

## The anaesthetic management of the malignant hyperthermia susceptible parturient

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*An overall management plan for malignant hyperthermia susceptible (MHS) parturients is presented based on the experience of managing 14 of these patients. A summary of the pertinent features of their deliveries and care plus a case report of one of these parturients is described.*

*Discussion centres around the problems of diagnosis of malignant hyperthermia susceptibility in pregnancy, the differential diagnosis and management of fever and tachycardia in a MHS parturient during labour and the use of dantrolene prophylaxis. Management of the MHS parturient in labour includes temperature and heart-rate monitoring, provision for cooling, and ready availability of a vapour-free anaesthetic machine. A large-bore intravenous infusion for hydration and for potential therapy of a MH crisis is essential. Epidural analgesia, using 2-chloroprocaine, is recommended.*

*Emergency and elective Caesarean section anaesthesia are discussed. The importance of being prepared for a potential crisis is stressed with particular emphasis on early diagnosis by monitoring of temperature at two sites, of heart rate and rhythm with a continuous ECG and of end-tidal carbon dioxide, should a general anaesthetic be required. Recommendations are made for appropriate anaesthetic agents for both regional and general anaesthesia. Treatment of a MH crisis is outlined, with emphasis on availability of appropriate resuscitative drugs.*

### Key words

ANAESTHESIA: obstetric; GENETIC FACTORS: malignant hyperthermia; DRUGS: dantrolene.

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Since Crawford first inquired in the letters column of *The Lancet* in 1972 "whether or not there was a record of a pregnant or newly born patient or animal having developed hyperpyrexia and second whether hyperpyrexia has been encountered in a patient undergoing an operation under regional block anaesthesia,"<sup>1</sup> there have been several case reports of the obstetrical management of malignant hyperthermia susceptible (MHS) patients.<sup>2-8</sup> To date an overall management plan for malignant hyperthermia susceptible patients during labour and delivery has not been published.

British Columbia has a large kinship of MHS patients, with over 200 members. This kinship first was identified in 1977 following the death of a family member, who developed a classic MH reaction during a Caesarean section, under general anaesthesia.<sup>9</sup> Several members of this kinship who have had children since 1977 are included in this report.

Since 1977, 14 MH susceptible parturients have given birth to 18 infants (one set of twins) at the Vancouver General Hospital and the Grace Hospital, Vancouver. There were seven Caesarean sections and ten vaginal births. Table I lists the pertinent features of these parturients and the type of anaesthetic care they received. Experience gained in the management of these deliveries by the authors has enabled the development of a management plan for analgesia/anaesthesia for this high risk group of parturients.

The following case report illustrates the management.

### Case report

This patient has a strong family history of MH. Two of her brothers and one sister have survived MH

TABLE I Clinical features

<i>Patient</i>	<i>Para/Gravida</i>	<i>Delivery</i>	<i>Analgesia/Anaesthesia</i>	<i>Dantrolene</i>	<i>MH Characteristics</i>
1	P0G1	CS after trial of labour	Epidural 2-chloroprocaine for labour & CS	Yes	Strong family history Elevated CPK Increased muscle bulk
	P1G2	CS & tubal ligation	Epidural 2-chloroprocaine	Yes	
2	P0G1	SVD	nil	No	Strong family history Elevated CPK Leg cramps, lax joints
3	P2G3	CS	Epidural 2-chloroprocaine	Yes	Daughter had MH episode Normal CPK Family history strabismus, scoliosis, inguinal hernia
4	P1G2 previous C.S. under spinal	CS	Epidural 2-chloroprocaine	No	*Positive family history Elevated CPK, muscle bulk
5	P1G2 previous C.S. under G.A. – no problem	CS	Epidural 2-chloroprocaine	Yes	Positive family history
6	P1G1	SVD	Epidural – 2CP	No	Positive family history
7	P0G1 P1G2	Forceps SVD	Epidural – 2CP Epidural – 2CP	No No	Positive family history
8	P1G2 previous C.S. under spinal	CS	Epidural – 2CP	Yes	Positive family history Elevated CPK
9	P1G2 previous C.S. under spinal	CS	Epidural – 2CP	No	History of unexplained tachycardia under G.A.; unlikely MH
10	P0G1 P1G2	SVD SVD	Epidural – 2CP Meperidine	Yes No	Positive family history Elevated CPK
11	P1G2	SVD previous forceps under epidural	Epidural – 2CP	Yes	Positive family history Normal CPK
12	P0G1 (twins)	SVD	Epidural – 2CP	Yes	Positive family history CPK 7000 i.u./l Increased muscle bulk
13	P0G1	SVD	Meperidine	No	Positive family history
14	P1G2	SVD	Nil	No	Positive muscle biopsy – K type

