MALIGNANT
HYPERthermia

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MALIGNANT HYPERTHERMIA (MH)

- An *inherited* disorder which causes sensitivity of skeletal muscle to certain inhaled anesthetic agents and/or depolarizing muscle relaxants

- Abnormally large amounts of calcium released from skeletal muscle leading to a life-threatening hypermetabolic state

- If not identified and treated promptly, it may progress and cause irreversible organ damage or death

- May occur at any time during the anesthesia process – including the early recovery phase

- MH-susceptible patients are *always* at high risk, even if they have had previous anesthesia without a reaction
TRIGGERING AGENTS

- **Inhaled General Anesthetic Agents:**
  - Halothane (Fluothane)
  - Isonflurane (Forane)
  - Desflurane (Suprane)
  - Sevoflurane (Ultane)
  - Enflurane (Ethrane)
  - Ether

- **Depolarizing Neuromuscular Blocking Agents:**
  - Succinylcholine (Anectine)
MH-SUSCEPTIBLE PATIENTS

- An inherited autosomal dominant genetic disorder

- Personal or Family history of:
  - Malignant Hyperthermia
  - Unexplained death during anesthesia
  - A fetus with a paternal history of MH-sensitivity (even if maternal history is negative)
  - Patients exhibiting prolonged Masseter muscle spasm (Trismus), or muscle rigidity after a triggering agent

- Predisposing disorders associated with MH-susceptibility:
  - Central core disease
  - Duchenne’s or Becker’s Muscular dystrophy
  - King-Deneborough syndrome
  - Myotonia

- Incidence rate: Adults 1:100,000  Children 1:50,000
Trigger
↓
Large quantities of Calcium released (from sarcoplasmic reticulum in skeletal muscle)
↓
Sustained increased calcium levels within the skeletal muscle
↓
Excessive stimulation of aerobic and anaerobic glycolytic metabolism
↓
Increased Carbon Dioxide production/Decreased Oxygen Supply
↓
Respiratory and metabolic acidosis
↓
Sustained muscle contractions
↓
Increased metabolism and heat production
↓
ATP stores within the cells are depleted
↓
Cells die
↓
Large amounts of potassium released into circulation

Hyperkalemia
↓
Cardiac Dysrhythmias

Myoglobin released
↓
Renal Failure
<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>EARLY</th>
<th>LATE</th>
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</thead>
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<tr>
<td>1. Tachycardia (usually 1st symptom – mistaken for light anesthesia)</td>
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<td>1. Fever (up to &gt; 110° - 114° F)</td>
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<td>2. Masseter spasm or trismus (severe, sustained contraction of jaw making intubation difficult)</td>
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<td>2. Sympathetic Nervous System activation</td>
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<td>3. Increase in end-tidal carbon dioxide (&gt;100 mmHg – unable to correct it)</td>
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<td>3. Edema (Cerebral/Peripheral)</td>
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<td>4. Tachypnea (pt’s attempt to correct hypercarbia)</td>
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<td>4. Cyanosis/Mottled Skin</td>
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<td>5. Hypoxia</td>
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<td>5. Myoglobinuria/Rhabdomylysis</td>
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<td>6. Acidosis (pH &lt; 7.0)</td>
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<td>6. DIC</td>
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<td>7. Hyperkalemia</td>
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<td>7. Multiorgan Failure (Cardiac/Renal)</td>
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<td>8. Hypertension</td>
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<td>8. Cardiac Arrhythmias</td>
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<td>9.</td>
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<td>9. Sudden Cardiac death in young patients</td>
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In the event of a MH emergency in the OR:

* Hyperventilate with 100% O₂ in an attempt to meet the requirements of the body during the crisis period.
* The Circulating RN shall call for additional help from the other OR suites, or from PACU
* Anesthesia staff will retrieve the Malignant Hyperthermia cart from the Anesthesia Work Room, and bring it to the OR
* Additional staff shall assist Anesthesia, mix the Dantrolene, assist with cooling the patient, deliver specimens to the Clinical Laboratory, documentation, run for supplies, etc.
* The surgeon should close the surgical wound, if possible. If not, the surgeon should pack the wound with saline-soaked surgical towels or laparotomy sponges. The Circulating RN should document, on the Intraoperative Nurses’ Notes, the number of towels/lap sponges used to pack the wound.
* Notify the Pharmacy
The Malignant Hyperthermia cart contains:
- 54 vials of Dantrolene
- Sterile water to reconstitute the Dantrolene (w/o bacteriostatic agent)
- Ice packs
- Various sizes of syringes and needles; 60 ml, 10ml, 3 ml
- Toomey Syringes

