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

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plastic surgery THE MEETING
AMERICAN SOCIETY OF PLASTIC SURGEONS
THE PLASTIC SURGERY FOUNDATION
ASMS
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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 (*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

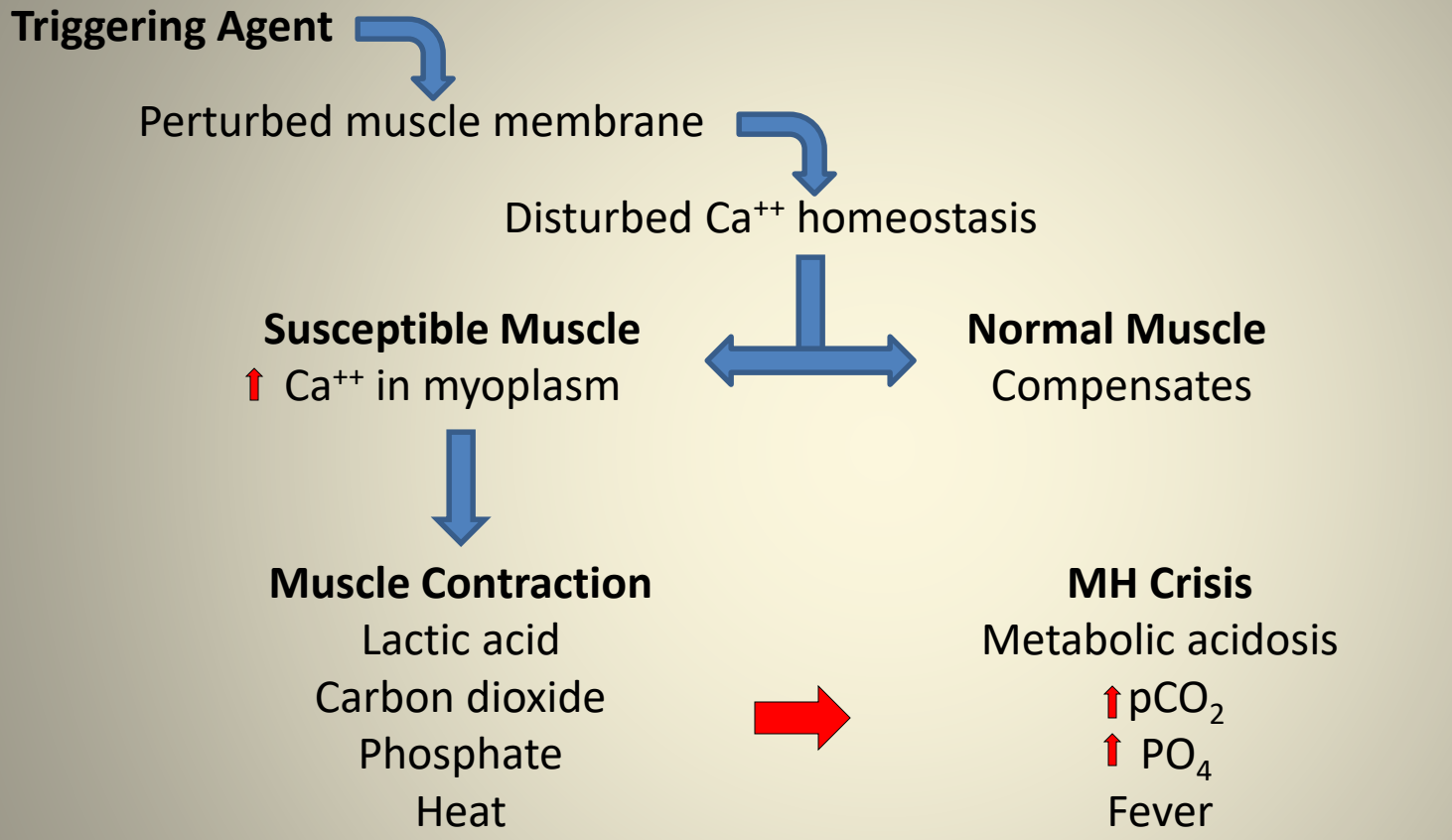
MH Susceptibility Testing

