

Malignant Hyperthermia

Basics

Definition

- A pharmacogenetic clinical syndrome that manifests as a hypermetabolic crisis when susceptible patients are exposed to an anesthetic triggering agent.

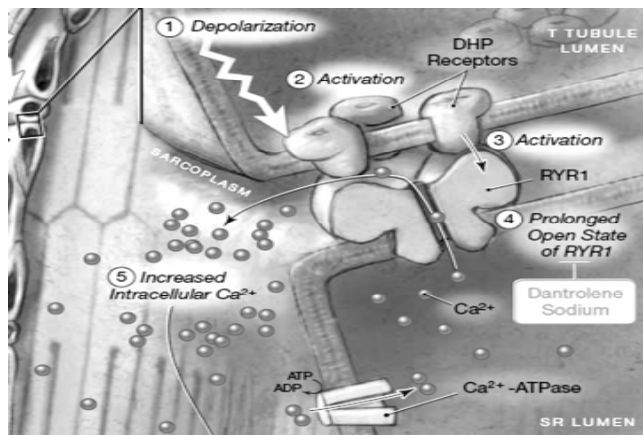
Genetics

- MH trait is found in 1:2000-3000 patients.
- Autosomal dominant with low penetrance.
- At least 4 chromosomal loci identified.
- Ryanodine receptor-1 (RYR-1) is best characterized.

Incidence

- 1 in 20,000-50,000 anesthetics, depending on the population and drugs used.
- May occur on a patient's 2nd exposure to triggers.

Excitation-Contraction Coupling



Risk Factors

- Prior history of MH
- Family history of MH
- Age (Pedi > Adult)
- History of unexplained fevers, muscle cramps, or weakness
- History of caffeine intolerance
- Trismus on induction (precedes 15-30% of MH)
- Comorbidities:
 - Central Core Disease
 - Dystrophinopathies (DMD, Becker's)
 - Other myopathies
 - King-Denborough Syndrome
- Type of Procedure:
 - Ortho (joint dislocation)
 - Ophtho (strabismus or ptosis repair)
 - ENT (cleft palate, T&A, dental procedures)

Sequence of Events

1. Triggers

- All potent inhalational agents (but not N₂O)
- Succinylcholine

2. Increased Cytoplasmic Free Ca²⁺

- Masseter muscle rigidity (trismus)
- Total body rigidity

3. Hypermetabolism

- Increased CO₂ production (most sensitive and specific sign of MH!)
- Increased O₂ consumption
- Increased heat production

Sequence of Events

4. Cell Damage

- Leakage of K⁺, myoglobin, CK

5. Compensatory Mechanisms

- Increased catecholamines - tachycardia, hypertension, cutaneous vasoconstriction
- Increased cardiac output - decreased S_{cv}O₂, decreased P_aO₂, metabolic acidosis
- Increased ventilation - increased ET_{CO2}, increased V_E
- Heat loss - sweating, cutaneous vasodilation

6. Temperature Rise

- A late and inconsistent sign of MH!
- Temperature can rise 1-2°C every 5 minutes.

Sequence of Events

7. Secondary Systemic Manifestations

- Arrhythmias
- DIC
- Hemorrhage
- Cerebral Edema
- Acute Renal Failure
- Compartment Syndrome
- Death

Differential Diagnosis

- Neuroleptic Malignant Syndrome (NMS)
- Thyroid Storm
- Sepsis
- Pheochromocytoma
- Drug-induced (e.g. ecstasy, crack, amphetamines, PCP, LSD)
- Serotonin Syndrome
- Iatrogenic Hyperthermia

Treatment (Acute Phase)

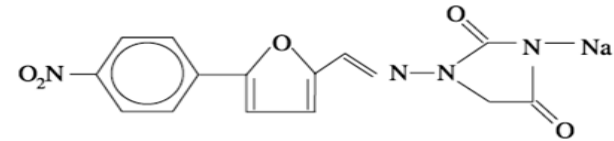
1. Get Help

- Call for help (Code Blue, 911, etc); get the MH cart.
- D/C volatile agents and succinylcholine.
- Notify surgeon; halt surgery ASAP, or continue with non-triggering agents if necessary.
- Call the MH Hotline 1-800-MH-HYPER.

