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# MALIGNANT HYPERTHERMIA

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Malignant hyperthermia is a subclinical myopathy due to an inherited abnormality in the skeletal muscle cells. The condition is triggered on exposure to potent inhalational agents and suxamethonium resulting in uncontrolled release of calcium from the muscle cells causing extreme hypermetabolism.The early detection and treatment with Dantrolene sodium is essential to prevent a fatal outcome.

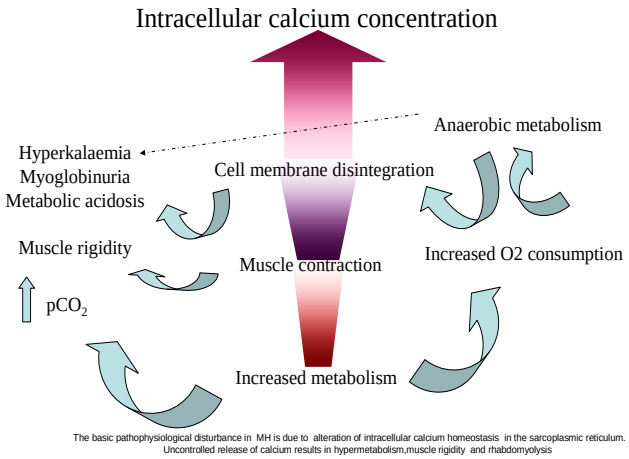
## Aetiology

Malignant Hyperthermia(MH)is an inherited autosomal dominant disorder with variable penetrance. The affected individuals are otherwise healthy and develop extreme hypermetabolism following exposure to triggering agents administered during general anaesthesia and rarely following severe stresses such as vigorous exercise and heat.

In the majority of MH susceptible (MHS) individuals the defect is due to a genetic mutation on chromosome 19 on the ryanodine receptor (RR) which is an intracellular calcium channel in the sarcoplasmic reticulum in skeletal muscle cells. At least 25 of the 90 mutations identified on RR are associated with MH. Individuals with Central Core Disease (CCD) an autosomal dominant non progressive myopathy due to a mutation of the RR gene are also susceptible to MH.

CCD should be suspected in children with proximal myopathies, hip dislocations and scoliosis who often require repeated anaesthetics.
All volatile anaesthetics influence calcium release from the sarcoplasmic reticulum while suxamethonium stimulates calcium release from T tubules in the muscle cell.

These triggering agents when administered to MHS patients induce a disturbance of the intracellular calcium homeostasis leading to uncontrolled metabolism and sustained muscle contraction.




## Clinical signs

### Metabolic symptoms:

Unexplained rapid rise of $ETCO_2$ end tidal carbon dioxide may be the earliest sign. Hyperthermia with increase in core temperature by 2°C/10mins - 1hour, usually occurs later during the anaesthetic or post operatively causing tachycardia, cyanosis, hypoxaemia, lactic and metabolic acidosis, hyperkalaemia and life threatening arrhythmias. Disseminated Intravascular Coagulation is the usual cause of death when body temperature exceeds 41°C.

### Muscular symptoms:

Masseter muscle rigidity following suxamethonium is often seen in young patients. Generalised muscular rigidity following a short or prolonged exposure to volatile agents is a relatively specific sign but not pathognomonic as this is seen even with myotonias. Rarely rapid

rhabdomyolysis may lead to severe hyperkalaemia, acute renal failure and compartment syndrome.

It is important to note that MH reaction can occur either per or postoperatively within 24hrs and may not necessarily develop with every exposure to anaesthesia and is usually seen after the 3rd exposure.

## Management of MH reaction

1. Discontinue volatile agents, disconnect vapouriser. Do not repeat Suxamethonium
2. Hyperventilate using 2-3 x Minute Volume with 100% Oxygen, high inspiratory pressures may be necessary due to muscle rigidity
3. Continue general anaesthesia with Total Intravenous Anaesthesia if the surgical procedure cannot be terminated immediately
4. Change the anaesthetic machine if possible
5. Give Dantrolene (specific calcium receptor antagonist)
   bolus dose 2mg/kg, repeat 1mg/kg up to 10mg /kg till symptoms recede followed by infusion 0.25-0.5mg/kg/hr 4 hourly for 24-48 hours if necessary
6. Start cooling measures,
   surface cooling with ice packs, cold intravenous fluids, nasogastric lavage, peritoneal dialysis if indicated & discontinue at 38°C to prevent a rebound effect.
7. Treat arrhythmias with beta blockers (avoid Calcium channel blockers)
8. Check blood gases, electrolytes, creatine phosphokinase, coagulation profile, serum & urine myoglobin
9. Correct hyperkalaemia, metabolic acidosis
10. Ensure adequate diuresis
11. Monitor central venous pressure, arterial blood pressure, core temperature, ETCO2 and hourly urine output for at least 36hrs
12. Refer patient and family members to a specialised MH testing centre

## Investigations

In vitro contracture test IVCT is currently the "gold standard" for diagnosis of MHS. This is carried out in specialised centres and relies on *in vitro* contracture response of biopsied muscle to Halothane and Caffeine. In MHS patients contractions occur on exposure to both halothane and caffeine. If only one test is positive the person is considered as MH equivocal if both are negative MH can be excluded.

MH can be verified by DNA analysis but is inconclusive if negative, due to numerous unidentified mutations on the ryanodine receptor gene.

## Differential diagnosis

During anaesthesia, sepsis, thyroid crisis, phaeochromocytoma, faulty apparatus, and allergic reactions causing hyperthermia can resemble MH but the temperature rise is progressive in MH.

Malignant Neuroleptic Syndrome (MNS) may present with clinical signs similar to MH This is due to an abnormal CNS response to dopamine antagonists such as Neuroleptics, Tricyclics and responds to treatment with Benzodiazepines. These patients have normal calcium channels in the muscle cells and diagnostic laboratory tests are not available for MNS

## Anaesthesia in known or suspected MHS patients

1. Use local, regional anaesthesia if possible or GA with intravenous anaesthetics and non depolarising muscle relaxants. Nitrous oxide and opioids can be used.
2. Use disposable or cleaned anaesthetic breathing systems and a fresh $CO_2$ canister
3. Disconnect the vapouriser,
4. Flush the anaesthetic machine including the ventilator with air or $O_2$ > 10l/ min for at least 10minutes prior to induction.
5. Pre treatment with Dantrolene is not recommended

## Monitoring of MHS

In addition to routine monitoring the core temp should be monitored in long operations & continued post operatively for 4 hours following short uncomplicated surgery and for 24 hours in all other patients

## Conclusion

During the past 30yrs, the mortality following MH has reduced from 80% to less than 5% due to the dramatic progress in understanding the clinical manifestations, pathophysiology and discovery of Dantrolene. A thorough anaesthetic history to identify patients at risk, a high degree of

awareness of the possibility of MH following administration of triggering agents and early initiation of treatment with Dantrolene is essential to prevent high mortality and morbidity in this rare condition. It is important to ensure that Dantrolene is readily available wherever anaesthesia is administered

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