\*Developed fever postoperatively – 39.2°(R), Arterial blood gases normal. Treated with antibiotics.

reactions and have positive muscle biopsies. The patient had not had a muscle biopsy but her CPK levels had been consistently elevated, the highest measuring  $1063 \text{ iu}\cdot\text{L}^{-1}$ . She is 172.5 cm tall and her prepregnancy weight was 114 kg. She had had two previous uneventful general anaesthetics for minor gynaecological procedures. She was initially seen in 1980 prior to the birth of her first child, at approximately 36 weeks' gestation. At that time, a full discussion of the implications of MH was undertaken, including a possible plan of anaesthetic management. The development of pregnancy induced hypertension necessitated her admission to hospital at 38 weeks gestation. Her weight on admission was 134 kg. As her blood pressure remained elevated it was decided to induce labour. She received dantrolene sodium orally  $4 \text{ mg/kg/24}$  hours beginning 48 hours preinduction. This produced symptoms of nausea, weakness, fatigue and headache.

On the day of induction, the delivery suite was fully prepared with a vapour-free anaesthetic machine, equipment for establishing arterial and central venous pressure lines, a heavy ply plastic sheet (which could be converted to an ice bath) and resuscitative drugs (intravenous dantrolene, sterile distilled water, sodium bicarbonate, procainamide, regular insulin, 50 per cent dextrose in water and propranolol). Ice and cold intravenous solutions were readily available. The patient's temperature was monitored orally every 15 minutes in early labour and more frequently as labour advanced. Skin temperature was also monitored. An epidural catheter was inserted early in labour as technical difficulties were anticipated, because of obesity. Analgesia, as required, was given through the epidural catheter and two per cent 2-chloroprocaine was selected as the local anaesthetic of choice. After 13 hours of labour and with little progress, a Caesarean section was performed for cephalopelvic disproportion. Anaesthesia to T4 had been achieved using three per cent 2-chloroprocaine through the existing epidural catheter. The vapour-free anaesthetic machine, equipment and drugs had been moved into the operating room from the delivery suite, and the ECG, BP, and temperature (rectal and axillary) were continuously monitored. The anaesthetic and subsequent postoperative period were uneventful. She received dantrolene orally for a

further 24 hours during which time her pulse and temperature were closely followed.

In 1983, the patient presented for a repeat elective Caesarean section and tubal ligation. This pregnancy was uncomplicated and she was seen as an out-patient at 37 weeks' gestation to discuss the anaesthetic management. She was admitted 24 hours preoperatively and started on oral dantrolene  $- 4 \text{ mg/kg/24}$  hours. This again resulted in symptoms of lethargy, weakness, nausea and headache. Her weight on this admission was 140 kg. Following an intravenous fluid "load" of 2000 ml of normal saline, an epidural catheter was inserted at L2-3 and incremental doses of three per cent 2-chloroprocaine were given to achieve an analgesia level of T4. The operating room had previously been prepared with a vapour-free anaesthetic machine, appropriate equipment and drugs as listed for the birth of her first child. The ECG was continuously monitored, and the blood pressure was taken every three minutes using an automatic blood pressure device. The axillary and skin temperature were continuously monitored. Oxygen per face mask was administered until the baby was born. Oral dantrolene therapy and temperature monitoring were continued for 24 hours postoperatively. There were no untoward sequelae in the mother or baby.

