Malignant Hyperthermia

"The Disease of Anesthesia"

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What It Is

- Inherited Disorder
- Autosomal Dominant, variable penetrance
- Hypermetabolic State
- Triggered by certain anesthetics
- Hyperkalemia
- Muscle Damage
- Hyperthermia
- Abnormal handling of intracellular calcium levels

What It Isn't

- "Allergy to Anesthesia"
- "Allergy to Succinylcholine"

History

- 1961- Denborough et al described a string of anesthetic related deaths in a family
- 1960's-Recognition of relationship of MH to Porcine Stress Syndrome
- 1971-Caffeine/Halothane Contracture Test
- 1975/1979-Dantrolene for treatment
- 1982-MHAUS and MH hotline
- Mid1980's- End tidal Carbon dioxide monitoring

Epidemiology

- Autosomal Dominant with incomplete penetrance
- Up to 30 mutations of genes for calcium release channels and slow calcium channels
- 1 in 50,000 general anesthetics
- MH trait in 1 in 2,000-3,000 patients

Triggering Agents

- Halogenated Anesthetic Agents
- Succinylcholine

Nontriggering Agents

- Everything else

Symptoms

- Hypercarbia
- Increased oxygen consumption
- Metabolic acidosis
- Tachycardia
- Hyperkalemia
- Dysrhythmias
- Increased Creatine Kinase
- Rhabdomyolysis
- Muscle Rigidity
- Masseter muscle spasm
- Hyperthermia

Pathophysiology

- Mutation of Ryanodine receptor of Sarcoplasmic Reticulum
- Triggering agent keeps receptor open
- Overpowers the pumping capacities of the Ca2+ ATPase
- Massive Ca2+ release in myoplasm
- Hypermetabolic state

Animal Model

- Landrace pigs-Porcine Stress Syndrome
- Acute Capture Myopathy-deer, ducks, turkey, antelope, rabbits

Mimics of Malignant Hyperthermia

- Heat gain in Operating Room
- Malfunctioning Ventilator
- Malfunctioning equipment or probes
- Thyroid Storm
- Cocaine, amphetamines, ecstasy
- Fever from infection, transfusion, etc.

Awake Triggering

- 12 year old boy after football game, Tmax-108 degrees
- Symptoms consistent with MH
- Had MH after sevoflurane treated with Dantrolene 6 months earlier
- Died despite Dantrolene therapy

ASSOCIATION WITH OTHER DISORDERS

- Neuroleptic malignant syndrome
- Duchenne's Muscular Dystrophy
- Strabismus
- Osteogenesis imperfecta
- King-Denborough syndrome (short stature, musculoskeletal abnormalities, and mental retardation)
- Hyperkalemic Cardiac Arrest in infants

Masseter Muscle Spasm

- In Pediatric Population
- Immediately after Sux
- Unable to open mouth to intubate
- Precursor of MH in 20-30%
- Elevated creatine kinase (10-20,000)
- Myoglobinuria
- 1% of children who receive Inhalational agent/Sux

Treatment

- Discontinue Triggering agents
- Switch to Nontriggering technique
- Hyperventilate with 100% 02
- Bicarbonate 1-2 mg/kg as needed
- Get additional help
- Dantrolene 2.5mg/kg Push. Repeat PRN
- Cool patient: gastric lavage, surface, wound
- Treat arrhythmias-***do not use calcium channel blockers***
- Arterial or venous blood gases
- Electrolytes, coagulation studies

Dantrolene

- Antispastic drug
- Found to work in MH
- Prevents the release of calcium in SR
- Restores metabolism to normal
- Pretreatment not reliable

Logistics of Dantrolene

- Very hard to mix
- Dosage 2.5mg/kg up to 10 mg/ kg
- 2.5 mg/kg = *9 vials* for 70 kg patient
- 10 mg/kg = *35 vials* for 70 kg patient
- Facilities using triggering agents need to have dantrolene available immediately
- MH kits and/or carts with supplies

Mixing

Table 1. Dantrolene Mixing Time by Dose and Diluent Temperature

Dantrolene Dose	2.5 mg /kg		10 mg /kg	
72-kg Adult	A Diluent	W Diluent	A Diluent	W Diluent
*Time / seconds	94 seconds	59 seconds	94 seconds	59 seconds
Number of Vials	9 vials	9 vials	36 vials	36 vials
1 Mixer / minutes	14 minutes	9 minutes	56 minutes	35 minutes
3 Mixers / minutes	5 minutes	3 minutes	19 minutes	12 minutes