- 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



MH Presentation

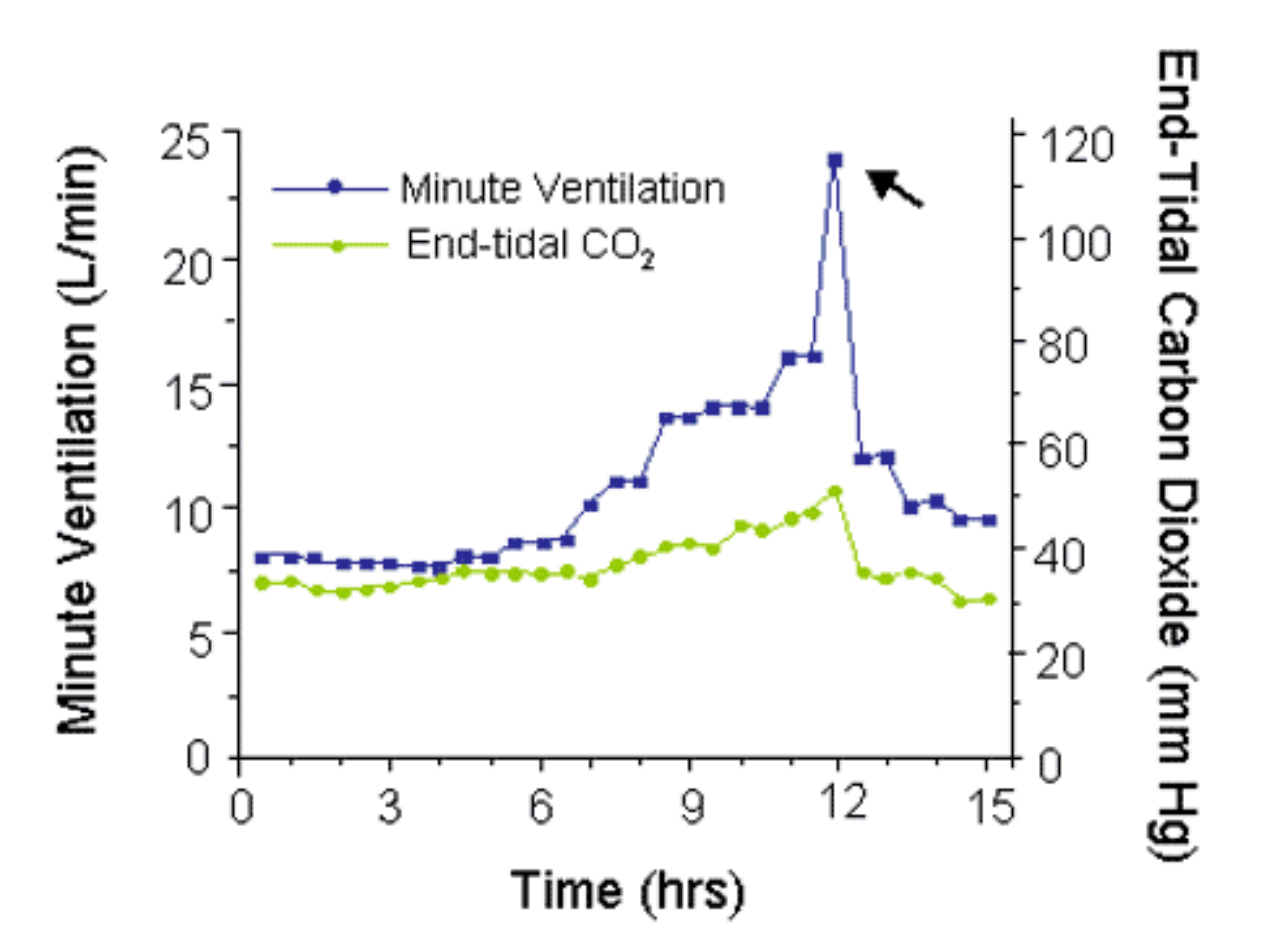
Clinical

- 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

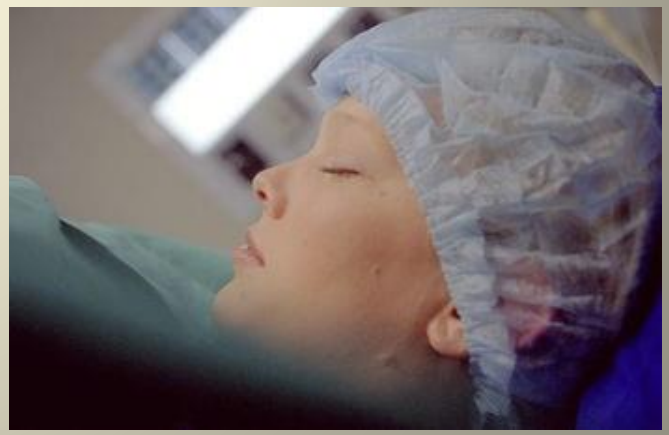
- Increased end-tidal CO_2 and increased $PaCO_2$
- Decreased pH (metabolic and respiratory acidosis)
- Decreased PaO_2
- Hyperkalemia (PVC, VT, VF)
- Increased CK
- Myoglobin in blood or urine
- Abnormal coagulation tests
- Increased plasma lactate level

