Classic diseases revisited

Malignant hyperthermia

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Summary

Malignant hyperthermia is a rare autosomal dominant trait that predisposes affected individuals to great danger when exposed to certain anaesthetic triggering agents (such as potent volatile anaesthetics and succinylcholine). A sudden hypermetabolic reaction in skeletal muscle leading to hyperthermia and massive rhabdomyolysis can occur. The ultimate treatment is dantrolene sodium a nonspecific muscle relaxant. Certain precautions should be taken before anaesthesia of patients known to be susceptible to malignant hyperthermia. These include the prohibition of the use of triggering agents, monitoring of central body temperature and expired CO₂, and immediate availability of dantrolene. In addition, careful cleansing of the anaesthesia machine of vapours of halogenated agents is recommended. If these measures are taken, the chances of an MH episode are greatly reduced. When malignant hyperthermia does occur in the operating room, prompt recognition and treatment usually prevent a potentially fatal outcome. The most reliable test to establish susceptibility to malignant hyperthermia is currently the in vitro caffeine-halothane contracture test. It is hoped that in the future a genetic test will be available.

Keywords: malignant hyperthermia; dantrolene

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Epidemiology

Malignant hyperthermia (MH) was first reported by Denborough and Lovell in 1960.¹ MH is a rare pharmacogenetic trait often manifested first when a susceptible individual is given general anaesthesia using triggering agents such as potent volatile anaesthetics and depolarising muscle relaxants (succinylcholine). The incidence of the MH reaction during anaesthesia is estimated to be 1/15 000 anaesthetics in children and 1/50 000 anaesthetics in adults.² However, data collected in Denmark has shown a frequency in the range of 1/260 000 with general anaesthesia and 1/60 000 when succinylcholine is used. This difference in incidence estimation is partly due to different rates of triggering agents utilised in different countries. The acute MH syndrome is more prevalent in young people with more than 50% of cases occurring before the age of 15 years.³ The patient is normally in apparent good health but suffers from subclinical myopathy which can be exposed in a violent way when triggering agents are used in anaesthesia. There is a tendency for MH to erupt dramatically in young people during anaesthesia, often for minor procedures, which may present the healthcare team with a difficult problem.

Pathophysiology and clinical manifestations

MH is a syndrome of intense and abrupt striated muscle hypermetabolic reaction resulting in hyperthermia and rhabdomyolysis. The clinical picture is often dramatic with intense tachycardia, overproduction of CO₂, muscular rigidity, respiratory and metabolic acidosis, hyperkalaemia and terminal haemodynamic collapse. The pathophysiology of the MH reaction involves an inherited oversensitivity to triggering agents. When these agents are used on MH-susceptible patients they can cause rapid accumulation of calcium in striated muscle myoplasm, resulting in muscle contracture followed by rhabdomyolysis and an intense heat-producing reaction. This muscular hypermetabolic reaction occurs due to massive elevation of myoplasmic Ca²⁺ levels. The muscle contracture often starts with masseter muscle rigidity and then spreads to all striated muscles of the body. Due to its abrupt onset and violent character, an MH reaction is a true medical emergency requiring immediate action from the responsible anaesthetist. The ultimate treatment is dantrolene, a nonspecific muscle relaxant which acts by blocking the release of calcium from the sarcoplasmic reticulum of skeletal muscle cells. Before the discovery of the utility of dantrolene in the treatment of MH reaction, the mortality was above 50%.⁴ Improved awareness and understanding of the MH syndrome, and better pre-anaesthetic identification of susceptible patients, together with improved intra- and post-operative monitoring and the early use of dantrolene, has resulted in a significant decrease in mortality from acute fulminant MH to 10%.⁵

The acute MH reaction occurs most often after induction. It may also occur during anaesthesia, and also during the course of the recovery. The condition may also be recurrent, and as a result patients should be closely monitored, especially during the first 48 hours after being exposed to triggering agents. Most often these reactions do not evolve to the fulminant form of MH, and major signs like tachycardia, fever, mixed acidosis and elevated serum creatinine are present, but to a lesser degree. Abortive forms can occur both during anaesthesia and in the recovery room.

The differential diagnosis of intra-operative fever, tachycardia, tachypnoea and muscle rigidity includes conditions such as sepsis, thyrotoxic state, pheochromocytoma and stimulation during light planes of anaesthesia. Hypoxic brain damage, particularly affecting the hypothalamus, can also lead to fever and rigidity. In small children, elevation of temperature during operation is sometimes a result of attempts to prevent heat loss by excessive covering, which prevents dissipation of endogenous heat.