### Discussion

Malignant hyperthermia is a symptom complex which occurs under certain specific conditions – in particular, in response to the challenge of certain volatile anaesthetic agents and muscle relaxants.<sup>10</sup> An apparently normal labour and delivery may suddenly change into a catastrophic situation, due to development of fetal distress, haemorrhage, abruptio placenta or cord prolapse and anaesthetic intervention may become necessary. Therefore, it is important that a plan of management for MHS parturients be devised for all hospitals where deliveries are performed. To date, there has only been one report of a newborn having had a possible MH reaction.<sup>11</sup>

The absolute diagnosis of malignant hyperthermia susceptibility is dependent on (1) a documented MH episode, or (2) a positive caffeine contracture response of a muscle biopsy.<sup>10</sup>

Patients who have a positive family history of MHS must always be treated as being susceptible

until a negative caffeine contracture test proves otherwise. Unfortunately, not all patients with a documented family history have ready access to a diagnostic facility. British Columbia does not yet have such a facility, the nearest is in Calgary, with a waiting list of 14 months. As well, not all patients choose to undergo the procedure.

Elevated creatine kinase (CK) levels are not always reliable indicators of susceptibility<sup>12</sup> but when coupled with a positive family history extra precautions must be taken. To date, there have not been any good studies of CK levels throughout pregnancy. Isherwood *et al.* examined CPK levels in 18 normal patients in the first trimester of pregnancy and then in 15 normal patients at the time of delivery and in the early puerperium. They concluded that CPK levels were elevated during normal pregnancy.<sup>13</sup> Studies involving greater numbers of patients need to be done to establish normal levels for pregnancy.

The current management plan at our hospital revolves around education, preparedness prior to admission of a MHS parturient and a protocol for treatment in the event of an unexpected reaction.

Malignant hyperthermia has been the topic of education sessions at our hospital for nursing staff, obstetricians and house staff. An increased awareness of this disorder by nursing and medical personnel ensures immediate notification of the anaesthesia department when a parturient with a suspicious history is admitted. Obstetricians also refer MHS parturients for counselling early in their pregnancy.

Once a MHS parturient has been identified, a copy of the consultation is sent to the admitting office to be placed on her chart on admission and another copy is posted in the anaesthetic workroom to alert the anaesthetic staff to the management plan. As well, the anaesthetic technician is alerted and he rechecks the vapour-free anaesthetic machine.

### Overall management plan

#### *Provision of a vapour-free anaesthetic machine*

In our hospital, a separate machine has been set apart for MH patients. It is readily available in a storage area in the operating room complex.

#### *Provision for cooling*

Calcium-free intravenous solutions are available in the refrigerator. These are periodically checked to ensure that they do not become outdated. Due to the expense of cooling blankets, a simplified measure such as a heavy ply plastic sheet (which can readily be converted to an ice bath by suspending the four corners to IV poles) is kept in a convenient location. Some hospitals have a MH cart which contains all of the emergency provisions necessary for a MH crisis. The cooling blanket, drugs and equipment to establish arterial and CVP lines would also be kept on the cart. Adequate ice is also available.

#### *Provision of appropriate resuscitative drugs*

These include dantrolene (at least 3 mg·kg<sup>-1</sup> – each vial contains 20 mg),<sup>14</sup> adequate sterile distilled water for mixing (60 ml/vial of dantrolene), regular insulin, 50 per cent dextrose in water (to treat hyperkalemia), sodium bicarbonate (to treat acidosis), procainamide, propranolol (to treat tachycardia and arrhythmias), and furosemide and mannitol (to promote diuresis).<sup>15</sup>

#### *Monitors*

A reliable method of continuously monitoring temperature must also be available. It should have at least two inputs so that two temperature probes can be used simultaneously. ECG and blood pressure monitoring is also essential. If an end-tidal CO<sub>2</sub> monitor is available, it should be in the room in the event a general anaesthetic is required. It will alert the anaesthetist to a developing reaction before the temperature begins to rise.

