It's getting hot in these genes: Malignant Hyperthermia in the Pediatric Patient

By: Ashley Evick, BSN,SRNA

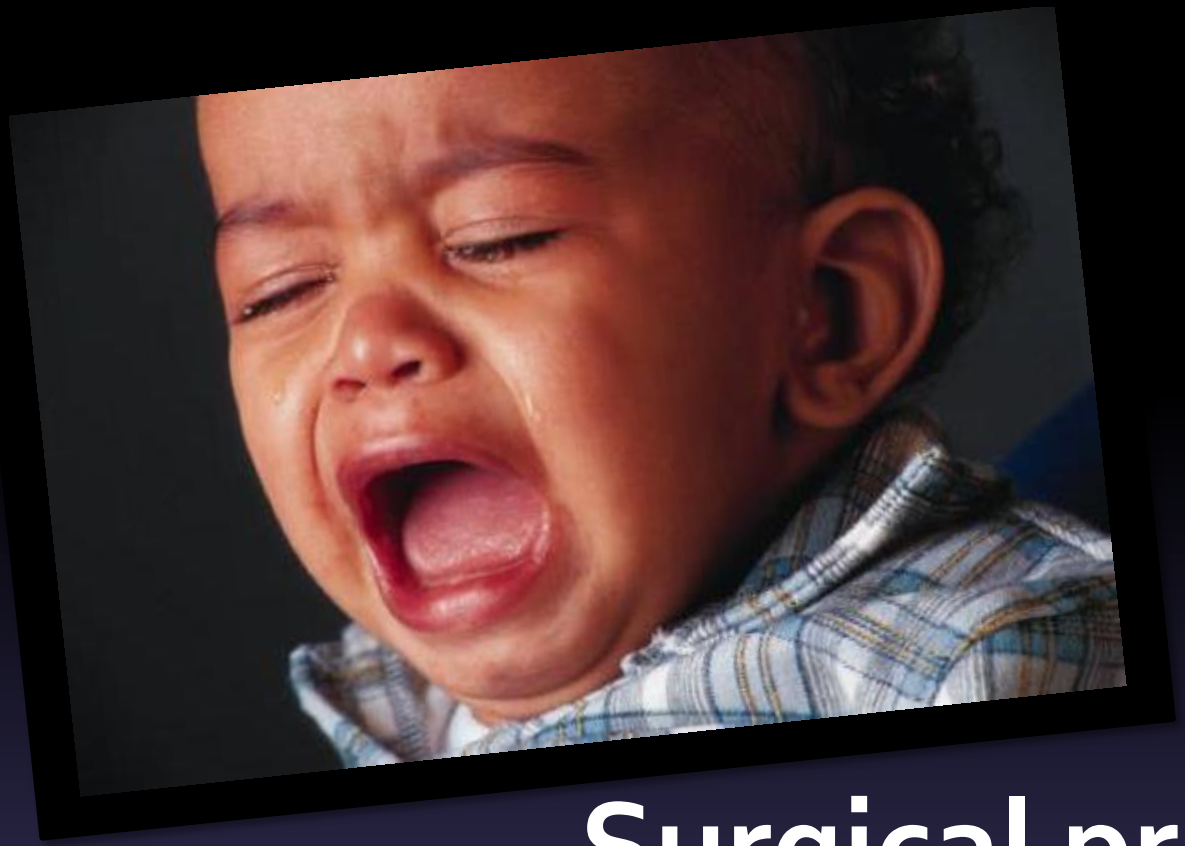
Objectives

- Be able to quickly assess/identify a malignant hyperthermia emergency in the operating room
- Be able to identify symptomology in the pediatric patient and how it can differ from the adult presentation
- Understanding of the treatment process for this emergency, and how it can impact outcomes for the pediatric patient

Case Discussion

History

- 4 month old male
- Wt. 6.48 kg
- NKDA
- No past surgical HX
- No medications
- HX of trigonocephaly and premature birth
- No family HX of surgery