Malignant hyperthermia

- pharmacogenetic disease
- more common in younger population
- estimated incidence 1/15 000–1/50 000
- no sex predominance
- if not treated, fatal

Box 1

Malignant hyperthermia: clinical and biological signs

- rapid elevation of core temperature
- generalised muscular rigidity
- tachycardia with arrhythmia
- metabolic acidosis, respiratory acidosis
- hyperkalemia
- elevated blood creatine kinase levels
- myoglobinuria
- disseminated intravascular coagulation

Box 2

Figure 1 Skeletal muscle contracture response to increasing concentration of halothane. MH-susceptible (MHS) vs MH-non-susceptible patient (MHN)

Genetics and population at risk

MH susceptibility is currently believed to result from a general inherited membrane defect that disrupts calcium metabolism in skeletal muscle. It is a clinically heterogeneous autosomal dominant pharmacogenetic disorder with a reduced penetrance and variable expression.⁶ Rarely, sporadic cases and a recessive autosomal hereditary pattern exist. As with most other genetic disorders, MH susceptibility is recognised only by an abnormal phenotype. Certain carriers of the genotype can develop an MH crisis after multiple anaesthetics while others will never develop the clinical syndrome. For some patients, the first exposure to triggering agents can be fatal.

The MH susceptibility phenotype is currently diagnosed on the basis of an abnormal *in vitro* caffeine–halothane contracture test (CHCT) performed on a freshly biopsied muscle strip.⁴ This abnormal *in vitro* reaction of skeletal muscle from a susceptible individual is characterised by an abnormal contracture in the presence of halothane (figure 1) and of caffeine (figure 2). In recent years a mutation in chromosome 19, which has been linked to a mutation in the ryanodine receptor gene, was found to be linked to a predisposition for MH susceptibility.⁷

The exact nature of the molecular defect is still unknown. The population at risk for developing a MH reaction during anaesthesia includes: survivors of a MH reaction or patients who have reacted positively with the CHCT; first degree relatives of such patients or members of known or suspected MH-susceptible families with neuromuscular disorders and/or increased levels of creatine kinase in serum⁸; patients who suffer from Duchenne muscular dystrophy, King-Denborough syndrome and central core myopathy (the latter is almost certainly related to MH susceptibility⁸; patients who have exhibited masseter muscle spasm during anaesthesia with halothane and succinylcholine; patients with a history of the neuroleptic malignant syndrome or past heat stroke, although the association with MH susceptibility may be coincidental.⁹

The caffeine–halothane contracture test

The caffeine–halothane contracture test (CHCT) was first published by Kelow in 1971 after noticing the increased sensitivity of muscle strips from MH-susceptible patients to the contracture effect of caffeine.¹⁰ Subsequently, Ellis reported an increasing sensitivity of MHS muscle strip to halothane and the combination of these two tests became the CHCT.¹¹ The CHCT measures contractures of isolated skeletal muscle fascicles induced by caffeine and halothane used separately. There is general agreement that contractures elicited by caffeine reflect facilitated opening of the Ca^{2+} release channels of the terminal cistern of the sarcoplasmic reticulum. This channel opening leads to the release of stored Ca^{2+} , similar to the pathophysiologic defect believed to be present in MH. The mechanism whereby halothane induces contractures in MH muscle *in vitro* remain unclear. Halothane alone produces significant contractures only in MH muscle, unlike caffeine which tends to produce contracture at high concentrations even in normal muscles. It is assumed that the effect of halothane on MH muscle is also connected to the abnormal regulation of the Ca^{2+} release channels of the sarcoplasmic reticulum in MH muscle. The CHCT should be performed on a fresh biopsy specimen of skeletal muscle. All the tests must be done within five hours of the biopsy. Most centres use regional blocks of the femoral and lateral cutaneous nerve, with or without sedation. Addition of local anaesthetics is contraindicated because this may change the muscle reactivity of the test. Sometimes, general anaesthetics can be used without triggering agents. In order to compare the data between centres, the muscle samples should be obtained from the vastus lateralis or medialis of the quadriceps. Good cosmetic healing and recovery of muscle function is normally achieved. It is advisable not to use diathermy before removing the muscle as this may cause depolarisation of the membranes and alter the reactivity of the excised muscle. Caution should be exercised when carrying out the procedure, so as not to tear the muscle while dissecting. The dissection should be parallel to the muscle fibres. Fragments of muscle bundles, 15–20 mm long and 2–3 mm in diameter are carefully dissected and then suspended in a tissue bath with Krebs solution at 37°C and adjusted to pH 7.4. The bath should be bubbled with 5% carbon dioxide (figure 3). After being attached to the tissue bath the muscle fascicles are connected to a force transducer and stimulated at 0.2 Hz with pulse duration of 1 ms and increasing voltage until optimal contraction and baseline is stabilised. Separate muscle bundles are exposed to increasing concentrations of halothane or caffeine. The contracture elicited is recorded on a paper chart. There are some differences

