

Malignant Hyperthermia Resource Kit

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Introduction

Malignant Hyperthermia (MH) is a rare pharmacogenetic disorder. MH reactions are potentially fatal if prompt appropriate treatment is not instituted.

MHANZ (the author of this resource kit) is a group of clinicians who are involved in malignant hyperthermia testing and research.

The recommendations in this kit are sourced from available evidence, guidelines developed by other groups, including the European Malignant Hyperthermia Group (EMHG), simulation testing and accumulated data from MH episodes. In some cases, the recommendations represent refined version of pre-existing documents.

An MH crisis is rare. Many anaesthetists will not experience one in their practicing career. There are many high priority tasks that must be attended to simultaneously. The complex coordination required combined with the rarity of an MH crisis and the rapidity of response needed are the reasons for the kit development.

Components of the resource kit

MH Poster – “MH – You’ve only got a few minutes”
MH Crisis Initial management
MH Crisis coordinators overview
MH Crisis task cards

Instructions for preparing the components

1. MH Poster

Print out the MH poster on A3, laminate and place in strategic places in each operating location.

2. MH Crisis Initial management

MH Crisis Initial Management is a page that should be printed, laminated and attached to each anaesthetic machine. This card will assist an anaesthetist in MH crisis diagnosis and initial management while the MH box and extra staff are being mobilised.

3. MH crisis coordinator overview

The coordinator overview page should be printed A4 size in colour and laminated.



The poster, cards, coordinators overview and MH crisis initial management pages are available for download from:

www.malignanthyperthermia.org.au

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4. MH Crisis Task Cards

The task cards are intended as way to delegate the multiple high priority tasks to available staff. The cards carry simple instructions and are designed for distribution both to staff who may not be familiar with MH crisis management and to skilled clinicians. The cards should be kept with the supply of dantrolene (see contents of an MH emergency box) and distributed by the coordinating anaesthetist to the most appropriate staff members

The printable cards represent a basic template for the management of MH crisis tasks. MHANZ recommends that they are printed and prepared with institutional specifics including locations of dantrolene and other emergency supplies and phone numbers. MHANZ actively encourages hospitals to modify the contents of the cards to suit local needs.

There are seven (7) cards to be printed as A6 and laminated. Holes punched and a suitable neck lanyard is recommended so that cards are easily read, roles are recognised and cards are not misplaced in a crisis. The cards have a colour key so printing in colour is highly desirable.

- 1 Anaesthetist 1: resuscitation
- 2 Dantrolene (recommended to print 3 of these) or ryanodex (if it is stocked in your institution)
- 3 Anaesthetic assistant
- 4 Anaesthetist 2: lines and investigations
- 5 Cooling
- 6 Surgical Team
- 7 Logistics

Dantrolene

Amount of stock

The dosing regimen of dantrolene should be based on actual body weight, dantrolene should be available wherever volatile anaesthetics or succinylcholine are used, and 36 vials (720 mg) of dantrolene should be immediately available with a further 24 (480 mg) vials available within 1 hour.

Borrowing from other local hospitals

MHANZ does not recommend reliance on dantrolene stocks from other hospitals for initial crisis management. Early and appropriate doses of dantrolene result in lowest morbidity and mortality. Dosing interval is every 10-15 minutes until signs of metabolism are normalised.

Replenishing supplies after use

Each hospital should consider where additional dantrolene for acute management or replacement will be obtained (recurrence of an MH crisis occurs in up to 25% of patients during the first 24 hours).

Water for mixing DANTRIUM®

It is extremely important that sterile water used for reconstituting dantrolene is not mistakenly infused into the patient. Suggestions to reduce the risk of this life-threatening error include:

- Use of 100 ml water for injections plastic bottles
- Additional labelling of sterile water bags (if 100 ml bottles are not available) in the MH box as "NOT for intravenous infusion"

DANTRIUM® mixing

Mixing dantrolene can be time consuming and rapid administration is critical. More than 36 vials may be required in the acute treatment of a large adult. It may be worth familiarising staff with dantrolene reconstitution utilising expired stock. Assignment of more than one staff member to the task of mixing may be appropriate if all the other tasks are being managed. This is why 3 dantrolene task cards are printed.

Vial access

Dantrolene reconstitution is ideally performed with a short, wide vial access needle. The BAXA TWO-FER 16-gauge short needle or the BRAUN MICRO PIN (MP2000) are 2 options tested by MHANZ.

RYANODEX® vs DANTRIUM®

Ryanodex® is dantrolene presented as sterile 250 mg lyophilised powder. Mix Ryanodex® with 5 ml of sterile water for injection to obtain a solution with a concentration of 50 mg/ml.

At the time of publication, RYANODEX® is only approved for use in Australia and New Zealand on a TGA exemption.

The following table outlines the differences in preparations of dantrolene in the event that RYANODEX is the preparation that is available.