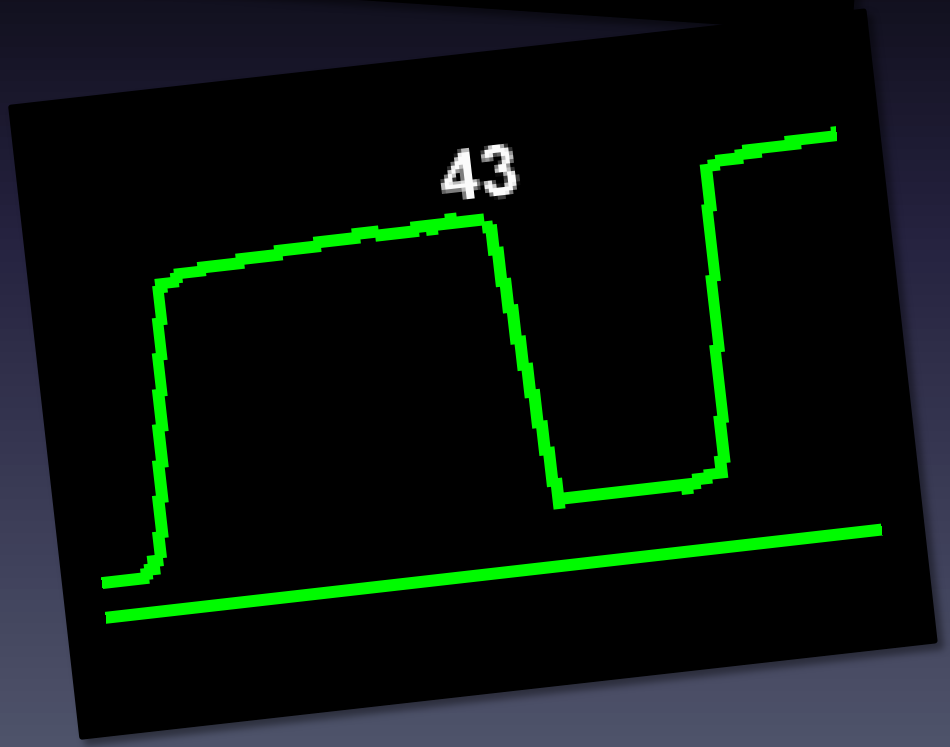


Surgical procedure

- Craniosynostosis
- GA with ETT
- Anticipation of large blood loss

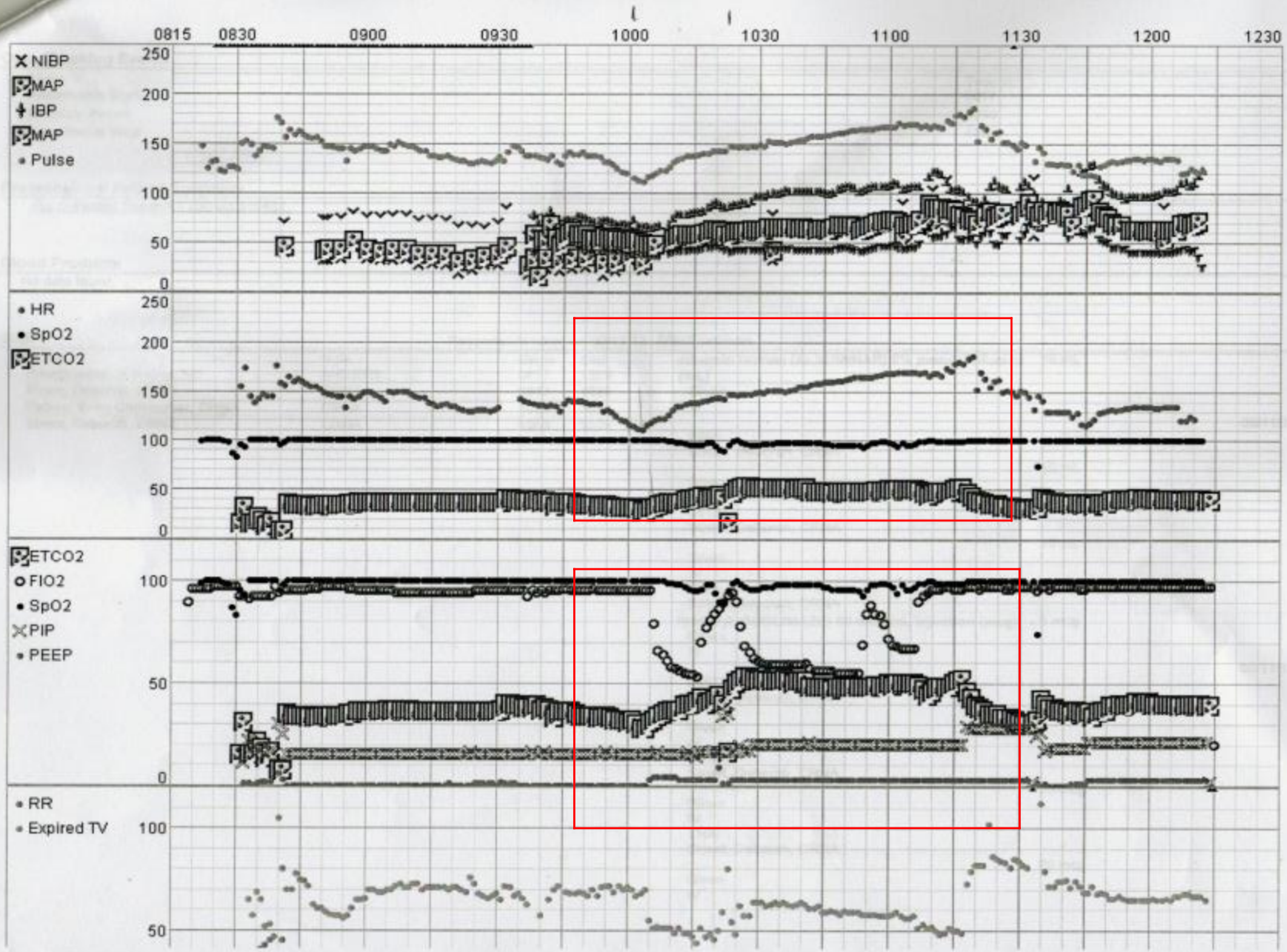
Anesthetic plan

- No premedication (child calm)
- Inhalation induction with N2O and sevo
- Intubation with ETT
- Rectal temp placed
- 22g, 24g, and 20g IV placed
- A-line placed (took quite a long time)
- Infant on under body blanket, heated circuit used, and room temperature increased
- Remi and precedex gtts used
- 0.9% NS and LR infusing
- Maintained on Sevoflurane
- Upper body blanket placed on infant, in addition to under body blanket



Case progression

- 90 minutes into case
- HR increased to 150s
- BP slight increase
- O2 saturation decreased to 97%
- EtCO2 gradually increasing to a peak of 53 (unresponsive to changes in ventilation)
- Temp. increasing 0.1 degree Celsius at a time (child hypothermic to begin 33 degrees Celsius)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ETCO2
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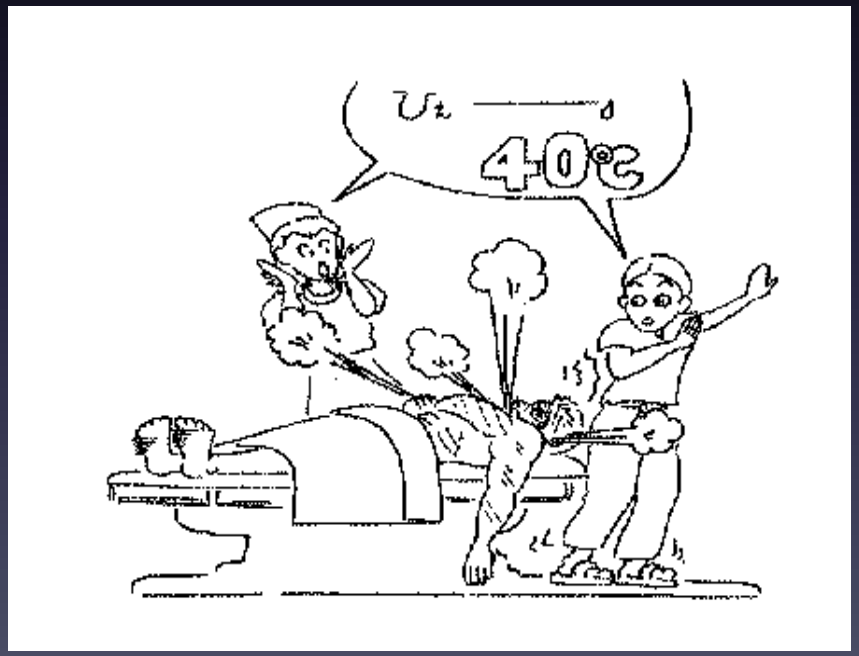
SpO2
PIP
PEEP
RR
Expired TV

Differential Diagnosis

- Gave fentanyl and remi boluses to assure child was not too light
- No change in $EtCO_2$ with ventilation changes
- ETT in good position and not obstructed

- MALIGNANT HYPERTHERMIA!!!!



Labs

time	1013	1112	1129	1200	1448
ph	7.29	7.17	7.29	7.21	7.39
CO_2	48	60	39	51	38
O_2	97	71	250	393	419
K	3.6	5.1	5.1	3.7	4.0
temp	33.5	38.1	37.2	35.0	
Bicarb	22.3	19.4	19.3	19.3	23.6
FiO_2	60	100	100	100	100
Ca	1.26	1.24	1.55	1.40	1.45

time	1130	1357	1911	0116	0500	0841	2350	0438
CK	155	192	197	245	199	202	213	83

Myoglobin in urine: negative

Treatment

- Call for help!!!!
- Sevo stopped, flows increased
- CO_2 absorber and circuit changed
- Ice applied to infant, warming blankets turned off, and room temp decreased
- Dantrolene 2.5 mg/kg initial dose
- Insulin R
- Dextrose
- Gtts changed to plasma-lyte
- Remi and precedex gtts ran as anesthetic agents
- Calcium chloride given
- MHAUS called and assisted in treatment plan
- Emergency algorithm guide used
- Versed given
- Subsequent doses of Dantrolene given at 1.5 mg/kg then 1 mg/kg
- Child transferred to PICU and remained on ventilator

Effective Sept. 2011

Emergency Therapy for MALIGNANT HYPERTHERMIA

MH Hotline: 1-800-644-9737 • Outside of the US: 001-303-389-1647

DIAGNOSIS

Signs of MH:

- Increasing $ETCO_2$
- Trunk or total body rigidity
- Masseter spasm or trismus
- Tachycardia/tachypnea
- Mixed Respiratory and Metabolic Acidosis
- Increased temperature (may be late sign)
- Myoglobinuria

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, evaluate and monitor the patient, and consider dantrolene treatment
- Follow CK and urine myoglobin for 36 hours.
- Check CK immediately and at 6 hour intervals until returning to normal. Observe for dark or cola colored urine. If present, liberalize fluid intake and test for myoglobin
- Observe in PACU or ICU for at least 24 hours

ACUTE PHASE TREATMENT

1. GET HELP.
GET DANTROLENE.
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, continue with non-triggering anesthetic technique.
- Don't waste time changing the circle system and CO_2 absorbant.

