# MALIGNANT HYPERTHERMIA (MH)

Malignant Hyperthermia
is a pharmacogenetic disease of skeletal muscle that may precipitate a potentially fatal sequence of metabolic responses in the presence of triggering anesthetics. The primary triggers for MH are - Inhalational Anesthetics and Succinylcholine.

Incidence estimated at 1:10,000 and 1: 150,000. Etiology involves the uncontrollable release of intramyoplasmic calcium ($Ca^{2+}$) that results in sustained muscle contractures, which in return produces a hypermetabolic response. The hypermetabolic response manifests as hypercarbia, hyperthermia, tachycardia, and if not treated early, a mixed metabolic and respiratory acidosis, muscle rigidity, severe rhabdomyolysis, circulatory shock and possibly death.

Cart (MH Cart) - An orange colored box containing the necessary drugs, equipment and treatment algorithm for the acute management of MH is available in Major OT Paeds recovery area, and day surgery OT outside OT2. It should be brought into theatre for any suspected case. If the "box" is opened at any time, the seal will be broken and the last person using it should check the contents thoroughly before applying a new seal.
ALWAYS RETURN THE CART AFTER USE to the respective OT areas.

## 1. RECOGNITION

Signs of MH:

- Unexplained increase in $ETCO_2$ AND
- tachycardia AND
- Unexplained increase in oxygen requirement (previous uneventful anaesthesia does not rule out MH)
    - Other signsTrunk or limb rigidity

- Masseter spasm or trismus
- Unstable/ rising blood pressure
- Respiratory and metabolic acidosis
- Temperature changes are a late sign

**2. IMMEDIATE MANAGEMENT**

**CALL FOR HELP, GET DANTROLENE, MH Kit.**

Allocate specific tasks:

- Stop all trigger agents [volatiles (and succinylcholine)]
- Notify surgeon

- Ventilate
- Install clean breathing system and HYPERVENTILATE with 100% $O_2$ 10L/min
- Maintain anaesthesia with intravenous agent
- ABANDON/FINISH surgery as soon as possible
- Muscle relaxation with non-depolarising neuromuscular blocking drug

**3. TREATMENT AND MONITORITNG**

**(A) Dantrolene 2.5mg/kg IV** bolus
Repeat bolus 1mg/kg until signs and symptoms of MH subside and titrate to HR, muscle rigidity and temperature (up to 10mg/kg)

**(B) Cool** the patient if T > 39℃ – cold IV saline, ice saline lavage, surface cold packs. Stop when T < 38℃ and falling.

**(C) Treat:**

- Hyperkalaemia: NaHCO3, hyperventilation, calcium chloride, glucose/insulin.
  Glucose/insulin:

10U soluble insulin / 50ml 50% dextrose (adult),
0.15U soluble insulin/kg / 10ml 50% dextrose/kg (child)
Calcium chloride 10mg/kg for life threatening arrhythmias

- Arrhythmias: magnesium/amiodarone/metoprolol AVOID calcium channel blockers - interaction with dantrolene (hyperkalaemia, cardiac arrest)
- Metabolic acidosis: hyperventilate, $NaHCO3^-$
- Myoglobinaemia: forced alkaline diuresis (mannitol/furosemide + $NaHCO3^-$); may require renal replacement therapy later
- DIC: FFP, cryoprecipitate, platelets
- Check plasma CK as soon as possible

**(D) Monitor**

Core & peripheral temperature
$ETCO_2$, $SpO_2$, ECG
Invasive blood pressure, CVP
Continue monitoring in ICU, repeat dantrolene as necessary
Monitor for acute renal injury and compartment syndrome

**(E) Investigate**

- ABGs
- U/E/S (K)
- FBC (Hct, platelets)
- Coagulation
- CK

**(F) Stabilize and send to ICU.**

Post-Crisis Problems

**A** **A**lkalinize urine & maintain diuresis, monitor for **acute renal failure**

**B** **B**eware hypothermic, hyperkalemic, hypokalemic, hypervolemic overshoot - serial monitoring of filling pressures, fluid balance, electrolytes, Temp, K, Ca, coagulation profile and Haematocrit may require correction.