Figure 2 Skeletal muscle contracture response to increasing concentration of caffeine. MH-susceptible (HMS) vs MH-non-susceptible patient (HMN)

Diseases possibly related to MH

- myotonia congenita
- periodic paralysis
- Schwartz-Jampel syndrome
- King-Denborough syndrome
- Duchenne muscular dystrophy

Box 3

Figure 3 Apparatus used in the CHCT

between the protocols used in Europe and in the US but the principle remains the same.^{12 13}

INTERPRETATION OF RESULTS

Three diagnostic groups are recognised: MH susceptible, with abnormal results of both halothane and caffeine tests; MH non-susceptible, with normal results of both tests, and MH equivocal, when only one test is positive. The latter group must also be classified as susceptible to MH and should not be exposed to triggering agents as the significance of these findings are still unknown. According to various reports, standardised CHCT is both highly sensitive (100%) and specific (85–90%) for determining MH susceptibility.^{14 15}

Due to the lethal character of the MH susceptibility trait, false-negative results are reason for concern. Recently, four cases of apparently false-negative results were reported from South Africa.¹⁶ All four cases suffered from a clinical and biochemical hypermetabolic reaction to anaesthesia using triggering agents. It is well known that many conditions may change the results of the tests, such as calcium entry blockers,¹⁷ or muscle fibre type discrimination.^{18 19} However, the technical details of these four negative tests were not reported, no description was given of the viability of the muscle specimens used, and no examples of the recording were provided. This seems to be the first report of false-negative results in CHCT, which has been used for many years. In contrast, several large studies have shown no complication after using triggering agents in patients whose biopsy has proven to be MH non-susceptible.¹⁴ All clinical biological tests have false-negative results. It seems that in the case of CHCT these numbers are very low and it is advised that patients in whom the clinical and biological scenario strongly suggest an episode of MH, even if CHCT proves to be negative, should be treated as MH susceptible.

Indication for testing

Identification of patients susceptible to anaesthesia-induced malignant hyperthermia may be accomplished on the basis of clinical history. Documentation of an episode of hyperthermia, muscle rigidity, acidosis and rhabdomyolysis during anaesthesia using triggering agents may be suggestive of MH. Often, the clinical diagnosis is only suspected when early signs of MH are recognised. Triggering anaesthesia is then discontinued. Any episode of masseter muscle spasm after giving triggering agents should be regarded as an abortive form of MH and testing is then highly recommended. In relatives of patients with proven susceptibility to MH, *in vitro* diagnostic CHCT is also recommended.

Other tests for the diagnosis of MH

Abnormalities in the Ca^{2+} release channel of skeletal muscle sarcoplasmic reticulum (the ryanodine receptor) proved to be responsible for the MH syndrome as biochemical and genetic linkage analysis showed it to be the site of the MH defect.⁷ Ryanodine, a naturally occurring alkaloid, was shown to be able to differentiate between muscle of MH susceptible and normal patients in terms of *in vitro* contracture response.^{20 21} Although the ryanodine contracture test seems to be more specific than the regular CHCT, it is not as widely accepted as the gold standard for diagnosis of MH.

CHCT has stood the test of time and has been proven to be highly sensitive and specific. Still, it is an invasive test needing surgical intervention. During the past decades significant effort has been invested in an attempt to develop a less invasive test that is as reliable. A large number of tests have been proposed, including biochemical counts and serum tests. Determination of the creatine kinase level, while useful in family studies, is unsatisfactory in that 30% of carriers are not detected. Increased creatine kinase activity in serum is a general sign of muscle disease which is nonspecific and not always present. A less invasive and adequately accurate genetic test is needed for an easier diagnosis of this potentially fatal disease. This is most likely to be realised when the exact molecular defects causing MH are identified.