2. Dantrolene 2.5 mg/kg rapidly IV through large-bore IV, if possible

To convert kg to lbs for amount of dantrolene, give patients 1 mg/lb (2.5 mg/kg approximates 1 mg/lb).

- Dissolve the 20 mg in each vial with at least 60 ml sterile, preservative-free water for injection.
- Repeat until signs of MH are reversed.
- Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.

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. Apply ice to surface.
- Infuse cold saline intravenously. Other cooling techniques may be applied at clinician's discretion.
- 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.**

Continued on other side...

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

Effective Sept. 2011

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ACUTE PHASE TREATMENT Continued

6. Hyperkalemia
Treat with hyperventilation, bicarbonate, glucose/insulin, calcium.

- Bicarbonate 1-2 mEq/kg IV.
- For **pediatric**, 0.1 units insulin/kg and 2 ml/kg 25% Dextrose or for **adults**, 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, serum myoglobin, 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 and give bicarbonate to alkalanize urine to prevent myoglobinuria-induced renal failure.
(See D below)

- 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.

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 4-6 hours or 0.25 mg/kg/hr by infusion for at least 24 hours and sometimes longer as clinically indicated. Further doses may be indicated.

C. Follow vitals and labs as above (see #7)

- Frequent ABG as per clinical signs
- CK every 8-12 hours; less often as the values trend downward

D. Follow urine myoglobin and institute therapy to prevent myoglobin precipitation in renal tubules and the subsequent development of Acute Renal Failure. CK levels above 10,000 IU/L is a presumptive sign of rhabdomyolysis and myoglobinuria. Follow standard intensive care therapy for acute rhabdomyolysis and myoglobinuria (urine output >2 ml/kg/hr by hydration and diuretics along with alkalinization of urine with Na-bicarbonate infusion with careful attention to both urine and serum pH values).

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.mhreg.org) and send a letter to the patient and her/his physician. Refer patient to the nearest Biopsy Center for follow-up.

NON-EMERGENCY INFORMATION:

MHAUS
1 North Main Street
PO Box 1069
Sherburne, NY 13460-1069

Phone: 1-800-986-4287
(607) 674-7901
Fax: (607) 674-7910
Email: info@mhaus.org
Website: www.mhaus.org

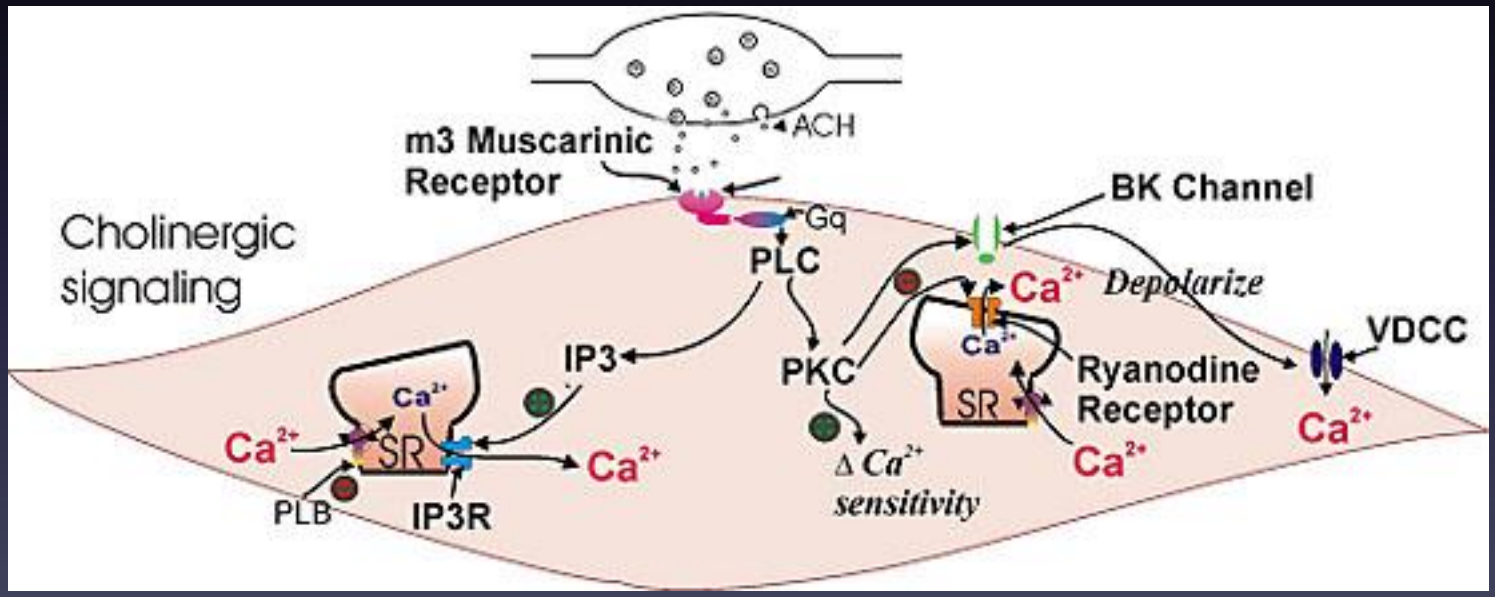
CAUTION! This protocol may not apply to all patients; alter for specific needs.

Benefits of an Algorithm

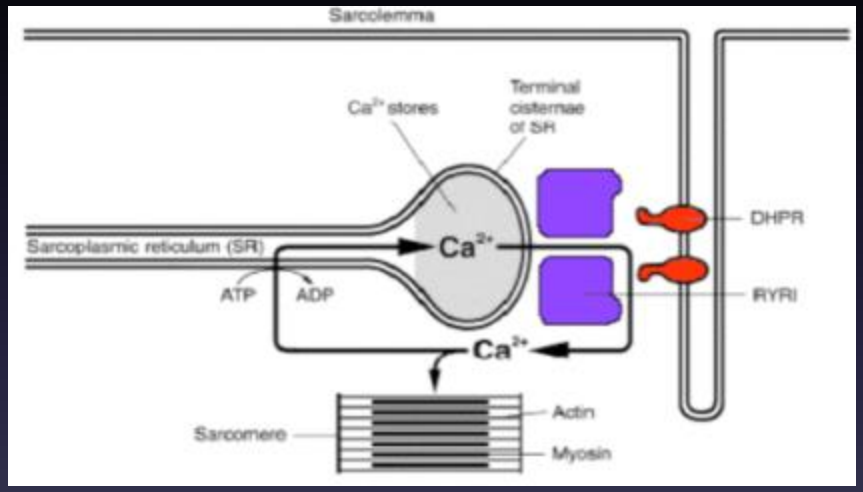
- An algorithm was used during this case
- Kept everyone on track
- Made sure every task was completed
- User friendly manual in every OR