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
- Hypoventialation

- Heat stroke
- Sepsis

- Hypoxic encephalopathy
- Intracranial hemorrhage
- Brain injury
- Meningitis

- Faulty equipment

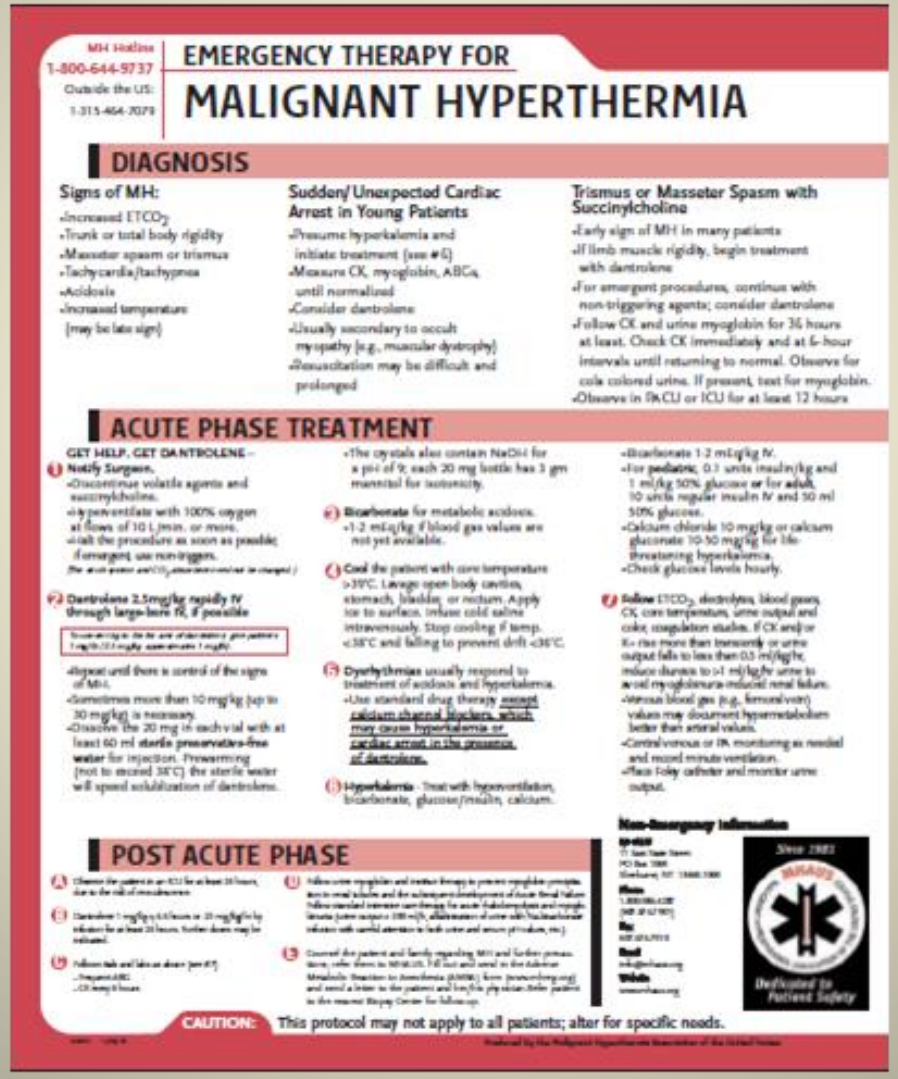
What to do if you Suspect MH

- 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 + opiod
- Hyperventilate with 100% O_2 at >10 L/min to remove excess CO_2
- Obtain core temperature

What to do if you Suspect MH

- Administer Dantrolene
- Repeat until the end-tidal CO_2 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 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.

2. **Dantrolene 2.5mg/kg rapidly IV through large-bore IV, if possible**
   - 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 solubilization 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 **except calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.**

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.

Non-Emergency Information