Product characteristic	RYANODEX®	DANTRIUM®
Presentation	Sterile 250 mg lyophilised powder, 20 mL vial injectable suspension for IV use	
Formulation	Active: 250 mg dantrolene sodium; Inactive: 125 mg mannitol, 25 mg polysorbate 80, 4 mg povidone K12, NaOH, HCl.	Active: 20 mg dantrolene sodium; Inactive 3 g mannitol, NaOH
Dosing	Dose 2.5 mg/kg - MHANZ, MHAUS* recommendation	Dose 2.5 mg/kg - MHANZ, MHAUS* recommendation
Reconstitution/ Administration	Mix with 5 mL WFI**; produces orange coloured suspension. For Intravenous push. Final concentration = 50 mg/mL, pH 10.3.	Mix with 60 mL WFI. Shake until solution is clear. Continuous rapid Intravenous push. Final concentration ~ 0.33 mg/mL, pH 9.5.
Warning/ Precautions/ Contraindications	Similar. Check full Product Information before prescribing.	Similar. Check full Product Information before prescribing
Storage/ Handling	Use within 6 hrs @ 20C - 25C, Protect from light	Protect from light, use within 6 hrs @ 15C - 25C

*MHAUS - Malignant Hyperthermia Association of the United States

** WFI - water for injection

MH Diagnosis and Differential Diagnosis`

Who is susceptible?

MH may occur in any patient given triggering agents, including patients who have previously had uneventful general anaesthesia.

The signs and symptoms

Not all of these need to be present to initiate treatment and not all occur in this order.

Early

- Prolonged masseter spasm
- Increased oxygen consumption
- Inappropriately raised end tidal carbon dioxide
- Inappropriate tachypnoea during spontaneous ventilation
- Inappropriate tachycardia
- Cardiac arrhythmias - particularly ventricular ectopic beats

Developing

- Rapid rise in temperature (0.5°C per 15 minutes)
- Mixed metabolic and respiratory acidosis
- Hyperkalaemia
- Profuse sweating
- Cardiovascular instability
- Decreased oxygen saturation
- Skin mottling
- Generalised muscular rigidity unresponsive to non-depolarising muscle relaxant

An arterial blood gas is the single most useful investigation to perform

Late

- Cola coloured urine (myoglobinuria)
- Generalised muscle aches (awake patient)
- Grossly raised serum Creatinine Kinase (CK)
- Coagulopathy
- Cardiac Arrest

Differential Diagnosis

- Inadequate anaesthesia/machine malfunction or analgesia
- Insufficient ventilation or fresh gas flow Phaeochromocytoma
- Sepsis or infection
- Thyroid Storm
- Serotonin Syndrome
- Recreational drug use (amphetamines)
- Neuroleptic malignant syndrome
- Ischaemia Intracerebral infection or haemorrhage
- Inadvertent overheating
- Elevated etCO₂ due to laparoscopic surgery

Recommendations for contents of an MH emergency box

Mobility and accessibility are important considerations for the type of container used. A 50 litre Esky/Chilly Bin on wheels is one suggestion.

Suggested contents:

Dantrolene

- 36 vials of Dantrium® (20 mg per vial)
- Sterile water for injection – either 100 ml bottles or, if larger bags are used these need to be clearly labelled as “not for intravenous infusion”
- Drawing up needles (see vial access – page 4)
- 60 ml syringes (5-10)

Or

- At least 2 vials of Ryanodex® (250 mg per vial)

Include local information on where to source additional dantrolene including contact details

Drugs

- 8.4% sodium bicarbonate (1 mmol/ml)
- 50% dextrose 50 ml
- Lignocaine 1%
- Amiodarone 300 mg

Cold Box (in fridge)

- 2 litres crystalloid for IV use
- Actrapid insulin

Pathology collection tubes with prewritten requests (if appropriate) for:

- Haematology
- Coagulation profile
- Electrolytes, creatinine, urea, creatinine kinase (CK)
- Blood cross match
- EDTA tube for Possible DNA testing (paediatrics)

Task Cards

- As described in the Resource Kit instructions

Management of an MH crisis

Start treatment as soon as an MH crisis is suspected.

The clinical presentation of MH varies and treatment should be modified accordingly.

Treatment:

Immediately

- Stop all trigger agents.
- Hyperventilate (use a minute volume 2–3 times normal) with 100% O₂ at high flow.
- Declare an emergency and call for help.
- Change to non-trigger anaesthesia (TIVA).
- Inform the surgeon and ask for termination/ postponement of surgery.
- Disconnect the vaporizer - do not waste time changing the circuit/anaesthetic machine.

