MALIGNANT HYPERTHERMIA

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OBJECTIVES

- Describe four triggers of malignant hyperthermia (MH)
- Explain three signs and symptoms of MH
- Examine four treatment modalities of MH

DEFINITION

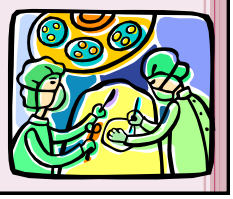
- Hypermetabolic disorder of skeletal muscles
  - First described in 1962
- Pharmacogentic disorder
  - Inherited disorder
  - Genetic autosomal dominance

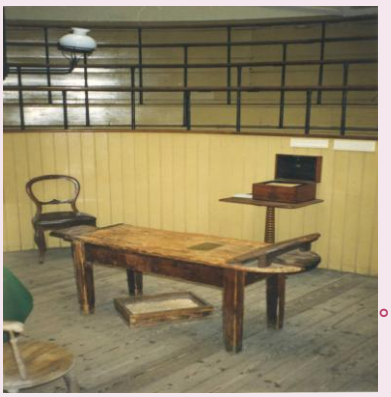
CAUSE

- Physiology
  - Defect in cell membrane that when combined with a trigger causes:
    - Release of calcium from sarcoplasmic reticulum resulting in hypermetabolic state
    - High oxygen consumption → ATP depletion → high production of lactic acid, CO_2, & heat→ leak of potassium from cell

TRIGGERS

- Depolarizing neuromuscular blockers
  - succinylcholine
- Inhalation anesthetics
  - Desflurane
  - Isoflorane
  - Sevoflorane
  - Halothane
  - Ether





- Operating Theater of St. Thomas Hospital, London England (Hess, 1998)

NON-TRIGGERING AGENTS

- Non-depolarizing neuromuscular blockers
  - atricurium
  - cisatracurium
  - curare
  - pancuronium
  - rocuronium
  - vecuronium

NON-TRIGGERING AGENTS

- Local anesthetics
  - Lidocaine
- Barbiturates
  - Thiopental
- Anesthetic agents
  - Propofol
  - Etomidate
  - Ketamine
- Inhalation agents
  - Nitrous oxide
- Benzodiazepines
  - Diazepam
  - Midazolam
  - Lorazepam
- Opioids
  - Fentanyl
  - Sufentanil
  - Morphine
  - Hydromorphone
  - Meperidine

MORE TRIGGERS

- Physical exertion
- Emotional stress
- Muscularity
- Heat stroke
- Trauma
- Statin treatment

OCCURRENCE

- Children 1:15,000
  - Rare in children less than 2 yrs. old
- Adults 1:50,000
- Males more than females
- Caucasian more than any other races
- Succs. & inhalation agents 1:4,200
- After prior unremarkable general anesthetics
- Onset can be seen
  - During induction
  - During procedure
  - Early postoperative period

MORTALITY

- Fatal if untreated
  - Cardiac dysrhythmias, acidosis, hyperkalemia, DIC, MSOF, cardiac arrest
- 70% in 1960's
- Less than 10%
  - 7% in hospital*
  - 21% in outpatient settings*
    - Mortality increases with treatment delay & rise of temperature*

* Rosenberg, 2011

Signs and Symptoms

- Temperature
  - Increase by 0.6 degree C (or 1 degree F) per one to two minutes
  - Late symptom

Signs and Symptoms

- Muscle rigidity
- Increase CO2
- Hypoxemia
- Increased respiratory rate
- Increase heart rate
- Cardiac arrhythmia
- Acidosis
- Hyperkalemia

Signs and Symptoms

- Labile blood pressure
- Flushed or rosy skin
- Mottling or cyanosis
- Coagulopathy
- “Dark” blood
- “Cola colored” urine
- Myoglobinuria
- Increased CPK

Watch for Misdiagnosis

- “Light” anesthesia
- Thyroid storm
- Pheochromocytoma
- Sepsis
- Neuroleptic malignant syndrome
  - Hypermetabolic reaction to antipsychotic agents from blockade of the dopamine receptor
- Cocaine toxicity

Diagnostic Tests

- History
- Masseter muscle rigidity
- Caffeine-halothane contracture test
  - First case of day
  - Combine skeletal muscle with caffeine and halothane
  - Assess rate of muscle contraction
  - Limited number of centers in North America perform test
  - $6,000

Diagnostic tests

- Molecular genetic testing
  - Mutation on chromsome 19 in the ryanodine receptor (RYR1)
  - 29 RYR1 mutations that cause MH
  - Have “predisposition” for MH
    - Detects about 30% of those at risk
  - Performed after CHCT
  - $800

Treatment

- Teamwork
- Plan
  - All members should act immediately
  - MH cart
  - Get additional personnel