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 6 hours or 10 mg/kg/hr by infusion for at least 24 hours. Further doses may be indicated.

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

D. Follow urine myoglobin and institute 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, administration of urine with 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.mhaus.org) and send a letter to the patient and his/her physician further patient to the nearest Biopsy Center for follow-up.

Since 1981 MHAUS Dedicated to Patient Safety

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

Endorsed by the Malignant Hyperthermia Association of the United States

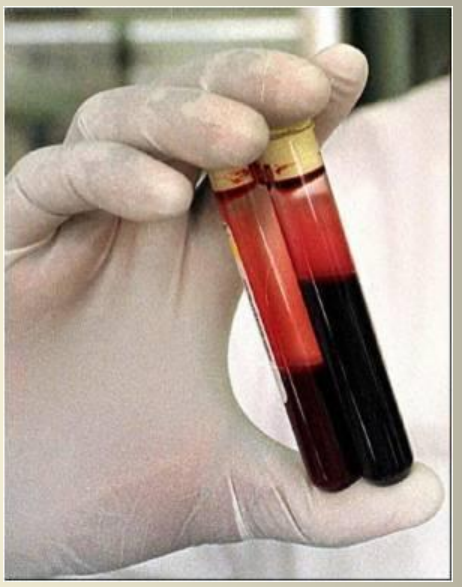
MH Cart

+ Ice Machine

Manage Hyperthermia

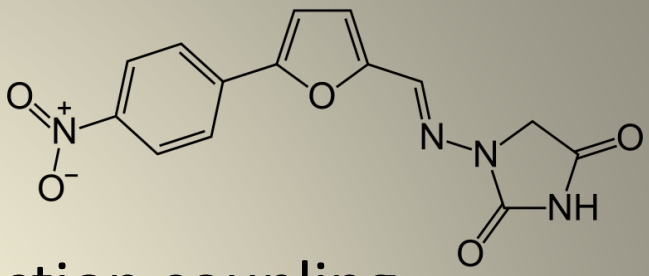
- **Cooling Measures to Lower Core < 38°C**
- Lower OR temperature
- Discontinue patient warming measures
- Place ice packs around patient
- Administer iced saline lavage by NG tube
- Irrigate surgical site with iced saline