Anatomy &
Physiology

The Normal Muscle Contraction and Relaxation Cycle



Skeletal Muscle Contraction



- **Sliding filament theory**
- **Multiple steps**

1. CNS produces an action potential transmitted down axon of alpha motor neuron

2. Activated voltage gated Ca channels in the NMJ

3. Ca influx causes vesicles to fuse with membrane and release AcH

4. AcH diffuses across synapse and binds/activates nicotinic AcH receptors opening Na/K channels

5. Na rushes in and K trickles out this triggers an action potential

6. Action potential spreads through the muscle depolarizing

7. Voltage gated Ca channels are activated in T-tubule membrane this also activates ryanodine receptors to release Ca from the sarcoplasmic reticulum

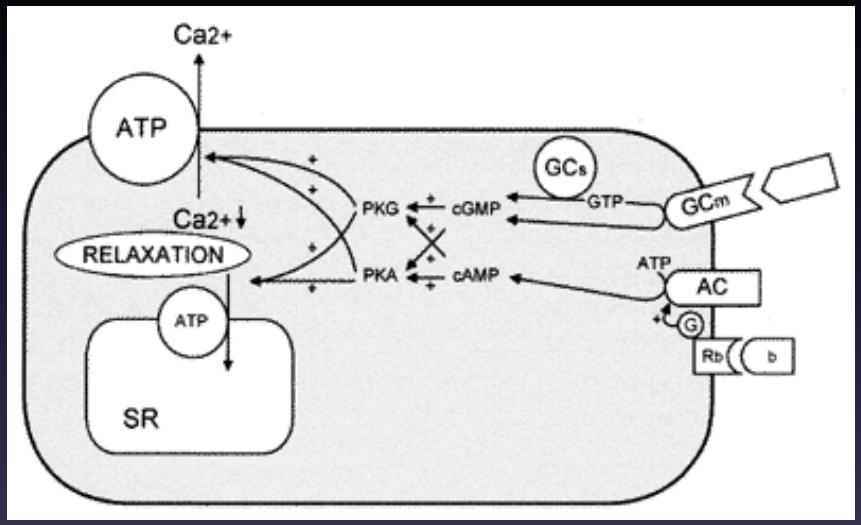
8. Ca binds to troponin C on actin thin filaments on myofibrils modulating tropomyosin

9. Troponin allows tropomysin to move unblocking sites

10. ATP binds to myosin releasing actin allowing movement of the crossbridge

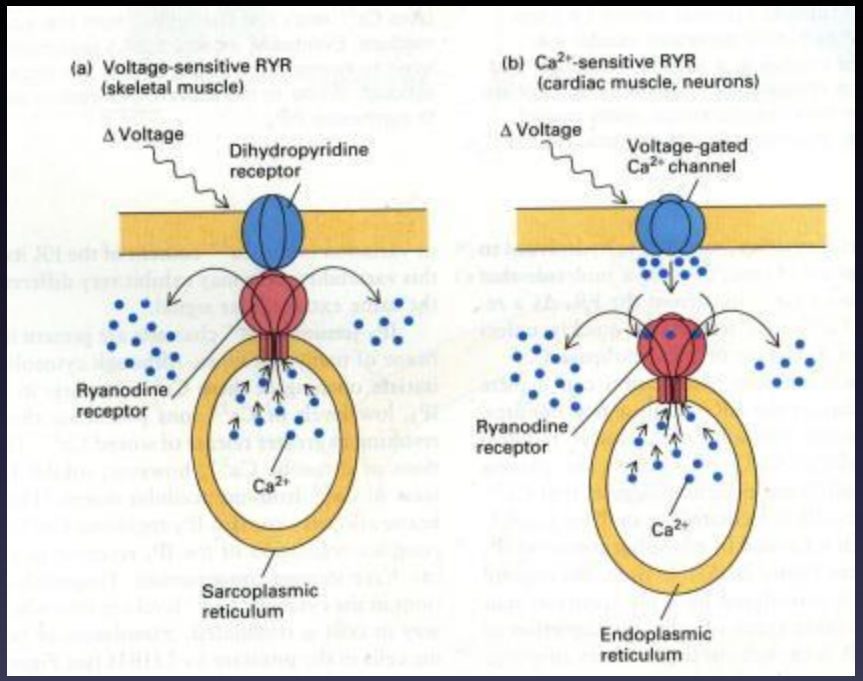
Skeletal Muscle Relaxation

- While the previous steps are occurring calcium is actively pumped back into sarcoplasmic reticulum
- The tropomyosin changes confirmation and blocks binding sites
- The contraction ceases



What is Malignant Hyperthermia??

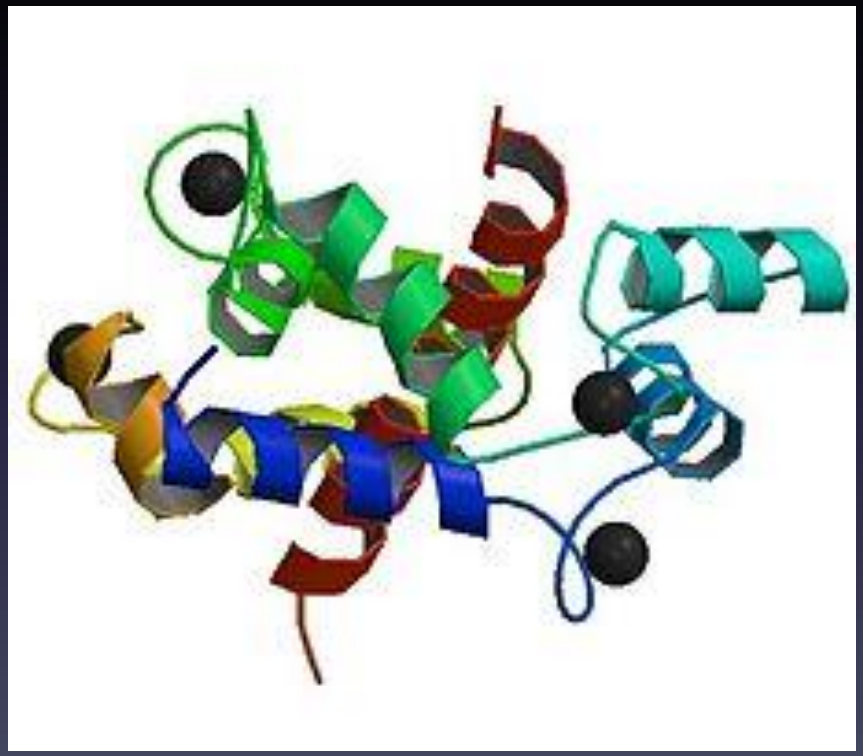
- Potentially life-threatening complication of anesthesia
- Autosomal dominant genetic disorder of ryanodine receptor gene (RYR1)



Some Statistics

- 1:2,000 occurrence
- May even be 1:500
- With dantrolene, mortality has decreased from 70%-80% to 6.5%-16.9%
- 1:5,000 to 1:10,000 with children

What is the role of the RYR1 receptor??