**C** **C**reatine Kinase (**C**K) levels track severity of *rhabdomyolysis*: if present, beware of renal failure, which may follow marked rhabdomyolysis. Monitor **CNS** function.

**D** **DIC** with *coagulopathy, thrombocytopenia, hemolysis, and abnormal bleeding*

**E** **E**levated liver functions are often observed 12-36 hours post-MH crisis.

Post-Acute Phase

**A** **A**wareness of recrudescence signs.

**B** **B**iopsy: Send the patient to a biopsy center for evaluation.

**C** **C**ounsel the patient and family regarding MH and further precautions

**D** **D**antrolene 1 mg/kg IV q 4-6h and continued for 24-48h after an episode of Malignant Hyperthermia. **D**ocumentation.

# Malignant Hyperthermia Crisis

AAGBI Safety Guideline

Successful management of malignant hyperthermia depends upon early diagnosis and treatment; onset can be within minutes of induction or may be insidious. The standard operating procedure below is intended to ease the burden of managing this rare but life threatening emergency.

## 1 Recognition

- Unexplained increase in $ETCO_2$ **AND**
- Unexplained tachycardia **AND**
- Unexplained increase in oxygen requirement
- (Previous uneventful anaesthesia does **not** rule out MH)
- Temperature changes are a late sign

## 2 Immediate management

- **STOP** all trigger agents
- **CALL FOR HELP.** Allocate specific tasks (action plan in MH kit)
- Install clean breathing system and **HYPERVENTILATE** with **100% $O_2$ high flow**
- Maintain anaesthesia with intravenous agent
- **ABANDON/FINISH** surgery as soon as possible
- Muscle relaxation with non-depolarising neuromuscular blocking drug

## 3 Monitoring & treatment

- Give **Dantrolene**
- Initiate active **cooling** avoiding vasoconstriction
- **TREAT:**
  - **Hyperkalaemia:** calcium chloride, glucose/insulin, $NaHCO_3$
  - **Arrhythmias:** magnesium/amiodarone/metoprolol **AVOID** calcium channel blockers – interaction with dantrolene
  - **Metabolic acidosis:** hyperventilate, $NaHCO_3$
  - **Myoglobinaemia**: forced alkaline diuresis (mannitol/furosemide + $NaHCO_3$) may require renal replacement therapy later
  - **DIC:** FFP, cryoprecipitate, platelets
- Check plasma CK as soon as able
- *For Paediatric Doses see Section 6*

**DANTROLENE**
2.5mg/kg immediate iv bolus. Repeat 1mg/kg boluses as required to max 10mg/kg

**For a 70kg adult**
- **Initial bolus: 9 vials dantrolene** 20mg (each vial mixed with 60ml sterile water)
- Further boluses of 4 vials dantrolene 20mg repeated up to 7 times

*For Dantrolene Doses in Paediatric patients see Section 5*

**Continuous monitoring**
Core & peripheral temperature
$ETCO_2$
$SpO_2$
ECG
Invasive blood pressure
CVP

**Repeated bloods**
ABG
U&Es (potassium)
FBC (haematocrit/platelets)
Coagulation

## 4 Follow-up

- Continue monitoring on IC U, repeat dantrolene as necessary
- Monitor for acute renal injury and compartment syndrome
- Repeat CK
- Consider alternative diagnoses (sepsis, phaeochromocytoma, thyroid storm, myopathy)
- Counsel patient & family members
- Refer to MH unit (see contact details below)

The UK MH Investigation Unit, Academic Unit of Anaesthesia, Clinical Sciences Building, St James's University Hospital Trust, Leeds LS9 7TF. Direct line: 0113 206 5270. Fax: 0113 206 4140. Emergency Hotline: 07947 609601 (usually available outside office hours). Alternatively, contact Prof Hopkins or Dr Halsall through hospital switchboard: 0113 243 3144.