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

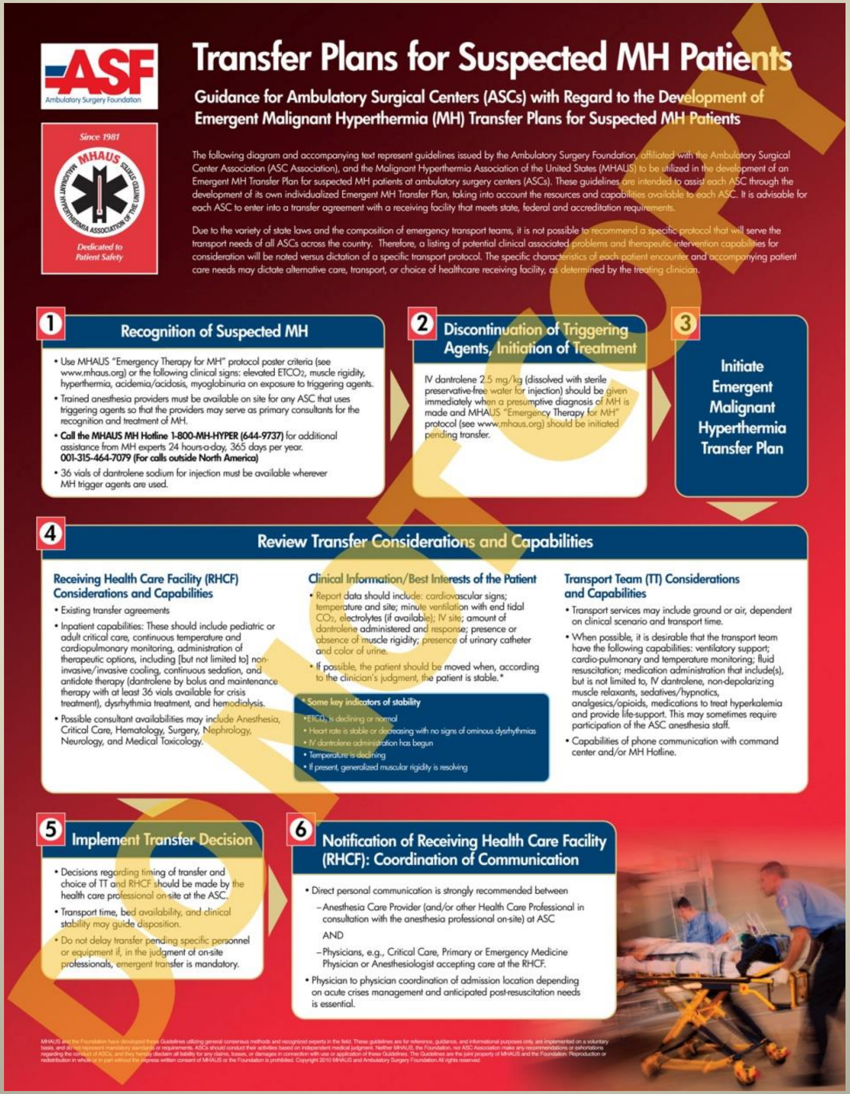
- Dantrolene (36 vials) + sterile nonbacteriostatic water
- Glucose + insulin + calcium
  - Treat hyperkalemia
- Bicarbonate
  - Treat metabolic acidosis
- Diuretic (Furosemide)
  - Maintain urinary output
- Antiarrhythmics

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

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How should an anesthesia machine be prepared for an MHS patient?