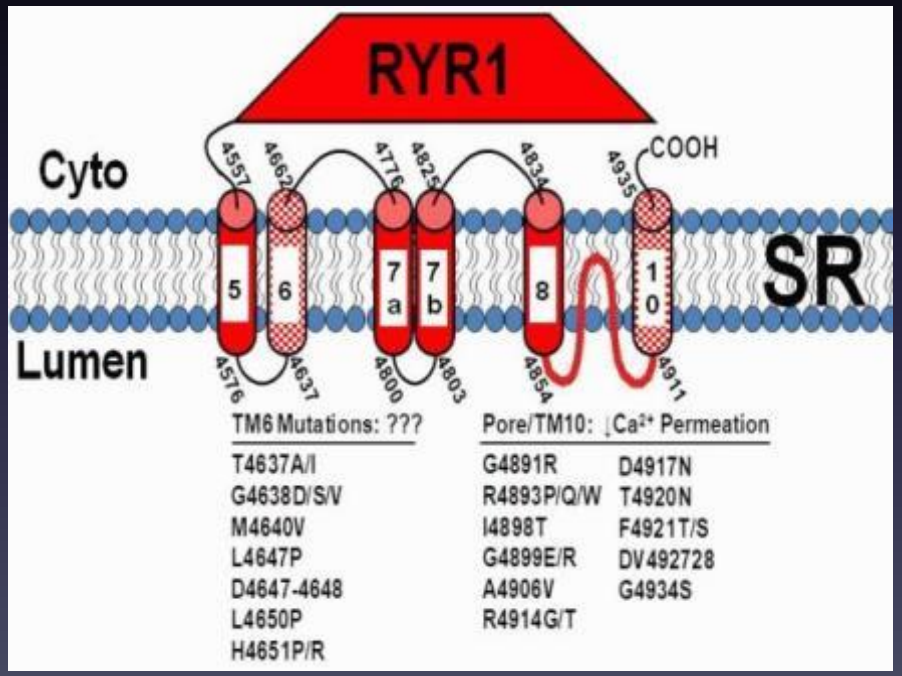


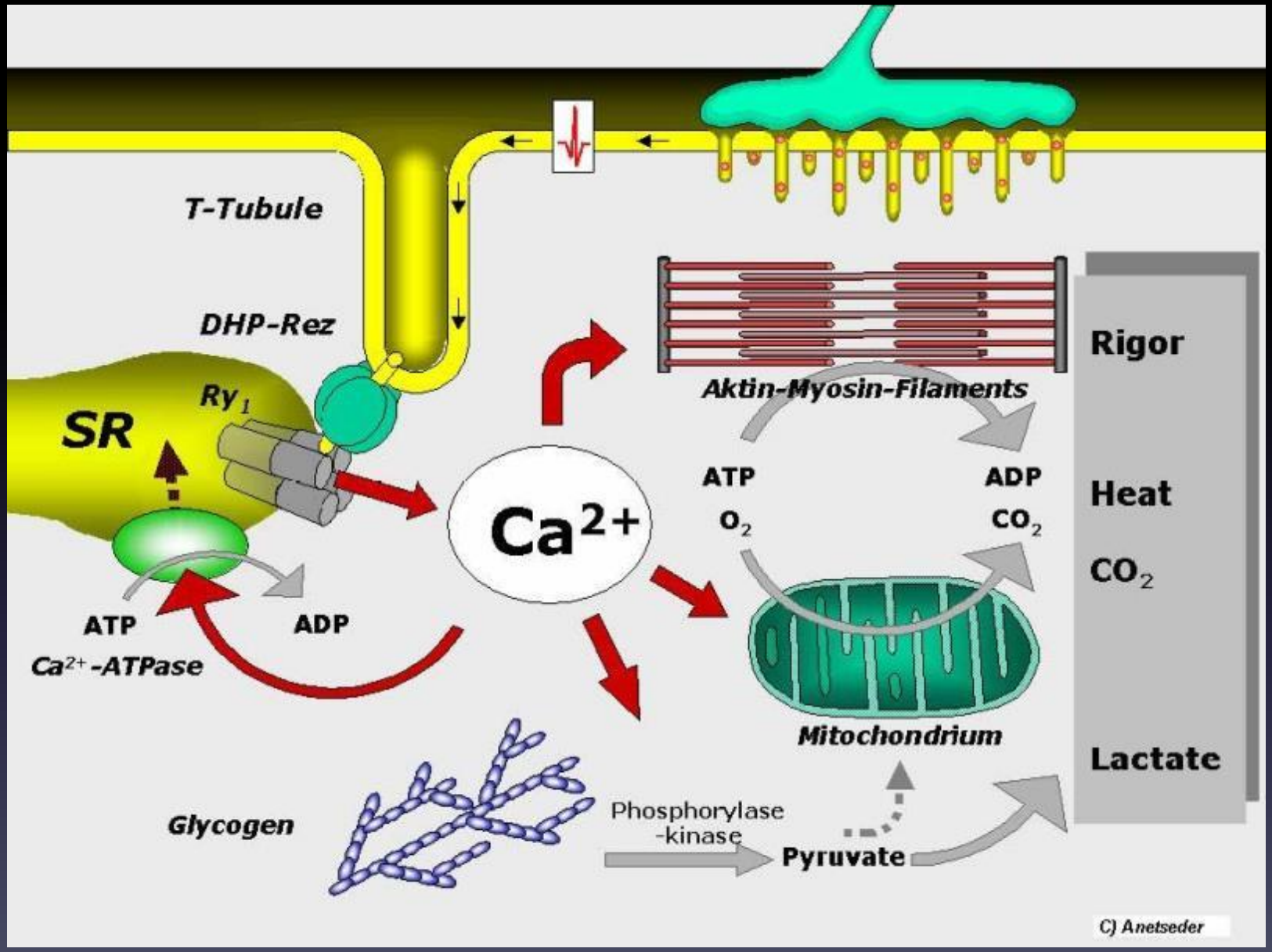
- Known as the skeletal muscle calcium release channel
- Protein in the membrane of the sarcoplasmic reticulum
- Various mutations have been noted

What is happening???

- Causes uncontrolled increase in skeletal muscle oxidative metabolism, overwhelming oxygen supply and removal of carbon dioxide, this reaction releases heat and causes acidosis and circulatory collapse