- At least 3 one liter bags of 0.9NS are kept in the refrigerator at all times
- Instructions for reconstituting the Dantrolene are taped to top of the MH cart
- The “Emergency Therapy For Malignant Hyperthermia” protocol, by MHAUS,
  is taped to the top of the MH cart
TREATMENT

ACUTE PHASE TREATMENT

✓ Dantrolene should be administered **within 10 minutes** of the diagnosis
  - initial dose 2.5 mg/kg IV
  - repeat dose q 5 minutes until reversal of the reaction occurs **OR** a total dose of 10mg/kg has been given
  - dissolve 20 mg in each vial with at least 60ml sterile-water (warming may speed it up)

✓ Halt the triggering event- If surgery must continue, maintain general anesthesia with IV non-triggering anesthetics (e.g. propofol)

✓ Hyperventilate with 100% Oxygen- To flush volatile anesthetics and ETCO2

✓ Draw labs and ABGs

✓ Anti-arrhythmic agents for dysrhythmias  (Do NOT use Calcium Channel Blockers)

✓ Cold saline IV, lavage with cold fluids, and cooling blanket  (for a core temperature > 39° C)

✓ Glucose/insulin, calcium, sodium bicarb for hyperkalcemia
DANTROLENE

Mechanism of Action
- Classified as a direct-acting, muscle relaxant – specific to skeletal muscle only
- Disassociates the excitation-contraction coupling within the muscle cells by acting on the rayodene receptor. (Where gene mutations occur)
- Interferes with the release of calcium from the Sarcoplasmic Reticulum, thus suppressing the rise in calcium in the muscle cells that triggers the MH crisis
- Reestablishes the normal level of ionized calcium in the myoplasm

Dosage and Administration
- Supplied in 36 ml vials
- Each vial contains 20 mg of Dantrolene Sodium, 3 grams of Mannitol, and Sodium Hydroxide (Sodium Hydroxide increases the pH to 9.5)
- Reconstitute with 60 mls of sterile water for injection, without Bacteriostatic Agent
- Vial is shaken until solution is clear - THIS MAY TAKE 2 – 4 MINUTES
- Give 2.5mg/kg RAPID IV Push (use a micron filter)
Dantrolene Dosage and Administration

- Large bore IV/Central line → inject close to the IV insertion site
- Its effects should be noticed within 2-3 minutes
- Repeat dose Q 5 minutes until MH crisis subsides
- Maximum doses 10 mg/kg - 30mg/kg
- Should be given via a separate line, not compatible with 0.9NS, D5W, or LR
- Primary line must be flushed with sterile water for injection USP (without a bacteriostatic agent) before administering the Dantrolene and after administration
- Tissue necrosis with IV extravasation (due to the high pH of the Dantrolene)
- Protect from light
- Use within 6 hours of mixing
- Half life is variable = 4°- 8°
- Shelf life of Dantrolene = 28 months
- Post Acute Treatment → Dantrolene 1mg/kg q 4-6 hours IV, 8 mg/kg/day in 4 divided doses, or 0.25 mg/kg/hr by continuous IV infusion until symptoms completely stop
DANTROLENE

Side Effects

- Lethargy
- Muscle weakness (↓ grip strength, Lower Extremities s affected more)
- ↓ Respiratory function
- Dizziness
- Double vision
- Nausea, vomiting, diarrhea
- Can potentiate the effects of NMB agents
- CV collapse if given with a Calcium Channel Blocker

Indications

- For relief of spasms, cramping, and tightness of muscles caused by certain medical conditions such as:
  - MS
  - Cerebral Palsy
  - Stroke
  - Spinal Injuries
POST ACUTE PHASE TREATMENT

✓ ICU monitoring for 24-36 hours

✓ Dantrolene 1 mg/kg q 4-6 hours or 0.25 mg/kg/hr by infusion for at least 24 hours

✓ Frequent ABG, BMP, CPK, CBC, and PT/PTT levels drawn until normalized

✓ Follow standard ICU therapy for acute rhabdomyolysis ad myoglobinuria
  - alkalinazation of urine with bicarb drip
  - urine output > 200 ml/hr

For help with an Emergency Situation call:
The Malignant Hyperthermia Hotline
1-800-644-9737

(Non-Emergency Information: 1-800-986-4287)
Conditions That Mimic MH

- Post surgery sepsis
- Thyrotoxicosis
- Duchenne’s dystrophy
- Becker’s musculodystrophy
- Myotonic dystrophy
- Neuroleptic malignant syndrome
- Iatrogenic hyperthermia
- Head trauma
- Drug toxicity
- Hyperthyroidism
- Hypokalemic periodic paralysis
- Pheochromocytoma
- Rhabdomyolysis
- Ventilation problems

- These conditions can mimic Malignant Hyperthermia, but are NOT actually MH.