Disable vaporizers

Flow 10L/min 0_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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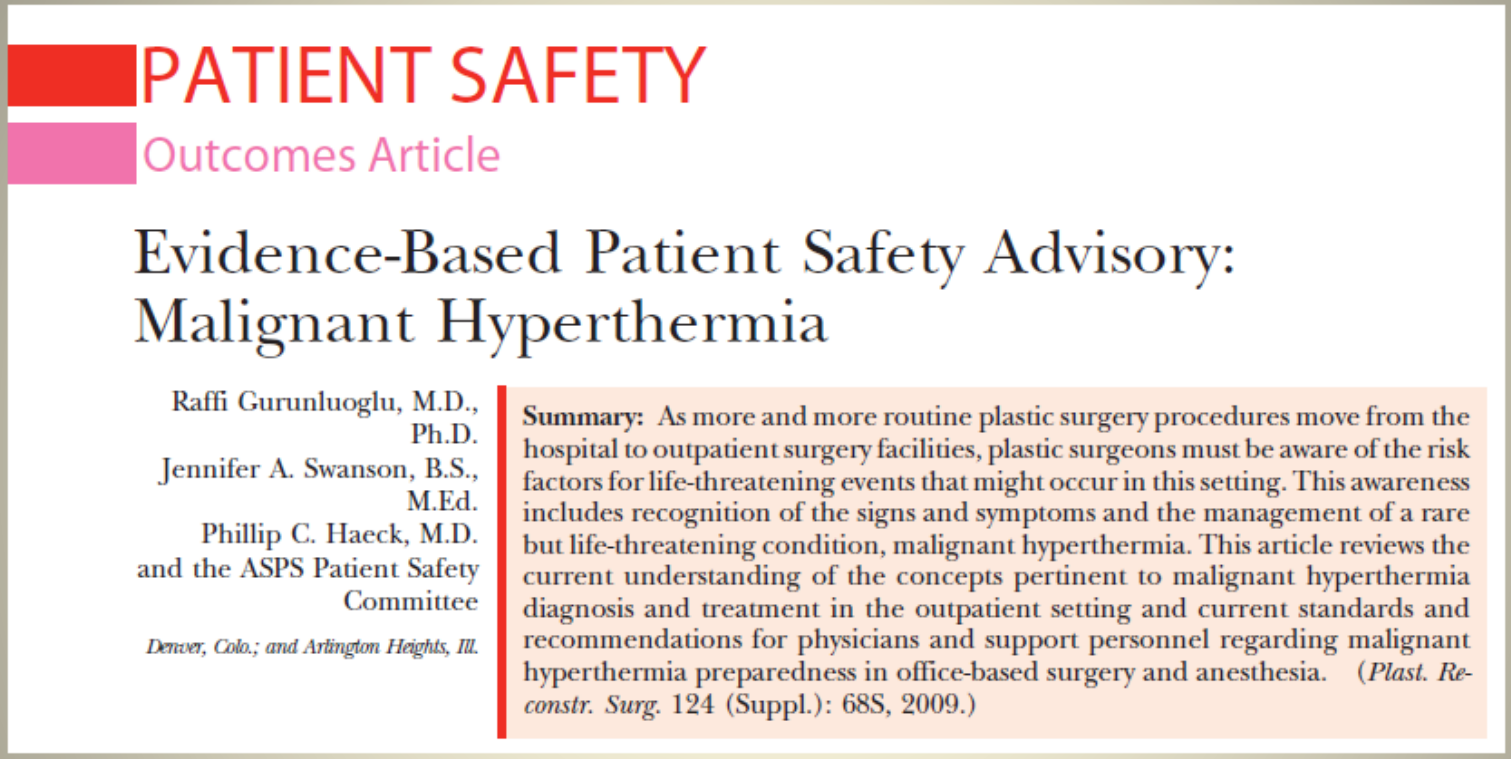
When should a MH susceptible patient be discharged after masseter spasm?

A patient with marked rigidity should **not** be discharged.

Overnight observation for temperature rise, myoglobinuria, elevated CK levels or progression to MH

Malignant Hyperthermia Association of the United States

More Information



PATIENT SAFETY

Outcomes Article

Evidence-Based Patient Safety Advisory: Malignant Hyperthermia

Raffi Gurunluoglu, M.D., Ph.D.
Jennifer A. Swanson, B.S., M.Ed.
Phillip C. Haeck, M.D.
and the ASPS Patient Safety Committee

Denver, Colo.; and Arlington Heights, Ill.

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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