#### **Dantrolene prophylaxis**

The management of anaesthesia for surgery in MHS patients has been made easier with the availability of dantrolene. As it is poorly absorbed orally,<sup>16</sup> it is now recommended that it be given intravenously prior to induction of anaesthesia. Flewellen recommended that it be given in a dosage of 2.4 mg·kg<sup>-1</sup> over 10–15 minutes preoperatively.<sup>17</sup> Dantrolene does cross the placenta<sup>18,19</sup> and newborns have demonstrated decreased muscle tone following its use. No evidence of respiratory or cardiovascular depression has been seen. It may provide protection for the newborn who may have inherited the MH genetic predisposition.

At present, if a vaginal birth is anticipated, dantrolene is not given prophylactically. The patient has her temperature (oral and skin or axilla) and ECG closely monitored throughout labour for any sign of a developing reaction.

The advantages and disadvantages of prophylactic dantrolene should be considered for the patient having a Caesarean section. If the patient is having a regional anaesthetic, the authors prefer to monitor the patient closely and to have dantrolene available, should a reaction occur. If the patient is having a general anaesthetic and has had a previous reaction or is muscle biopsy positive, then serious consideration should be given to the use of intravenous dantrolene prior to induction of anaesthesia. The relative risks of developing a MH reaction, which would be promptly treated with intravenous dantrolene, or of administering prophylactic dantrolene with its concomitant transfer to the fetus must be discussed with each patient.

#### **Analgesia for labour**

Fortunately, most of the agents used to provide labour analgesia are non-triggering for MH. Nitrous oxide mixed with oxygen (Entonox® or Nitrox®) is safe, as are the narcotic analgesics.

There are definite advantages to the use of epidural analgesia during labour in MHS parturients. It has been demonstrated that circulating catecholamines decrease after epidural analgesia is administered.<sup>20</sup> As stress and sympathetic responses have been implicated in the development of MH<sup>10</sup>, it is advantageous to provide good analgesia and decrease the sympathetic response to pain. Early placement of the epidural catheter, when the patient is more cooperative, allows its immediate use when labour becomes distressing. It also is available if operative intervention (forceps or Caesarean section) becomes necessary. Due to theoretical considerations, an ester type local anaesthetic is preferred. One and one-half to two per cent 2-chloroprocaine is the agent of choice. It provides excellent analgesia, and is rapidly metabolized in the mother and newborn. Its only disadvantage lies in its short duration of action.

The use of amide local anaesthetics is somewhat controversial. Several case reports of their use for obstetric analgesia have been published.<sup>3</sup> The Malignant Hyperthermia Association of the United

States has now removed amide local anaesthetics from the list of triggering agents.<sup>21</sup> The use of small amounts of the amide local anaesthetics was advocated by Gronert in 1980<sup>10</sup> and their use for labour analgesia is probably safe. However, Rosenblatt has reported a potential enhancement of the toxicity of bupivacaine by dantrolene.<sup>22</sup> This, coupled with the need for large volumes and high concentrations for Caesarean section anaesthesia, would suggest caution in using these agents, at present, for Caesarean section.

#### **Anaesthesia for Caesarean section**

If an elective Caesarean section is planned the patient should be admitted 24 hours preoperatively in order to rest and to allow time for any further laboratory investigations. At this time, a follow-up discussion regarding prophylactic dantrolene should be held. If the patient is at high risk, i.e., has had a previous MH reaction, has a very high CK or a positive muscle biopsy, and there are contraindications to a regional anaesthetic, then the benefits of prophylactic dantrolene must be strongly emphasized. The patient must fully understand the risks associated with the development of a MH crisis.

The operating room should be prepared with the vapour-free anaesthetic machine, appropriate resuscitative drugs, provision for cooling and monitors as outlined in Table II.

Regional anaesthesia, either spinal with tetracaine or epidural with three per cent 2-chloroprocaine, is preferred unless there are specific contraindications. A large-bore intravenous cannula is essential, both to adequately fluid preload the patient and to facilitate treatment of a reaction. Normal saline is a preferred "preload" as it does not contain calcium. As sympathomimetic agents, such as ephedrine, are relatively contraindicated in MHS patients, a large (2000 ml) fluid "preload" is necessary to prevent hypotension. Epinephrine, to prolong the duration of the block, is best avoided until further information on its clinical use in MH is available.