- See next slide for illustration

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DHP-Rez
SR
Ry 1
Ca2+
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ADP
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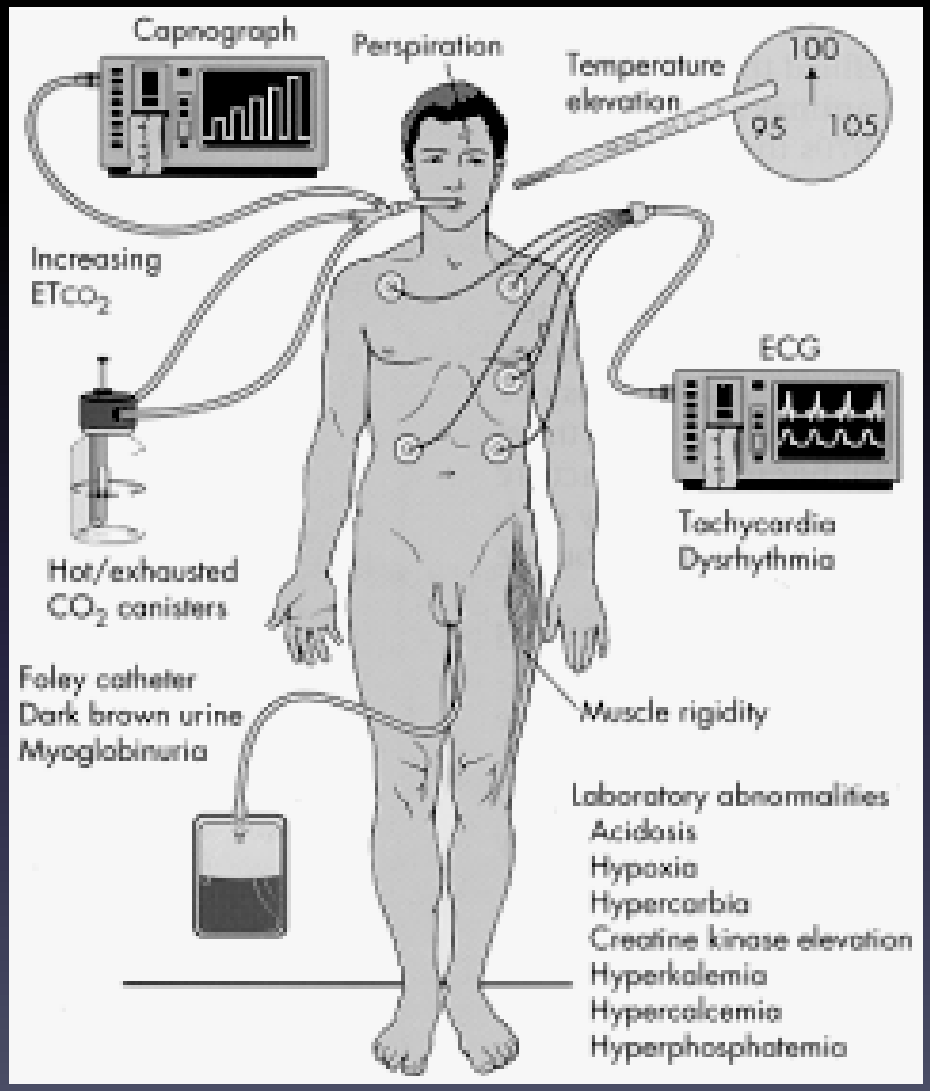
ADP
CO2
Mitochondrium
Rigor
Heat
CO2
Lactate
Glycogen
Phosphorylase
-kinase
Pyruvate
C) Anetseder

Signs of Malignant Hyperthermia

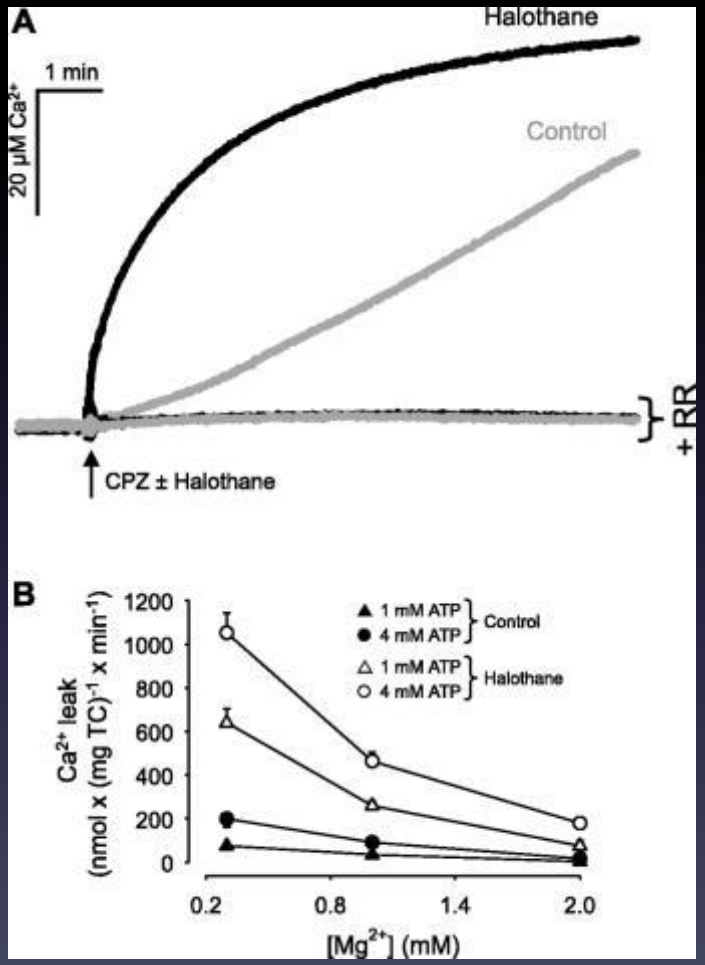


- elevated temperature
- increases HR
- increased RR
- acidosis
- hypoxia
- rigid muscles
- rhabdomyolysis
- myoglobin in urine
- CK elevation

What are the triggers??

Testing for MH

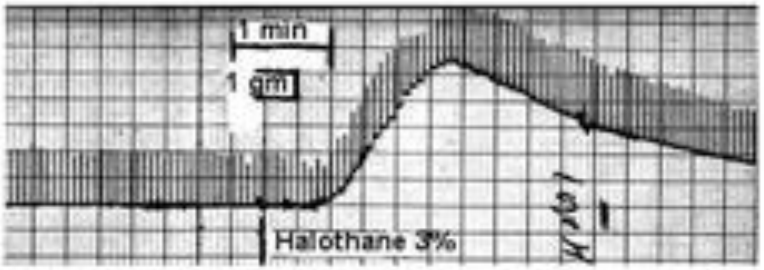
- Caffeine halothane contracture test
- In vitro contracture test
- 2 g muscle for biopsy from quadriceps test within 5 hours of testing
- Tested 3 times for each test agent
- 4 centers in US: *Bethesda, MD; Davis, CA; Minneapolis, MN ; Winston-Salem, NC*



Testing Continued

HALOTHANE TEST

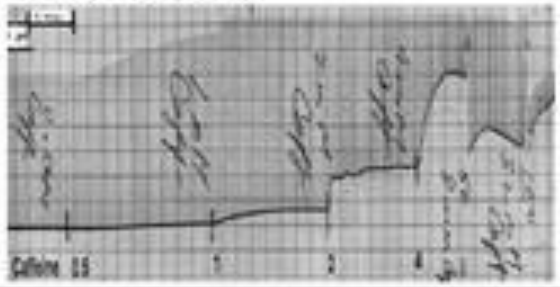
- Halothane (3%) is administered.
- Normal muscle will not change its baseline by more than 0.5 grams (half a box).