2. Get Dantrolene

- 2.5 mg/kg IV push.
- Dissolve 20 mg in 60 ml sterile, preservative-free H₂O (for a 70 kg pt, you need 175 mg = 9 vials).
- Repeat until signs of MH are controlled.
- Sometimes, more than 10 mg/kg is necessary (= 35 vials of dantrolene!).

Dantrolene



- A hydrophobic, hydantoin derivative
- Interferes with excitation-contraction coupling by binding the RYR-1 Ca²⁺ channel
- Relatively safe drug; causes generalized muscle weakness (including respiratory muscles).
- Can also be used to treat NMS or thyroid storm.

Treatment (Acute Phase)

3. Treat acidosis

- Hyperventilate patient with 100% O₂ at > 10 L/min.
- Bicarbonate 1-2 mEq/kg until ABG available.

4. Treat hyperthermia

- Cool if T > 39°C, but D/C if T < 38°C.
- Apply ice to body surfaces.
- Cold NS via IV.
- Lavage stomach, bladder, or rectum PRN.

5. Treat dysrhythmias

- Standard therapies, but avoid CCBs in the presence of dantrolene (may promote hyperkalemia).

Treatment (Acute Phase)

6. Treat hyperkalemia

- Hyperventilate
- Bicarbonate
- Insulin & glucose (10 units in 50 ml D50)
- Calcium (10 mg/kg CaCl₂, or 10-50 mg/kg Ca gluconate)

7. Maintain UOP

- Mannitol (0.25 g/kg), and/or
- Lasix (1 mg/kg)

8. Continue to monitor

- ET_{CO2}, Temp, UOP & color, Electrolytes, ABG, CK, PT/PTT/INR

Treatment (Post Acute Phase)

1. **Observe in ICU for at least 24 hours.**
 - Recrudescence rate is 25%.
2. **Dantrolene**
 - 1 mg/kg IV q4-6hrs for at least 36 hours.
3. **Follow labs**
 - ABGs, CK, myoglobinuria, coags, electrolytes, UOP and color
4. **Counsel patient and family**
 - Future precautions.
 - Refer to MHAUS.
5. **Refer patient and family to nearest Biopsy Center for follow-up.**

Susceptibility Testing

Caffeine-Halothane Contracture Test (CHCT)

- Gold Standard
- Requires fresh muscle biopsy
- Sensitivity >97%, Specificity 80-93%
- Available at 9 U.S. testing centers

Molecular Genetics

- *RYR1* mutation screening
- Low sensitivity, but high specificity
- Typically reserved for patients with a positive CHCT, relatives of known MH susceptibility, or patients with highly suspicious MH episode.

Prevention

Machine

- Change circuit and CO₂ absorbant
- Remove vaporizers
- Flush machine at FGF of 10 L/min for 20 minutes.

Monitors

- ASA monitors, especially temperature and ET_{CO2}

Anesthetic

- Avoid succinylcholine and volatiles
- All other non-triggering agents are OK (including N₂O)

Emergency

- Know where to find the MH cart.
- Have dantrolene available.

References

- Litman RS, Rosenberg H. 2005. Malignant hyperthermia: update on susceptibility testing. *JAMA*, **293**: 2918-24.
- Morgan GE, Mikhail MS, and Murray MJ. *Clinical Anesthesiology, 4th ed.* New York: McGraw-Hill Companies, Inc., 2006.
- Malignant Hyperthermia Association of the United States (MHAUS, <http://www.mhaus.org>)
- UCLA Department of Anesthesiology (<http://www.anes.ucla.edu/dept/mh.html>)