Dantrolene

- Give dantrolene 2.5mg/kg i.v. (ampoules of 20 mg are mixed with 60 ml sterile water).
- Obtain dantrolene from other sources, for example, pharmacy/nearby hospitals - 36–50 ampoules may be needed for an adult patient.
- Dantrolene infusions should be repeated until the cardiac and respiratory systems stabilise.
- The maximum dose (10mg/kg) may need to be exceeded.

Monitoring

- Continue routine anaesthetic monitoring (SpO₂, ECG, NIBP, EtCO₂).
- Measure core temperature.
- Establish good i.v. lines with wide-bore cannulas.
- Consider inserting an arterial and central venous line, and a urinary catheter.

- Obtain samples for measurement of K⁺, CK, arterial blood gases, myoglobin, and glucose.
- Check renal and hepatic function and coagulation.
- Check for signs of compartment syndrome.
- Monitor the patient for a minimum of 24 h (ICU, HDU, or in a recovery unit).

Symptomatic Treatment

Treat Hyperthermia

- 2000–3000 ml of chilled (4°C) crystalloid
- Surface cooling: wet, cold sheets, fans, and ice packs placed in the axillae and groin.
- Other cooling devices if available.
- Stop cooling once temperature is <38.5 C°.

Treat Hyperkalaemia

- Dextrose: 50%, 50 ml with 50 IU insulin (adult dose).
- CaCl₂: 0.1 mmol/kg, i.v. (e.g. 7 mmol/10 ml for a 70 kg adult).
- Dialysis may be required.

Treat Acidosis

- Hyperventilate to normocapnoea.
- Give sodium bicarbonate i.v. if pH , 7.2.

Treat arrhythmias

- Amiodarone : 300mg for an adult (3mg/kg slow IV)
- b-blockers (e.g. propranolol/metoprolol/esmolol)- if tachycardia persists.
- Maintain urinary output >2 ml/kg
- Furosemide 0.5–1 mg/kg
- Mannitol 1g/kg
- Fluids: crystalloids (e.g. lactated Ringer's solution or 0.9% saline) i.v.

Guidelines for managing the elective MH susceptible patient

Who should receive trigger free anaesthesia?

Patients with one of the following should be treated as susceptible

- 1 Previous malignant hyperthermia reaction
- 2 Positive in vitro contracture test (IVCT) from muscle biopsy designated MHShc, MHSh or MHSc
- 3 Positive genetic test for MH
- 4 If an IVCT has not been done and the patient has a relative with a positive IVCT or suspected clinical reaction
- 5 Patient has a negative genetic test for MH (but has not yet had a confirmatory IVCT)

Patients in whom it is not necessary to treat as susceptible

1. Patient has had a negative in vitro contracture test
2. Patient's parent (from the MH susceptible side of the family) has had a negative IVCT and there is no evidence of MH in the other parents' family.

Preparing the operating theatre

Prepare the anaesthesia workstation (see below)

- Add "Susceptible to Malignant Hyperthermia" to the surgical safety checklist and make all personnel aware of the precautions required
- Remove volatile anaesthetic cassettes or canisters from the workstation
- Remove suxamethonium from the specific operating room anaesthetic drug trolley

Intraoperative monitoring

- Standard ANZCA intraoperative monitoring with temperature monitoring

The post anaesthesia care unit

- Patients susceptible to MH may be managed in the normal post anaesthetic care unit and do not need to be isolated from other post-operative patients. Volatile anaesthetic levels in parts per million safe for occupational exposure are also safe for susceptible patients.
- Standard post-operative monitoring as per ANZCA guidelines including standard PACU discharge criteria is appropriate

Charcoal Filters

MHANZ Recommendations the following for the use of activated charcoal filters (ACF) in the preparation of anaesthetic workstations for patients at risk for MH susceptibility:

- 1 Remove vaporisers from the anaesthetic machine
- 2 Flush circuit for 90 seconds with oxygen or air at 10 litres/min using the ventilator with a 2-litre test lung attached.
- 3 Change full breathing circuit and soda lime whilst maintaining flushing at 10 litres/min (the ventilator is left unchanged).
- 4 Insert activated charcoal filters on both the inspiratory and expiratory ports of the breathing system.
- 5 Maintain fresh gas flow of 10 litres/min for 90 mins from the commencement of the anaesthetic.
- 6 After 90 mins it is safe to reduce FGF to 3 litres/min.
- 7 ACFs can be used at 3 litres/min until a total of 12 hours has elapsed from the commencement of the anaesthetic.
- 8 ACFs are single use items.
- 9 In the event of an MH crisis, If available activated charcoal filters should be placed in the inspiratory and expiratory limbs of the anaesthetic circuit
 - Clinical priorities in an MH crisis remain: dantrolene administration (2.5mg/kg), high fresh gas flows, treatment of arrhythmia/acidosis and active cooling.

Up to date information on referrals,
contacts, genetics and in vitro contracture testing
is available on the MHANZ website

www.malignanthyperthermia.org.au