Initial treatment

- Surgery should be postponed and/or anesthesia changed to a non-triggering method
  - Transport to hospital if in outpatient setting
- Hyperventilate with 100% O2
- Give Dantrolene sodium

TREATMENT...DANTROLENE

- Skeletal muscle relaxant
  - Exact mechanism of action is unknown
  - Also has 3 gms mannitol per vial
- Inhibits release of calcium from cell by binding to ryanodine receptor
- Dose
  - 2.5 mg/kg
  - Repeat dose every 5 minutes until symptoms subside
  - Max dose is 10 mg/kg
  - Continue maintenance dose with I mg/kg every four- six hours for 24 – 48 hours after the event
- May be given through peripheral or central line

PREPARTION

- Dantrolene sodium
  - Comes in 20 mg vials
  - Prepare with 60 ml of preservative free water
  - May need to shake vial and warm vials in basin of water
  - 36 vials will be needed for a 70 kg patient for 10mg/kg dosing

SIDE EFFECTS OF DANTROLENE

- Muscle weakness
- Drowsiness
- Fatigue
- Dizziness
- Blurred vision
- Heptotoxicity
- Gastrointestinal
- Nausea
- Diarrhea

MEDICATIONS

- Lasix
- Methylprednisolone
- Sodium bicarb
- Procainamide or lidocaine
  - No calcium channel blockers
    - May cause hyperkalemia
- Oxygen
- Hyperkalemia cocktails
- No lactated ringers
- Narcotics for muscle pain

TREATMENT

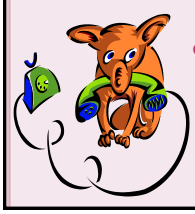
- Cooling measures
  - NG & rectal lavage
  - Cooled IV fluid
  - Cooling blanket
  - Ice packs
  - Bypass

TREATMENT

- Monitoring devices
  - Foley output 2ml/kg/hr
    - Monitor for myoglobinuria
  - EKG
  - Core temperature
  - Capnographic
  - Labs

POST-EVENT EVALUATION

- Emotional support to patient and family
- Report to North American Malignant Hyperthermia Registry and/or MHAUS hotline
- Evaluation of team's performance
  - Prepared
  - Conduct more drills
  - Were policies followed



Patient Teaching

- Educate patient
  - Future surgeries should be performed without triggering agents
  - Medical alert bracelet
  - Testing
- Choose medical care location carefully
- MH association of US
  - MHAUS founded 1981
  - 1-800-MH-HYPER
  - www.mhaus.org

Prevention…Inquire about medical history

- "Has anyone ever told you that you had a bad reaction to anesthesia?"
- "Has anyone in your family ever experienced a bad reaction to anesthesia?"
- "Have you or a family member every experienced a high fever while undergoing anesthesia?"
- "Has anyone in your family died unexpectantly in the OR?"
- "Have you or anyone in your family ever experienced sunstroke or heatstroke which required hospitalization?"
- History of Central Core Disease, Duchenne's or Becker's muscular dystrophy

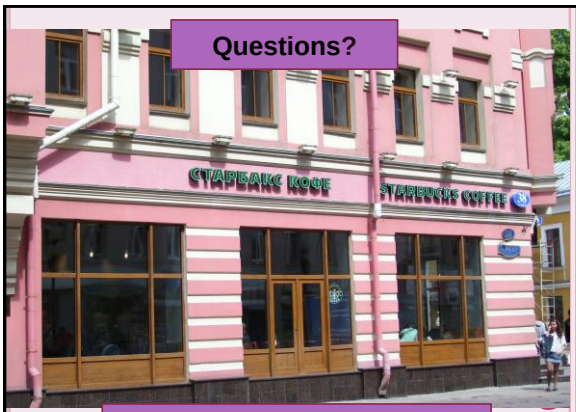
Case Study:

- 88kg female
- Robotic surgery for uterine fibroid
- Induction: Propofol, Rocuronium, desflurane
- Immediate rise in ventilation requirement & ETCO2
- Temp 37-38.1 C
- Desflurane discontinued and labs drawn
- ABG: pH 7.29, PaO2 513, PaCo2 48
- K: 4.9
- High minute ventilation continued with result in lowering ETCO2 to 29 and temp to 37.1 C
- Surgery aborted
- CPK peak 12,000 without myoglobinuria

April 2010 Case of the month from http://medical.mhaus.org/

Key

- Early identification
- Discontinue triggering agents
- Rapid administration of Dantrolene
- Control of acidosis and hyperkalemia
- Appropriate cooling measures



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WEBSITES

- Malignant Hyperthermia Association of America http://www.mhaus.org
- North American Malignant Hyperthermia Registry
- The Society for Ambulatory Anesthesia http://www.sambahq