Treatment of the acute MH crisis

Whenever a suspicion of acutely developing crisis of MH emerges, immediate discontinuation of all volatile anaesthetics and succinylcholine is mandatory. The next step is to hyperventilate the patient with 100% oxygen at a fresh gas flow of at least 10 l/min. Changing the anaesthesia machine to a non-contaminated one is no longer considered necessary in the acute stage. The key to a successful early abortion of the crisis is rapid intravenous administration

of dantrolene sodium. The initial bolus should be given rapidly at a dose of 2–3 mg/kg with increments up to 10 mg/kg total. Administration of dantrolene sodium is important and should be continued until signs of MH (eg, tachycardia, rigidity, increased end-tidal CO₂, and temperature elevation) are controlled. Occasionally, a total dose greater than 10 mg/kg may be needed. Administration of bicarbonate is recommended to correct the metabolic acidosis as guided by blood gas analysis. The initial dose should be 1–2 mEq/kg. Simultaneously an effort should be made to cool the patient. This can be done by administration of intravenous saline, lavage of stomach, bladder and rectum with iced saline, and surface cooling. The patient should be monitored closely for arrhythmias, which usually respond to treatment of hyperkalaemia and acidosis. Anti-arrhythmic agents may be used with the exception of calcium channel blockers (which may cause hyperkalaemia and cardiovascular collapse). Monitoring of end-tidal CO₂, blood gases, serum potassium, clotting studies and urine output are mandatory.

In the post-acute phase, patients should be observed in the intensive care unit for at least 48 hours since recrudescence of MH may occur, particularly following a fulminant case. Renal protection therapy to prevent myoglobinuric renal failure is desirable. Disseminated intravascular coagulation can occur in this period and the usual protocol for its treatment must be followed. The guidelines for continuing treatment with dantrolene after the acute event are not fixed. A conservative approach is to continue dantrolene 1–2 mg/kg every four hours intravenously, for at least 24–36 hours. Some clinicians prefer conversion to oral dantrolene 4–6 mg/kg per day for several days.

Anaesthesia for MH-susceptible patients

An individual known to be susceptible to MH should not be denied general anaesthesia on this basis. Elective anaesthesia, however, should only be carried out in hospitals with the knowledge and equipment needed to handle MH reaction. It has been recommended that out-patient surgery for these patients should be avoided,²² but it is now clear that out-patient surgery can be performed safely if patients are closely monitored postoperatively for at least four hours. In addition to routine pre-operative evaluation, baseline ECG and creatine kinase levels should be obtained.

PREPARATION OF THE OPERATING ROOM

The operating room must be free of anaesthetic vapors. Mechanical ventilation of MH-susceptible patients requires an anaesthesia machine that has not been contaminated with volatile anaesthetics. The minimum trace concentration of volatile anaesthetics is still unknown, and keeping a dedicated machine for MH-susceptible patients is expensive. A protocol for dealing with contaminated anaesthesia machines has been outlined.²³ This can be done by removing vaporisers, flushing with oxygen at a rate of 10 l/min for 5 min, replacing the fresh gas outlet hose and using a new disposable circle. Reservoir bags, ventilator bellows and soda lime should also be changed. These precautions are necessary as all volatile anaesthetics, especially halothane, have a high solubility in rubber and by removing these parts of the circulatory system a more rapid washout can be accomplished. Systems incorporating a non-rebreathing valve and bath system are not recommended in these cases unless a very high O₂ flow can be provided.

DANTROLENE

A supply of at least 36 vials of dantrolene should be available in the operating room for immediate use (20 mg per vial). This corresponds to a total dosage of 10 mg/kg in a 70 kg adult. This is the therapeutic dose needed in an acute attack.²⁴ The question of dantrolene prophylaxis is still being debated in the literature. Dantrolene was first discovered to be of value in the treatment of MH crises in pigs by Harrison,²⁵ its value has since been confirmed in a number of case reports,²⁶ and it has subsequently become the drug of choice in the prevention and treatment of acute MH crises. Dantrolene sodium is a diphenylhydantoin analogue which is poorly soluble in water. It is manufactured in a lyophilised formulation which also contains mannitol and sodium hydroxide. Each vial contains 20 mg of dantrolene, 3 g of mannitol and enough sodium hydroxide to raise the pH to 9.5. The lyophilised contents of each vial must be reconstituted with 60 ml of water. Although the mechanism of action is still unclear, it appears to inhibit release of calcium from the sarcoplasmic reticulum to the myoplasm.²⁵ In view of the low incidence of the MH reaction^{26–27} in MH-susceptible patients who received a trigger-free anaesthetic for minor elective surgery (under 0.62%), the common practice is not to use dantrolene pre-operatively as a routine.^{27–28} This practice eliminates the muscle weakness and nausea frequently associated with this treatment.²⁹ In patients with myopathy, prophylaxis with dantrolene is not