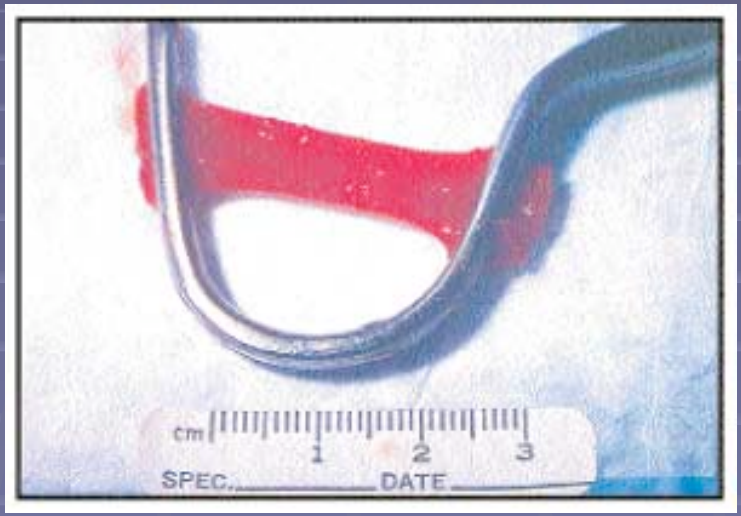
A = Ambient (22° C), W = Warmed Diluent Temperature (41° C)

*Comparative Study Results, Mean Times

- Dantrolene 1mg/kg q 4 hours for 24-36 hours
- Treat in an ICU setting
- Recrudescence rate is 25%
- Post-event counseling

Diagnosis

- Caffeine-Halothane Contracture Test
- Requires live fresh skeletal muscle from biopsy
- Test Sensitivity: 100%
- Specificity: 80%-93%
- Expensive
- Invasive


cm
1
2
3
SPEC.
DATE

- Only done in a few centers in USA
  - Bethesda, MD
  - Chicago, IL
  - Los Angeles, CA
  - Minneapolis, MN
  - Philadelphia, PA
  - Rochester, MN
  - Sacramento, CA
  - Winston Salem, NC

MHAUS

- Malignant Hyperthermia Association of the United States
- http://www.mhaus.org
- Education and support for families, medical staff
- 24 hour hotline

MH Hotline
1-800-644-9737
Outside the US:
1-315-464-7079

EMERGENCY THERAPY FOR MALIGNANT HYPERTHERMIA

DIAGNOSIS

Signs of MH:

- Increased $ETCO_2$
- 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 hyperkalemia 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 Succinylcholine

- 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 36 hours at least. Check CK immediately and at 6-hour intervals until 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 –

1 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 non-triggers.

(The circle system and CO_2 absorbent need not be changed.)

2 Dantrolene 2.5mg/kg rapidly IV through large-bore IV, if possible

To convert kg to lbs for amt of dantrolene, give patients 1 mg/lb (2.5 mg/kg approximates 1 mg/lb).

- Repeat until there is 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 solublization of dantrolene.
- The crystals also contain NaOH for a pH of 9; each 20 mg bottle has 3 gm mannitol for isotonicity.

3 Bicarbonate for metabolic acidosis.

- 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.

5 Dysrhythmias usually respond to treatment of acidosis and hyperkalemia.

- Use standard drug therapy <u>except calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.</u>

6 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 ml 50% glucose.
- Calcium chloride 10 mg/kg or calcium gluconate 10-50 mg/kg for life-threatening hyperkalemia.
- Check glucose levels hourly.

7 Follow $ETCO_2$, 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 0.5 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

A Observe the patient in an ICU for at least 24 hours, due to the risk of recrudescence.

B Dantrolene 1 mg/kg q 4-6 hours or .25 mg/kg/hr by infusion for at least 24 hours. Further doses may be indicated.

C Follow vitals and labs as above (see #7)
- Frequent ABG
- CK every 6 hours

D Follow urine myoglobin and institue therapy to prevent myoglobin precipitation in renal tubules and the subsequent development of Acute Renal Failure. Follow standard intensive care therapy for acute rhabdomyolysis and myoglobinuria (urine output > 200 ml/h, alkalinization of urine with Na-bicarbonate infusion with careful attention to both urine and serum pH values, etc.).

E Counsel the patient and family regarding MH and further precautions; refer them to MHAUS. Fill out and send in the Adverse Metabolic Reaction to Anesthesia (AMRA) form (www.mhreg.org) and send a letter to the patient and her/his physician. Refer patient to the nearest Biopsy Center for follow-up.

Non-Emergency Information

MHAUS
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PO Box 1069
Sherburne, NY 13460-1069
Phone
1-800-986-4287
(607-674-7901)
Fax
607-674-7910
Email
info@mhaus.org
Website
www.mhaus.org

Since 1981 MHAUS Malignant Hyperthermia Association of the United States Dedicated to Patient Safety

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

ORPO 7/05/1a

Produced By the Malignant Hyperthermia Association of the United States

Summary

- Autosomal Dominant
- Triggered by certain anesthetics
- Hypermetabolic state
- Hypercarbia, metabolic acidosis
- Dantrolene is only known treatment
- Survivable
- Caffeine-Halothane Contracture test


"That's
all
folks!"