Left uterine displacement should be achieved to avoid aortic caval compression. Oxygen by face mask is administered until the baby is born. Oxytocin is considered safe while ergometrine is contraindicated. Monitors should include ECG, blood pressure, and temperature. Rectal tempera-

TABLE II Checklist for MH-susceptible parturients

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1	<i>Counselling:</i> genetics and anaesthesia regarding risks
2	<i>Education:</i> patient as to risks, medical and nursing staff about ramifications of crisis and treatment
3	<i>Notification:</i> of nursing and anaesthesia staff regarding admission of MHS parturient
4	<i>Pre-admission checklist:</i>
	(a) vapour-free anaesthetic machine in good working order, disposable circuit, if required
	(b) MH cart containing all drugs and other equipment listed below
	(c) provision for cooling – adequate ice, cooling blanket or heavy ply plastic sheet, calcium-free intravenous solutions in refrigerator
	(d) drugs: dantrolene with adequate sterile distilled water to mix (see text for required amount), sodium bicarbonate (to treat acidosis), regular insulin, 50 per cent dextrose in water (to treat hyperkalemia), procainamide, propranolol (to treat tachycardia and arrhythmias), furosemide and mannitol (to promote diuresis)
	(e) monitors: ECG, temperature monitor with 2 probes, end-tidal CO <sub>2</sub> monitor, equipment for arterial and CVP lines
5	<i>Anaesthesia plan:</i>
	<i>Vaginal birth:</i>
	monitor temperature and ECG closely, analgesia as required – if high risk, early placement of epidural catheter, use of 2-chloro-procaine, vapour-free anaesthetic machine in labour/delivery room, MH cart in the room.
	<i>Caesarean section:</i>
	prophylactic intravenous dantrolene (if having general anaesthetic), large bore intravenous cannula for fluid infusion, treatment and prophylaxis and operating room prepared with vapour-free anaesthetic machine, MH cart, end tidal CO <sub>2</sub> monitor, temperature monitor, ECG, BP monitor and methods for producing cooling. Thiopentone, pancuronium, and narcotics available, in case general anaesthesia necessary.
6	<i>Avoid:</i>
	sympathomimetics (epinephrine, ephedrine), calcium salts, ergometrine, halogenated agents, muscle relaxants other than pancuronium, cardiac glycosides.
7	Treatment protocol for MH posted in each labour/delivery room and operating room
8	<i>Remember:</i>
	basic accepted principles of anaesthetic care.

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ture and skin or axillary temperature should be monitored continuously.

If a general anaesthetic is necessary, a rapid sequence induction-intubation with cricoid pressure must be done after preoxygenation. Thiopentone and pancuronium have been shown to be safe. Pancuronium must be administered in a dose of 0.15–0.2 mg·kg<sup>-1</sup> in order to allow rapid endotracheal intubation. This may necessitate prolonged mechanical ventilation in the recovery room. Nitrous oxide, oxygen and narcotic analgesia are considered safe for anaesthetic maintenance.

Close monitoring of temperature and heart rate, and dantrolene therapy (if previously initiated) should be continued for 24 hours postpartum. MH reactions have been reported in the immediate postoperative period.<sup>23</sup>

The paediatrician caring for the baby must be made aware of the diagnosis of MH and specifically of the use of dantrolene.

### Diagnosis and treatment of a MH crisis

Clinical signs of a crisis during surgical anaesthesia are increased muscle tone, tachycardia, arrhythmia, tachypnoea (if patient is breathing spontaneously) and a rapid increase in temperature. Laboratory confirmation includes acidosis, hypercarbia, elevated CK and hyperkalemia.

