Management of Emergency Cases in the OR: Identifying & Treating Malignant Hyperthermia

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Learning Objectives

• Understand pathophysiology of MH
• Identify patients at risk for MH
• Recognize onset of MH
• Know treatment & stabilization of acute MH
• Incorporate MH awareness & treatment plans in your surgical facility
Malignant Hyperthermia

- Inherited myopathy
- Hypermetabolic reaction/crisis to certain volatile anesthetic gases & succinylcholine
- Worldwide attention after published series of anesthetic deaths in a family (1960)
Malignant Hyperthermia

• MH susceptibility
  – 1 in 200 in certain populations

• MH incidence during anesthesia encounters
  – Between 1 in 5000 and 1 in 50,000 to 100,000
  – More common in males & children

• Mortality
  – 70% in 1960, now <5%
  – Accurate diagnosis, timely recognition, treatment
MH Genetics

Inherited skeletal muscle disorder

• Autosomal dominant with variable penetrance

• Ryanodine receptor type 1 gene (RYR1)
  – >100 associated mutations identified
  – Present in >50% of MH susceptible patients
    • Almost all families with central core disease

• Mutation at 1S subunit of dihydropyridine receptor
  – <1% of MH susceptible families worldwide
Agents that Trigger MH

- Halothane (most potent)
- Enflurane
- Isoflurane
- Desflurane*
- Sevoflurane*

* Less potent, gradual MH onset

- Succinylcholine (explosive MH onset)
Other Triggering Agents

- d-Tubocurarine*
- Ether derivatives and chloroform
- Rapid intravenous $K^+$
- Theophylline, aminophyllin, phosphodiesterase inhibitors in supertherapeutic doses
Safe Non-Triggering Agents

- Anticholinergics
- Anticholinesterases
- Barbiturates (e.g., thiopental)
- **Benzodiazepines**
- Droperidol
- Etomidate
- **Ketamine**
- Local anesthetics
- Narcotics

- Nitrous oxide
- Nondepolarizing muscle relaxants
  - Vecuronium
  - Rocuronium
  - Pancuronium
  - Atracurium
  - Mivacurium
  - Cisatracurium
- NSAIDS
- **Propofol**
- IV Anesthetics

**Use with care**
- Haloperidol
- Catecholamines
  - May cause secondary sympathetic response (not a trigger)
- Phenothiazines (e.g., chlorpromazine, prochlorperazine)
  - May cause neuroleptic malignant syndrome (confused with MH)
Non-Triggering Agents Triggering MH

MH can be triggered in < 1% of MH susceptible patients by “non-triggering” agents

Keep MH diagnosis in mind in any case with clinical presentation
Patient Evaluation

• MH susceptible patients may undergo anesthesia several times before a clinical episode occurs

• Preop questions:
  – Family history of adverse outcomes after general anesthesia
  – Conditions that predispose to true MH
    • Evans myopathy, King-Denborough syndrome, central core disease

• Patients with MH in 1st degree relatives are considered MH susceptible until proven otherwise
  – Must not receive triggering agents
  – Counseled and referred for evaluation
Musculoskeletal Disorders

• Duchenne muscular dystrophy
  – Risk life-threatening hyperkalemia with succinylcholine
  – Do not exhibit classic signs of malignant hyperthermia
• Patients with any form of myotonia should not receive succinylcholine
• No triggering agents for patients with:
  – Hypokalemic periodic paralysis
  – Central core disease
  – Multi-minicore disease (\textit{RYR1-related} forms)
  – Duchenne or Becker muscular dystrophy
  – Paramyotonia
  – Myotonia fluctuans
Associated with MH?

Heat Stroke
- Anecdotal reports of MH and death from heat stroke
- Many anesthesiologists believe a patient with history of heat stroke & rhabdomyolysis should be considered susceptible to MH

Exercise-related Rhabdomyolysis
- Some patients with exercise-induced rhabdomyolysis developed MH-like clinical syndrome and were found to be susceptible to MH on biopsy testing and genotyping
- Many anesthesiologists consider patients with exercise-induced rhabdomyolysis to be susceptible to MH

Neuroleptic Malignant Syndrome (NMS)
- Many of the same manifestations as MH
- Triggered by neuroleptic antipsychotics
- Many features similar to MH but no definitive association
- Most anesthesiologists do not consider patients with NMS to be susceptible to MH
MH Susceptibility Testing