Drugs contraindicated in MH-susceptible patients

- halothane, enflurane, isoflurane and all other volatile anaesthetics
- succinylcholine
- Ca-channel blockers

Box 4**Drugs considered safe to be administered to MH-susceptible patients**

- barbiturates
- narcotics
- benzodiazepines
- propofol
- pancuronium, vecuronium atracurium
- nitrous oxide
- local anaesthetics without adrenaline

Box 5

recommended due to its tendency to cause postoperative weakness and respiratory complications.^{30 31} The prophylactic dose is 2 mg/kg intravenously 10–15 minutes before induction.²⁴

Obstetric patients pose potential problems as dantrolene prophylaxis can cause uterine atony leading to excessive blood loss.³² It also can cross the placenta causing neonatal weakness; as a result dantrolene prophylaxis is avoided in obstetric patients. If elective Caesarean section is planned, regional anaesthesia is preferred, and if emergency Caesarean section is required, then a rapid sequence induction using safe agents with high dose of non-depolarising muscle relaxants for relaxation is recommended.

OTHER PREPARATIONS

Other drugs that may be used in the acute treatment of MH crises must be present in the operating room. Drugs such as procainamide, sodium bicarbonate, furosemide, mannitol, regular insulin, 50% glucose and propranolol should be available. Supplies of tubes, syringes and means of taking multiple arterial and venous blood samples should be available. Equipment for resuscitation, insertion of arterial and central lines, bladder catheterisation and a cooling machine with blankets should be available.

PREMEDICATION

The MH-susceptible patient should be scheduled first on the operating list in order to minimise the possibility of exposure to volatile anaesthetic vapours. Pre-operative sedation to reduce anxiety is an important part of anaesthetic management. Barbiturates, benzodiazepines and opiates can be used, although phenothiazines should be avoided because of the possible connection between MH and neuroleptic malignant syndrome. The use of atropine is not recommended because it can enhance sympathomimetic activity which can induce stress hypermetabolic reaction. There are reports about possible worsening rigidity and mortality when MH reaction occurs in the presence of atropine.³³ However, parasympatholytic drugs like atropine and glycopyrrolate have been used safely in MH-susceptible patients. In the case of children, administration of atropine during induction may offer certain advantages, such as prevention of bradycardia. Some authors recommend that an intravenous infusion be started several hours before operation in order to minimise the emotional stress.

Enhancement of body fluid volume before induction of anaesthesia is advisable to prevent hypotension. This should be done as soon as possible, as vasopressor agents are contraindicated in these cases.³³

INDUCTION AND MAINTENANCE OF ANAESTHESIA

Anaesthesia for MH-susceptible patients should be designed to be as stress-free as possible. Careful monitoring of temperature (rectal or oesophageal) and end-tidal CO₂ is mandatory. Elevation of end-tidal CO₂ has been shown to be an early sign of possible impending reaction.³⁴ Whenever suitable, local or regional anaesthesia is advisable because these techniques are reported to be safer.³⁵ When using general anaesthesia, all volatile anaesthetics, including the newer desflurane and sevoflurane, must be avoided.³⁶ The use of depolarising relaxer is absolutely forbidden.

NON-TRIGGERING ANAESTHETICS*Barbiturates*

There is consensus that barbiturates are non-triggering agents. It has been suggested that they might play a role in protection and inhibition of MH crises in humans, as they do in pigs.

Benzodiazepines Benzodiazepines are also considered safe for use in anaesthesia of MH-susceptible patients.³

Etomidate Etomidate was shown experimentally not to cause MH syndrome in susceptible pigs; compared to thiopental it has less protective effect.³⁷

Propofol A number of studies have shown that it is safe to administer propofol to MH-susceptible patients as it has been shown not to cause MH episodes in MH-susceptible pigs.³⁸ Propofol has frequently been given to MH-susceptible patients without any problems. Furthermore, there are many reports on the use of propofol in patients with myopathies which are possibly connected to MH without untoward effects.³⁹ Because of its rapid recovery time, propofol seems an ideal choice for short procedures in MH-susceptible patients under general anaesthesia.