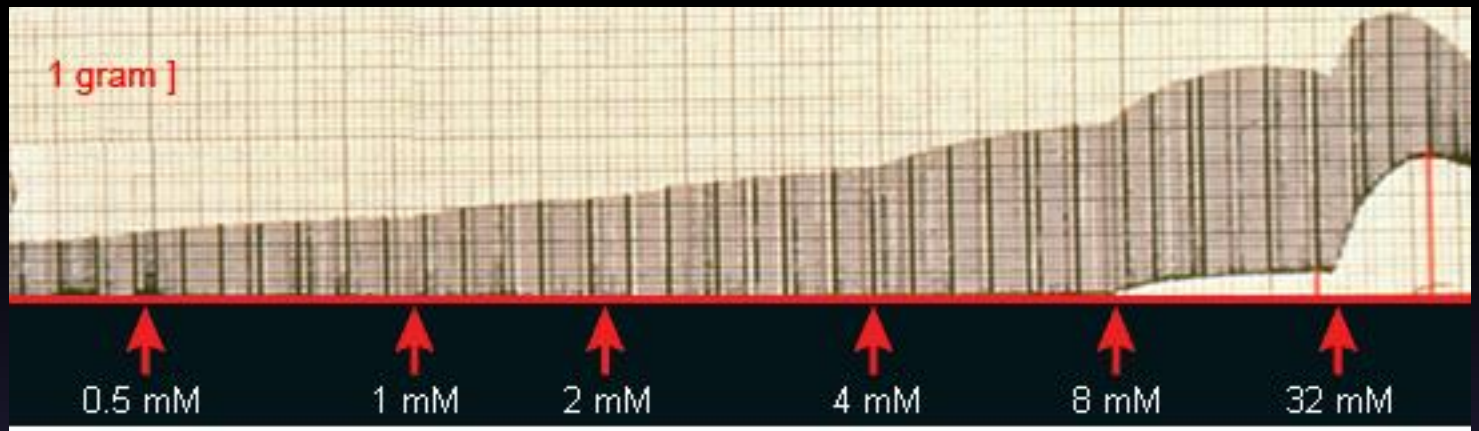
Abnormal halothane test

CAFFEINE TEST

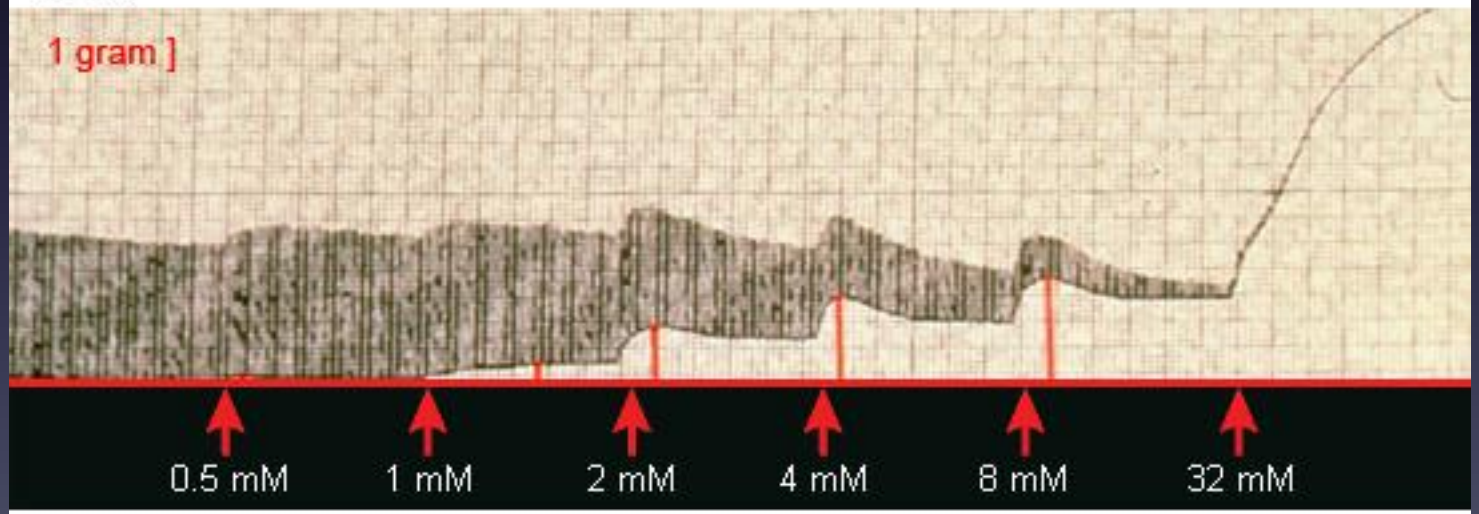
- Abnormal muscle is indicated by any response >0.2 gram evoked by 2 mM caffeine.
- In the graph below, 1 mM caffeine evokes an increase of 0.6 gram, and at 2 mM a further 1.8 gram.



Testing continued



Normal



Positive

Genetic testing

- Centers within the United States :
- *Pittsburgh, PA*
- *Marshfield, WI*

Can the presentation be different in pediatric patients???

Differences in pediatrics

- A study analyzed 264 records: 35 in the youngest age group (0-24 months), 163 in the middle age group (25 months- 12 years), and 66 in the oldest group (13-18 years).
- Sinus tachycardia, hypercarbia, and rapid temperature increase were more common in the oldest age cohort. Higher maximum temperatures and higher peak potassium values were seen in the oldest age cohort.
- Masseter spasm was more common in the middle age cohort.
- The youngest age cohort was more likely to develop skin mottling and was approximately half as likely to develop muscle rigidity. The youngest age group also demonstrated significantly higher peak lactic acid levels and lower peak CK values. The youngest subjects had greater levels of metabolic acidosis.

(Nelson, 2013)

Labs

time	1013	1112	1129	1200	1448
ph	7.29	7.17	7.29	7.21	7.39
CO_2	48	60	39	51	38
O_2	97	71	250	393	419
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Ca	1.26	1.24	1.55	1.40	1.45

time	1130	1357	1911	0116	0500	0841	2350	0438
CK	155	192	197	245	199	202	213	83

Myoglobin in urine: negative

A Published Case Report

The Case:

- 7-year-old boy with cholesteatomas underwent tympanoplasty.
- Three previous anesthetics with sevoflurane induction and maintenance with propofol infusion were not associated with MH symptoms.
- No family history of MH or muscle disease
- A minor rise of end tidal CO_2
- Increased rectal temperature
- Rhabdomyolysis and his father's positive IVCT results

Discussion:

- MH-susceptible patient responds differently to various agents
- Atypical MH forms are problematic
- It is possible that the speed of onset reflects the rate of increase of the intracellular Ca^{2+} concentration, which depends on the particular drug used, its concentration in muscles and any number of physiological variables that dictate the efficacy of Ca^{2+} homeostatic processes in each patient.

(BONCIU, 2007)

Another Case Report

- Two cases of MH triggered by sevoflurane:
- First Case: 6 year old girl stabismus repair 30 min after induction, $etCO_2$ was over 60 mmHg. Muscle rigidity of legs and elevation in temperature. Maximum esophageal temperature was noted to be 40.4 degrees Celsius. CK was 252 post-op and 1690 the next day.
- Second Case: 1 year and 9 month boy undergoing accessory ear resection. Sevoflurane used. 40 min after induction temperature was 38.6 degrees Celsius, HR 191, and oxygen saturation 93%. Muscle rigidity of the legs was noted. Highest temperature was 39.3 degrees Celsius. Both parents had no history of MH.

(Kinouchi,2001)

MHAUS Recommendations

Preparing for the MH patient

Per MHAUS:

- Anesthetic vaporizers are disabled by removing, or taping in the "OFF" position.
- Some consultants recommend changing CO_2 absorbent (soda lime or baralyme).
- Flow 10 L/min O_2 through circuit via the ventilator for at least 20 minutes
- During this time a disposable, unused breathing bag should be attached to the Y-piece of the circle system and the ventilator set to inflate the bag periodically.

Continued

- Use new or disposable breathing circuit.
- Use the expired gas analyzer to confirm absence of volatile gases, as some newer machines are not so easily cleaned of volatile agents.
- Newer anesthesia "work stations" may require up to 60 minutes for purging residual gases; consult manufacturer's information and information on the MHAUS website.
- Adding commercially available charcoal filters to the circuit will remove anesthetic gases and therefore obviate the need for purging the system as described However, the filters should be replaced every hour.