- May have many similar signs and symptoms, but the mechanism responsible is not the same as MH.
EMERGENCY THERAPY FOR MALIGNANT HYPERThERMIA

DIAGNOSIS

Signs of MH:
- Increased ETCO₂
- Trunk or total body rigidity
- Masseter spasm or trismus
- Tachycardia/tachypnea
- Acidosis
- Increased temperature (may be late sign)

Sudden/Unexpected Cardiac Arrest in Young Patients
- Presume hypercalcemia and initiate treatment (see #6)
- Measure CK, myoglobin, ABGs, until normalized
- Consider dantrolene
- Usually secondary to occult myopathy (e.g., muscular dystrophy)
- Resuscitation may be difficult and prolonged

Trismus or Masseter Spasm with Succinyicholine
- Early sign of MH in many patients
- If limb muscle rigidity, begin treatment with dantrolene
- For emergent procedures, continue with non-triggering agents; consider dantrolene
- Follow CK and urine myoglobin for 56 hours at least. Check CK immediately and at 6-hour intervals returning to normal. Observe for cola colored urine. If present, test for myoglobin.
- Observe in PACU or ICU for at least 12 hours

ACUTE PHASE TREATMENT

GET HELP. GET DANTROLENE - NOTIFY SURGEON.
- Discontinue volatile agents and succinylcholine.
- Hyperventilate with 100% oxygen at flows of 10 L/min. or more.
- Halt the procedure as soon as possible, if emergent, use nontriggers.
- (The cycle system is not often best need not be changed)

Dantrolene 2.5mg/kg rapidly IV through large-bore IV, if possible
- Give 0.5mg/kg in 30-60 min
- Repeat until control of the signs of MH
- Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.
- Dissolve the 20 mg in each vial with at least 60 ml sterile preservative-free water for injection. Prewarming (not to exceed 38°C) the sterile water will speed solubilization of dantrolene.
- The crystals also contain NaOH for a pH of 9; each 20 mg bottle has 3 gm mannitol for scotonicity

- 1.2 mEq/kg if blood gas values are not yet available.

4. Cool the patient with core temperature >39°C. Lavage open body cavities, stomach, bladder, or rectum. Apply ice to surface. Infuse cold saline intravenously. Stop cooling if temp. >38°C and falling to prevent drift <36°C.

Dysrhythmias usually respond to treatment of acidosis and hyperkalemia.
- Use standard drug therapy accept calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.

Hyperkalemia - treat with hyperventilation, bicarbonate, glucose/insulin, calcium.
- Bicarbonate 1.2 mEq/kg IV
- For pediatric, 0.1 units insulin/kg and 1 ml/kg 50% glucose or for adult 10 units regular insulin IV and 50 mEq 50% glucose.
- Calcium chloride 10 mg/kg or calcium gluconate 10-50 mg/kg for life-threatening hyperkalemia.
- Check glucose levels hourly.

Follow ETCO₂, electrolytes, blood gases, CK, core temperature, urine output and color, coagulation studies. If CK and/or K⁺ rise more than transiently or urine output falls to less than 6.5 ml/kg/hr, induce diuresis to >1 ml/kg/hr urine to avoid myoglobinuria-induced renal failure.

Venous blood gas (e.g., femoral vein) values may document hypermetabolism better than arterial values.
- Central venous or PA monitoring as needed and record minute ventilation.
- Place Foley catheter and monitor urine output.

POST ACUTE PHASE

Observe the patient in an ICU for at least 24 hours, due to the risk of recrudescence.
- Dantrolene 1 mg/kg 46 hours or 0.25 mg/kg/h infusion for at least 24 hours. Further doses may be indicated
- Follow vital and lab as above [see #7]
- Gentamicin
- CK every 6 hours

Follow urine myoglobin and institution therapy to prevent myoglobin precipitation in renal tubules and the subsequent development of acute renal failure.
- Follow standard treatment for acute renal insufficiency and myoglobinuria (urine output < 60 ml/h), alizarin staining of urine with Naphthol AS-TRatamin (see text). If needed, refer patient to the nearest biopsy center for follow-up.

CAUTION:
This protocol may not apply to all patients; alter for specific needs.

Non-Emergency Information
MHAS
11 East State Street
PO Box 1049
Oswego, NY 13126-0105
Phone: 1-800-666-MHAS
Fax: 315-674-7910
Email: info@mhast.org
Website: www.mhas.org
References