• Caffeine-halothane contracture test
  – Requires muscle biopsy
  – Done at specialized centers (8 in US)

• Genetic testing
  – RYR1 mutation screen
  – High specificity
  – Low sensitivity
    • Negative test requires caffeine-halothane contracture test
MH Susceptible Patients

• Minor procedures
  – Simple excisional surgery with topical or local anesthesia in the office or ambulatory surgical center
  – No evidence that local anesthetics, vasoconstrictors, or patient anxiety increase the chance of a MH reaction in this setting

• Complex procedures
  • Minimal or moderate IV or IM sedation/analgesia
  • General anesthesia
  • Major conduction blockade
  – Refer to an accredited ASC or hospital
Cascade of MH

Triggering Agent → Perturbed muscle membrane → Disturbed Ca\(^{++}\) homeostasis

Susceptible Muscle
- \(\uparrow\) Ca\(^{++}\) in myoplasm

Muscle Contraction
- Lactic acid
- Carbon dioxide
- Phosphate
- Heat

Normal Muscle Compensates

MH Crisis
- Metabolic acidosis
  - \(\uparrow\) pCO\(_2\)
  - \(\uparrow\) PO\(_4\)
  - Fever

Mitochondria Uncoupled
- \(\downarrow\) ATP production
- \(\uparrow\) ATP & O2 consumption

Ion Transport Dysfunction
- \(\uparrow\) K\(^+\)
- \(\uparrow\) PO\(_4\)
- \(\uparrow\) Mg\(^{++}\)
- Myoglobinemia
MH Presentation

**Clinical**
- Tachycardia
- Markedly increased minute ventilation (when breathing spontaneously)
- **Muscle rigidity**
- Skin mottling
- **Hyperthermia (late sign)**
  - Increase 1° to 2° C every 5 min
- Cola-colored urine
- Disseminated intravascular coagulation

**Laboratory**
- Increased end-tidal CO₂ and increased PaCO₂
- Decreased pH (metabolic and respiratory acidosis)
- Decreased PaO₂
- Hyperkalemia (PVC, VT, VF)
- Increased CK
- Myoglobin in blood or urine
- Abnormal coagulation tests
- Increased plasma lactate level
Increased Minute Ventilation vs $pCO_2$
Masseter Muscle Rigidity (MMR)

• Inability to open mouth after receiving a triggering agent
• 1% of children after succinylcholine + inhalation agent
• Usually can provide bag-mask ventilation
• Normal effect of succinylcholine is to increase masseter muscle tension above baseline
  – Significant MMR signals MH in up to 30% of cases
• If MMR is observed
  – Stop all triggering agents
  – Cancel surgery if possible
  – Observation for MH
Aborted or Subclinical MH

- Nonspecific hypermetabolism after inhalational anesthetic
- Postoperative muscle pain, myoglobinuria, or elevated K⁺ or CK
- Hospital observation for MH
  - Serial CK & K⁺
  - ABG if increased minute ventilation (mixed metabolic and respiratory acidosis)
Differential Diagnosis

- Anticholinergic syndrome
- Extrapyramidal syndrome
- Serotonin syndrome
- Neuroleptic malignant syndrome
- Contrast induced neurotoxicity
- Pheochromocytoma
- Thyrotoxicosis
- Drug withdrawal
- Drug toxicity
- Iatrogenic overheating
- Hypoventilation
- Heat stroke
- Sepsis
- Hypoxic encephalopathy
- Intracranial hemorrhage
- Brain injury
- Meningitis
- Faulty equipment
What to do if you Suspect MH

• Call for help
• Discontinue volatile agents & succinylcholine
• Get MH cart & Dantrolene
• Notify OR team that you suspect MH
• Finish procedure as fast as possible
  – If surgery must continue use nontriggering anesthetic
  – Propofol + opioid
• Hyperventilate with 100% O₂ at >10 L/min to remove excess CO₂
• Obtain core temperature
What to do if you Suspect MH

• Administer Dantrolene
  • Repeat until the end-tidal CO₂ begins to decline
    – Doses > 10 mg/kg may be necessary
    – If a dramatic response does not occur within minutes consider alternative diagnoses