Ketamine Its use in MH-susceptible patients remains controversial. Most experts do not recommend it because of its sympathomimetic effects.

Opiates Opiates are all considered safe non-triggering agents.

Fentanyl It has been reported that muscle biopsies in England and North America are being done with the aid of general anaesthesia, including fentanyl,²¹ alfentanil,⁴⁰ and sufentanil,⁴¹ without causing any complications.

Nitrous oxide Nitrous oxide is considered a safe agent for use, although in one report it was considered to possibly have had a slight triggering effect. However, it has been used frequently in MH-susceptible patients without any problems.⁴²

Non-depolarising muscle relaxants There have been some reports that d-tubocurarine and gallamine are not suitable for use in MH-sensitive patients. There are some published reports on other non-depolarising muscle relaxants, especially pancuronium, for which a possible protective effect in pigs was demonstrated.⁴³ Atracurium has been shown to be safe in pigs⁴⁴ and in humans.⁴⁵ Vecuronium has been also been shown to be safe. The safety of neuromuscular block reversal in MH-susceptible patients has been questioned. As a result of unpublished reports of asystole following reversal with neostigmine and atropine, some clinicians prefer to ventilate the patient until the neuromuscular junction recovers spontaneously, although others utilise it without hesitation.^{26 45}

EMERGENCE FROM ANAESTHESIA AND EXTUBATION

Emergence and extubation should be smooth and stress-free. If residual neuromuscular block persists, or if dantrolene is given in doses higher than 3.5 mg/kg, it is recommended that mechanical ventilation be continued until full recovery. Episodes of hypoxia or hypercarbia should be avoided as they can trigger MH. MH has been reported in the postoperative period even when a non-triggering anaesthesia was used. Therefore, continued supervision in the recovery room for at least four hours, including monitoring of heart rate and temperature is recommended.

OTHER MEDICATIONS USED IN ANAESTHESIA

Agents with sympathomimetic activity, especially the alpha-agonist type should not be used since they can aggravate crises of MH. The use of alpha-antagonists and beta-blockers for arrhythmia is not restricted. All medication which can augment calcium concentration in the myoplasm, eg, digoxin, methylxanthines and calcium salts, should be avoided. However, in cases of severe asthma or when there is an urgent need to treat hyperkalaemia, aminophylline and calcium can be administered, respectively. The use of calcium channel blockers is contraindicated for fear of causing acute hyperkalaemia when associated with dantrolene.⁴⁶

MH consultation

An MH reaction is fortunately rare. However, in recent years awareness of MH has greatly increased, and more patients are being tested, increasing the likelihood of confronting a patient who is MH-susceptible or a member of a MH-susceptible family. As prevention is an important issue in MH, it should be explained to patients and their relatives that administration of general anaesthesia is quite safe provided that certain rules are kept (ie, no triggering, the right monitoring, availability of dantrolene). The autosomal dominant transmission of MH should be explained and the anaesthetist should encourage patients and their families to attend special diagnostic centres. It should also be explained that MH susceptibility does not carry any increased risk for heart disease or sudden infant death syndrome. Sport can be practised safely, although strenuous physical activity is not desirable, especially in hot weather.⁴⁷ It is recommended that certain occupations be avoided, for example, occupations in which individuals are exposed to halogenated hydrocarbons, organ solvents, and the solvents used in the dry cleaning industry.⁴⁸

In view of the increased trauma risk, it is understandable that military authorities are not enthusiastic about enlisting MH-susceptible individuals. It seems reasonable, however, that a limited military service could be undertaken without additional risk. With regard to the medicolegal aspect of MH susceptibility, it is advised that anaesthetists adopt a more rigorous monitoring of temperature and expired CO₂. With adequate monitoring, a MH reaction can be detected long before serious complications occur. In case of suspected MH reaction, serum potassium, creatine kinase, and myoglobin levels should be

documented. The patient should then be referred for an appropriate consultation after a full explanation from the responsible anaesthetist is given. Patients found to be positive should be provided with bracelets noting 'susceptible to malignant hyperthermia: no potent inhalational anaesthetics or succinylcholine'. Patients should also be instructed that, whenever anaesthesia may be required, they must inform the anaesthetist about their special sensitivity.

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