During labour, some of these clinical signs may be present due to reasons other than development of a crisis. Tachycardia and tachypnoea are normal responses to pain or fever. Fever may be a sign of dehydration and/or sepsis (chorioamnionitis). Intravenous hydration will prevent dehydration and adequate pain relief, with epidural analgesia, will allow the development of tachycardia, tachypnoea and fever to assume diagnostic significance. If a MHS parturient develops persistent tachycardia, fever and/or arrhythmia then arterial blood gases should allow the differential diagnosis between development of a MH crisis and sepsis. Certainly,

the development of a persistent tachycardia, arrhythmia, muscle rigidity and/or fever during anaesthesia for Caesarean section should lead to prompt treatment.

Therapy for a crisis includes discontinuation of any triggering agents, hyperventilation with 100 per cent oxygen, institution of cooling, both external (by means of an ice bath or cooling blanket), and internal (with cold intravenous solutions and peritoneal lavage with cold solutions), intravenous dantrolene ( $2 \text{ mg} \cdot \text{kg}^{-1}$ ) to lower myoplasmic calcium, treatment of acidosis with sodium bicarbonate, treatment of hyperkalemia with regular insulin plus 50 per cent dextrose in water, maintenance of adequate urine output with fluids and furosemide and treatment of cardiac arrhythmias with procainamide or propranolol. If a crisis occurs and the baby has not been born, the neonatologist must be alerted to the fact that he may have a depressed, acidotic baby to treat. In each of the labour/delivery rooms and operating rooms a treatment protocol for MH should be posted. An excellent one is available from the Malignant Hyperthermia Association of the U.S.A.\*

#### Follow-up

Genetic counselling (if not previously performed) is arranged while the patient is still in hospital. The use of Medic-Alert identification is also stressed for the patient and her family. There are Malignant Hyperthermia Associations in both the United States and Canada which provide patients with up-to-date information about their condition.\*

#### Conclusion

A suggested method of handling parturients with a diagnosis of MH susceptibility has been presented. Included in Table II is a checklist to ensure that adequate preparations have been made. These recommendations are based on the experience of successfully managing 14 MHS parturients through 17 deliveries, of which seven were Caesarean sections.

\*Malignant Hyperthermia Association – 2 Bloor Street West, Box 144, Toronto, Ontario M4W 3E2.

Malignant Hyperthermia Association of U.S.A. (MHAUS) – Box 3231, Darien, CT 06820, U.S.A.

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### Résumé

*Une conduite générale pour les patientes susceptibles de développer une hyperthermie maligne (MHS) est présentée se basant sur l'expérience avec 14 de ces patientes. Un résumé des caractéristiques pertinentes de leur accouchement et soins est présenté en même temps qu'une histoire de cas d'une de ces patientes.*

*Les discussions tournent autour des problèmes du diagnostic de susceptibilité d'hyperthermie maligne lors de la grossesse, du diagnostic différentiel et de la conduite thérapeutique en face d'une fièvre et une tachycardie ainsi que de l'usage du dantrolène en prophylaxie. La conduite thérapeutique lors du travail inclut la surveillance de la température ainsi que la fréquence cardiaque la disponibilité d'un système de refroidissement et d'une machine d'anesthésie n'ayant jamais été contaminée par les agents anesthésiques. Le rétablissement d'une voie intra-veineuse avec un cathéter de gros calibre est essentiel pour l'hydratation et le traitement de la crise d'hyperthermie maligne. L'utilisation de l'analgésie épidurale par 2-chloroprocaine est recommandée.*

*L'indication de césarienne électorale ou d'urgence est discutée. L'importance d'être préparé pour une crise potentielle est mise en valeur. L'emphase particulièrement sur un diagnostic précoce par la surveillance de la température à deux sites et de la fréquence du rythme cardiaque avec un électrocardiogramme continu et un CO<sub>2</sub> en fin d'expiration si une anesthésie générale est requise. Des recommandations sont faites pour les agents anesthésiques appropriés tant pour une anesthésie générale que régionale. Le traitement de la crise d'hyperthermie maligne est décrit en mettant l'emphase sur la disponibilité des médicaments appropriés pour la réanimation.*