MALIGNANT HYPERTHERMIA

DEFINITION/EPIDEMIOLOGY

Malignant hyperthermia (MH) is a progressive, severe hyperthermic reaction occurring during general anesthesia.

The tricky part to MH is the presentation and onset are variable. Patients may be exposed several times before the onset of MH or the first exposure to a triggering agent. The initial signs are often variable as well. The reasons for this are not entirely clear but it could be related to the surgery duration, inhalational anesthetic, and the concentration delivered during the surgery.

PATHOPHYSIOLOGY

The most common defects leading to MH susceptibility at the molecular level are mutations in RYR1, the gene encoding the skeletal muscle isoform of RyR (40–80% of cases). Approximately, 1% of cases result from mutations in CACNA1S, which is the gene encoding the principal subunit of the DHPR.

DIAGNOSIS

The gold standard for testing remains the vastus muscle contracture test.

Episodes of MH now occur less frequently for three reasons:

- Decreased use of triggers
- Delay in triggering of MH by volatile agents, due to the use of nondepolarizers, tranquilizers, sedatives, or opioids
- Protective effect of minor hypothermia

MH is now detected earlier because of better awareness and more sophisticated monitoring.

DIFFERENTIAL DIAGNOSIS

Neuroleptic malignant syndrome- characterized by hyperthermia, muscle rigidity with extrapyramidal signs (dyskinesia), altered consciousness, and autonomic lability in patients receiving antidopaminergic agents. The syndrome is caused by an imbalance of neurotransmitters in the central nervous system. A functional dopamine deficiency

Thyroid storm- hypokalemia is very uncommon; generally develops postoperative

Pheochromocytoma- associated with dramatic increases in heart rate and blood pressure but not end-tidal CO or temperature.

Serotonin syndrome- These drugs appear to markedly increase serotonin activity in the brain, causing hyperthermia, confusion, shivering, diaphoresis, hyperreflexia, and myoclonus. Combinations associated with this "serotonin syndrome" include monoamine oxidase inhibitors (MAOIs) and meperidine, and MAOIs and selective serotonin reuptake inhibitors (SSRIs).

Iatrogenic hyperthermia

Brain stem/hypothalamic injury- Brain stem or hypothalamic injury near the hypothalamus and brain stem can be associated with marked hyperthermia

Sepsis- hares several characteristics with MH, including fever, tachypnea, tachycardia, and metabolic acidosis. This can be a difficult differential diagnosis if there is no obvious primary site of infection.

Transfusion reaction

MH, however, is associated with more dramatic degrees of metabolic acidosis and venous desaturation than are any of these diseases.

TRIGGERING AGENTS

Neuromuscular blocking agents Succinylcholine

Volatile anesthetics Halothane, isoflurane, sevoflurane, enflurane, desflurane, ether, and methoxyflurane

INCREASED RISK

Diseases:

- **Duchenne's muscular dystrophy**
- **Central-core disease** is an inherited condition that involves muscle weakness and skeletal abnormalities
- **Osteogenesis imperfecta**
- **King-Denborough syndrome** is consistently associated with MH. This syndrome is seen primarily in young boys with short stature, cryptorchidism, mental retardation, kyphoscoliosis, pectus deformity, slanted eyes, low-set ears, webbed neck, and winged scapulae.

Surgeries:

- **Orthopedic cases- joint-dislocation repair**
- **Ophthalmic surgery- ptosis and strabismus correction**
- **Head and neck procedures- cleft palate repair, tonsillectomy and adenoidectomy, and dental surgery**

Others:

- **Family history** of anesthetic complications
- **Intolerance to caffeine-containing foods**
- **History of unexplained fevers or muscular cramps**. Prior uneventful anesthesia and absence of a positive family history are notoriously unreliable predictors of susceptibility to MH, however. The CRNA should exercise extreme caution in any patient in whom trismus develops during induction of anesthesia.

SYMPTOMS

The cardinal and most consistent clinical features of an MH reaction are a rise in $ETCO_2$ (tachypnea if the patient is breathing spontaneously). Then, symptoms may include unexplained tachycardia, hyperthermia, and muscle rigidity.

If MH is not addressed early, metabolic hyperactivity and muscle breakdown will lead to progressive hypercapnia, tachycardia, hyperthermia, muscle rigidity, rhabdomyolysis, hyperkalemia, acidosis, hypoxia, and DIC. Arrhythmias and possibly cardiac arrest are likely to result from hypercarbia, sympathetic stimulation, hyperkalemia, and acidosis.

TREATMENT

- Notifying the surgeon
- Discontinuing volatile agents or succinylcholine
- Giving 100% O_2
- Stopping anesthesia or continuing with non-triggers
- Dantrolene 2.5 mg/kg
- Hyperventilation for respiratory acidosis
- Bicarbonate for metabolic acidosis
- Cooling for high temperatures

Gastric lavage is the best treatment for decreasing body temperature. Therefore, esophageal monitoring of temperature provides an inaccurate reflection of body temperature. It is best to measure core temperature at several locations, e.g. bladder, rectal, nasal.

- Diuresis
- Treat hyperkalemia: insulin/dextrose; Calcium chloride; or hemodialysis
- Dantrolene should be continued for 24 h, 7 mg/kg every 6 h, as there is a 50% recurrence rate.

Dantrolene is a calcium channel blocker. It acts at the ryanodine receptor to decrease the calcium level in the skeletal muscle cell by decreasing the release of calcium from the sarcoplasmic reticulum. Skeletal muscle relaxation occurs when the supply of calcium to the contractile proteins is impaired.

- If necessary, consult on-call physicians at the 24-hour MHAUS hotline.
- **1-800-MH-HYPER.**

Each 20 mg vial of dantrolene needs to be dissolved by vigorous mixing with 60 mL of water for injection which is time-consuming. Adult patients will require multiple vials for the starting dose (e.g. 10 vials for a patient of 80 kg). At least one person should be assigned the responsibility of continuously preparing the drug.