**Your nearest MH Kit is stored** .....

# Malignant Hyperthermia Crisis

AAGBI Safety Guideline

## 5 Paediatric Adminstration of Dantrolene

- Mix 20mg (one vial) of Dantrolene with 60ml of sterile water to make a Dantrolene solution of 1mg in 3ml.
- Give an initial bolus of *7.5ml/kg* of the Dantrolene solution (=2.5mg/kg)
- Repeat further doses of *.3 ml/kg* (=1mg/kg) up to a maximum of 30ml/kg in total of Dantrolene.
- For a 10kg infant :
  *Give an initial bolus of 75mls (2.5mg/kg) of Dantrolene solution followed by 30ml (1mg/kg) boluses as required up to a maximum of 300mls (10mg/kg) of Dantrolene solution in total.*
- Remember to include the Dantrolene solution administration in the overall fluid bolus totals i.e. 300mls of Dantrolene Solution in a 10kg child = 30ml/kg of fluid.

## 6 Paediatric Administration of Supportive Therapy

**ARRHYTHMIAS**:

- Magnesium: 0.2 mmol/kg (50mg/kg). Give slowly by IV injection not >10mg/kg/min
- Amiodarone: 5mg/kg over 20 minutes then 300micrograms/kg/hr. Max 1.2g in 24 hours
- Esmolol: *Loading dose of 500mcg/kg over 1 min then an infusion of 50mcg/kg/min over 4 mins Re-load with 500mcg/kg if inadequate response and increase infusion by 50mcg/kg/min Repeat until effective or a maximum infusion of 200mcg/kg/min is reached.*
- AVOID calcium channel blockers they interact with Dantrolene

**HYPERKALAEMIA:** ***Calcium Gluconate 10%:*** 0.5ml/kg to a maximum of 20mls
10% Dextrose (5mls/kg) + Insulin (0.1 Units/Kg) over 20 minutes.
Monitor Blood Sugar.

**ACIDOSIS:** Correct with *SODIUM BICARBONATE* 0.5-1.0 mmol/kg
*(0.5-1.0 ml of 8.4%* NaHCO3/ kg).

**URINE OUTPUT:** Need to maintain urine output at least 2 ml/kg/hr *If required use:*
*MANNITOL* 0.5 - 1.0 g/kg *(2.5 – 5 ml/kg of 20% solution)* and/or
*FRUSEMIDE* 1 mg/kg IV

**DIC**:

| | |
|---|---|
| FFP | 10ml/kg |
| Cryoprecipitate | 5ml/kg body weight up to 30kg<br>5 units at a time are issued to children >30kg |
| Platelets | <30kg 10ml/kg<br>>30kg one pool of donors |

Drug doses references from the BNF for children. The drugs advised are for the initial management of MH. For ongoing and definitive treatment please contact your regional Paediatric Intensive Care Unit.

## ANAESTHESIA FOR MH-SUSCEPTIBLE PATIENT

**A** **A**naesthesia machine preparation: change circuits, disable or remove vaporizers, flush machine at a rate of 10 L/min for 20 minutesContinue to use high gas flow rates to prevent rebound phenomena.

**A**nesthesia: Use local or regional anesthesia but general anesthesia with non-triggering agents is acceptable. Safe drugs include: barbiturates, benzodiazepines, opioids, nondepolarizing neuromuscular blockers and their reversal drugs, and nitrous oxide.

**B** **B**ody temperature monitoring.

**C** **Ca**pnography: **C**lose monitoring for early signs of MH.

**D** **D**antrolene available. **D**ischarge, if no problems, after 2.5 hours.

**References:**

1. MHAUS (Malignant Hyperthermia Association of the United States. http://www.mhaus.org 24h Hotline : 800-644-9737
2. Malignant Hyperthermia Crisis. AAGBI Safety Guideline 2011.