• Ensure adequate IV access
  – Consider central line placement

• Insert an arterial line & urinary bladder catheter

• Call 1-800-MH-HYPER for management assistance

• ICU admission or transfer
Have Treatment Plan Available
MH Cart

+ Ice Machine
Manage Hyperthermia

• Cooling Measures to Lower Core < 38°C
• Lower OR temperature
• Discontinue patient warming measures
• Place ice packs around patient
• Administer iced saline lavage by NG tube
• Irrigate surgical site with iced saline
Laboratory Studies

• Electrolytes
• Coagulation studies
• Complete blood count
• Creatine kinase
• Myoglobin
• Lactate
• Urinalysis
  – If heme positive, confirm probable myoglobinuria by absence of red blood cells on microscopic examination
• Urine myoglobin
Dantrolene

• Binds to ryanodine receptor
  – Depresses muscle excitation-contraction coupling
  – Decreasing intracellular calcium concentration

• May interact with Ca^{++} channel blockers (diltiazem/verapamil)
  – Cardiovascular collapse, arrhythmias, hyperkalemia

• Dissolve the 20 mg dantrolene in each vial with 60 mL warmed, sterile, preservative-free water

• One vial of dantrolene contains 3 g of mannitol
Dantrolene

• Initial dose 2.5 mg/kg IV push (up to 10 mg/kg)
• If no response to 20 mg/kg consider other diagnosis
• Once the initial signs have resolved
  – Start at 1 mg/kg
  – Titrate to clinical signs of hypermetabolism
  – Continue every 6 hrs x 36 hrs
  – Alternative: Infusion (0.1-0.3 mg/kg/hour)
MH Drugs to Stock in OR Suite

• Dantrolene (36 vials) + sterile nonbacteriostatic water
• Glucose + insulin + calcium
  – Treat hyperkalemia
• Bicarbonate
  – Treat metabolic acidosis
• Diuretic (Furosemide)
  – Maintain urinary output
• Antiarrhythmics
Treat MH Complications

• Metabolic acidosis
  – Bicarbonate

• Hyperkalemia
  – Hyperventilation
  – Glucose + insulin + Ca++

• Ventricular arrhythmias
  – Usually respond to treatment of acidosis & hyperkalemia
  – ACLS protocols except calcium channel blockers
  – Cardiopulmonary bypass as last resort

• Rhabdomyolysis
  – Furosemide + bicarbonate
Annual MH Mock Drill
Have a Transfer of Care Plan
Common MH Questions

Are MH susceptible patients candidates for outpatient surgery?
Yes, if non-triggering anesthetics are used
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Prophylaxis is not recommended for most MH-susceptible patients  
Use non-triggering anesthetics
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How should an anesthesia machine be prepared for an MHS patient?
Disable vaporizers
Flow 10L/min $O_2$ through circuit for at least 20 minutes.
Use a new breathing circuit.
Newer anesthesia machines may require up to 60 minutes of preparation
Common MH Questions

How long should MHS patients be monitored after uneventful anesthesia?

- May be discharged on the day of surgery
- Minimum 1 hour in PACU
- Additional hour in phase 2 PACU /step down unit
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When should a MH susceptible patient be discharged after masseter spasm?
- A patient with marked rigidity should not be discharged.
- Overnight observation for temperature rise, myoglobinuria, elevated CK levels or progression to MH
Welcome

Malignant Hyperthermia (MH):
Did you know...?

Start your visit with this short video overview of the disorder called "malignant hyperthermia" and the history of the MHAUS organization.

Whether you are a patient or a medical professional, MH resources are here for you. Contact us directly if you have any additional questions you need help with, or if you want to talk to the MHAUS administrative office staff about a specific need or concern.

We are here to help!
Evidence-Based Patient Safety Advisory: Malignant Hyperthermia

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Summary: As more and more routine plastic surgery procedures move from the hospital to outpatient surgery facilities, plastic surgeons must be aware of the risk factors for life-threatening events that might occur in this setting. This awareness includes recognition of the signs and symptoms and the management of a rare but life-threatening condition, malignant hyperthermia. This article reviews the current understanding of the concepts pertinent to malignant hyperthermia diagnosis and treatment in the outpatient setting and current standards and recommendations for physicians and support personnel regarding malignant hyperthermia preparedness in office-based surgery and anesthesia. (Plast. Reconstr. Surg. 124 (Suppl.): 68S, 2009.)

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