MH cart

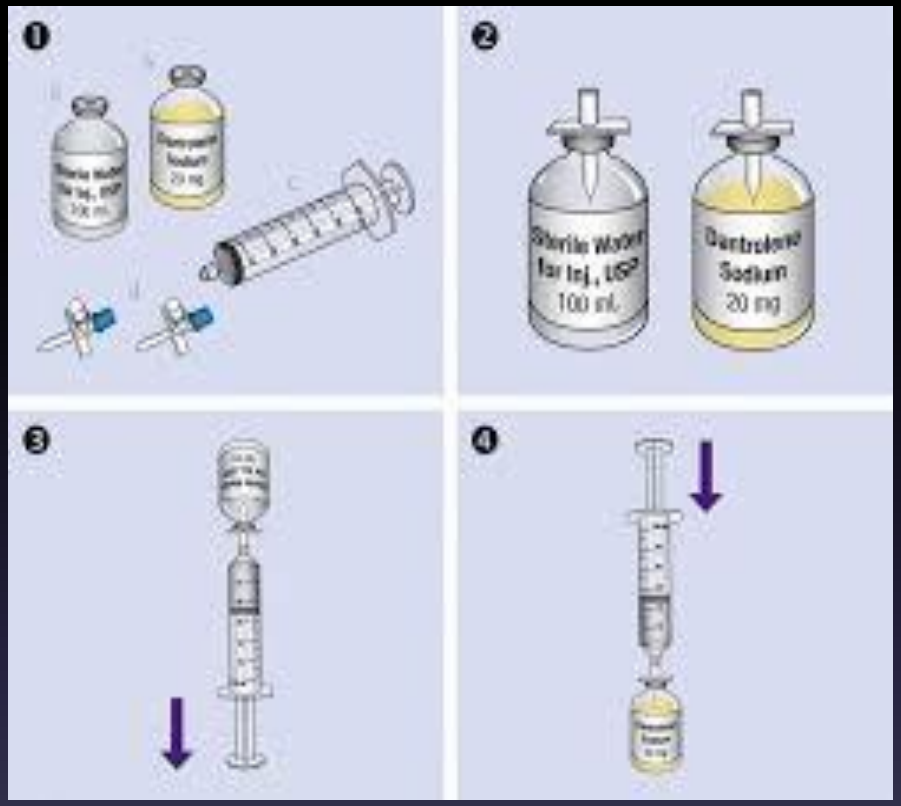
- Dantrolene
- Sterile water for injection USP
- Sodium bicarbonate
- Dextrose 50%
- Calcium chloride (10%)
- Regular insulin
- Lidocaine for injection (2%)
- Refrigerated cold saline solution
- Equipment: NGT, IV, syringes, temp probes, CVP kits, transducers, blood collection supplies

Dantrolene

- 36 vials should be available in each institution where MH can occur
- diluted at the time of use with 60 ml sterile water for injection (without a bacteriostatic agent)
- the vial is shaken until the solution is clear.
- It is mandatory to get dantrolene to its effective site, the skeletal muscle.
- MHAUS advises that the sterile water be stored in 100 ml vials, not bags, to avoid accidental IV administration of this hypotonic solution.

MHAUS

MALIGNANT HYPERTHERMIA ASSOCIATION OF THE UNITED STATES



MH emergency treatment

- Call MHAUS
- Discontinue volatile agents and succinylcholine
- Get help and notify surgeon;
- Dantrolene Sodium for Injection 2.5 mg/kg rapidly IV through large-bore IV
- Bicarbonate for metabolic acidosis
- Cool the patient
- Dysrhythmia treatment
- Hyperkalemia treatment
- Follow: $ETCO_2$, electrolytles, blood gasses, CK, serum myoglobin, core temperature, urine output and color, and coagulation studies.

New innovations

- Carbon absorber
- Single Use
- Do not have to remove vaporizers or soda lime

How to Use: Proactive use

- Turn the fresh gas flow up to 10 l/min for 90 seconds
- Place one of the Vapor-Clean canisters on the inspired port of the anesthesia machine and the other canister on the expired port of the anesthesia machine.
- Replace the breathing bag and connect a new breathing circuit between the patient and the Vapor-Clean canisters
- Maintain fresh gas flows at 10l/min for duration of the case
- Hook your patient up
- The Vapor-Clean filters are good for up to 12 hours. If your case goes longer than 12 hours, swap the filters for a new pair

How to Use: With MH episode

- Turn the anesthetic gas off
- Place the Vapor-Clean filters between the machine and the breathing circuit
- Turn the fresh gas flow up to 10 l/min
- The Vapor-Clean filters are good for 1 hour. If your case goes longer than 1 hour, swap the Vapor-Cleans for a new pair
- Shorter time is due to concentration of gas both on the patient and in the anesthesia machine
- Removing the vaporizers or soda lime is optional
- Treat the patient as prescribed by MHAUS

How to anesthetize the MH patient?

- Should be first patient of the day
- Prepare machine as discussed
- TIVA
- Can use NMB other than succ

Take Home Message

- Kids can present with MH differently than adults
- If MH is suspected treat with MH protocols
- Early interventions have the best outcomes
- Think with every kid (patient) this can happen

References

- BONCIU, M., DE LA CHAPELLE, A., DELPECH, H., DEPRET, T., KRIVOSIC-HORBER, R., & AIMÉ, M. (2007). Minor increase of endtidal CO_2 during sevoflurane-induced malignant hyperthermia. *Pediatric Anesthesia*, *17*(2), 180-182. doi:10.1111/j.1460-9592.2006.02051.

- Kinouchi, K., Okawa, M., Fukumitsu, K., Tachibana, K., Kitamura, S., & Taniguchi, A. (2001). [Two pediatric cases of malignant hyperthermia caused by sevoflurane]. *Masui. The Japanese Journal Of Anesthesiology*, *50*(11), 1232-1235.

- Nelson, P., & Litman, R. (2013). Malignant Hyperthermia in Children: An Analysis of the North American Malignant Hyperthermia Registry. *Anesthesia And Analgesia*.

- Gunter JB, Ball J, Than-Win S. Preparation of the Draeger Fabius anesthesia machine for the malignant hyperthermia susceptible patient. Anesth Analg,2008; 107:1936–1945.

- Wappler F; Anesthesia for patients with a history of malignant hyperthermia; Current Opinion in Anaesthesiology 2010, 23:417–422

- Birgenheier NM, Westenskow DR, Orr JA; Using Activated Charcoal Filters To Prepare Newer Anesthesia Machines for MH-Susceptible Patients, Proceedings 2009 ASA Annual meeting abstract A302

- Gunter JB, Ball J, Than-Win S. Preparation of the Draeger Fabius anesthesia machine for the malignant hyperthermia susceptible patient. Anesth Analg,2008; 107:1936–1945.

- Prinzhausen H, Crawford MW, Petroz GC; Preparation of the Drager Primus anesthesia workstation for malignant hyperthermia susceptible patients, Anesthesiology 2005; 103: A1276

- Shinkaruk KS, Nolan K, Crossan M;. Preparation of the Datex-Ohmeda Aestiva anesthetic machine for malignant hyperthermia cases, Anesthesiology 2008; 109 A279

- Official MHAUS Home Page - Malignant Hyperthermia Association .... (2014, January 1). *MHAUS*. Retrieved April 19, 2014, from http://www.mhaus.org/

- Kim, T., Rosenberg, H., & Nami, N. (). Current Concepts in the Understanding of Malignant Hyperthermia. *Anesthesiology News*, , 1-6.

Thank You

Questions?