HYPERTHERMIE MALIGNE

MALIGNE

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Objectifs

- Décrire l’évaluation pré-opératoire d’un patient à risque pour l’HM
- Proposer une approche anesthésique sécuritaire pour ce patient
- Décrire le traitement d’urgence d’une crise d’HM
- Proposer une approche sécuritaire pour les soins post-opératoires de ces patients

Agents déclencheurs de l’hyperthermie maligne

- Agents anesthésiques volatils
- Bloqueurs neuromusculaires dépolarisants

La Spirale….

- Exposition à un agent déclencheur
- Perturbation de l’homéostasie du calcium intracellulaire
- Contracture musculaire
- Hypermétabolisme
- Crise d’HM
- Diagnostic et traitement précoces!

Défintions

- Maladie pharmacogénétique rare caractérisée par un état hypermétabolique aigu déclenché par les agents anesthésiques volatils et/ou la succinylcholine
- Aussi rarement pour des exercises vigoureux et la chaleur
- Myopathie subclinique reliée à une homéostasie anormale du calcium intracellulaire

Anesthésie du patient susceptible à l’HM

- Appareil d’anesthésie sans volatils
- Chariot d’urgence HM
- Monitorage standard avec T
- Anesthésie loco-régionale
- AG mais avec TIVA
- Surveillance post-op 4h
- Ambulatoire c’est possible

Appareil d’anesthésie

- Appareil ‘nettoyé’ avec O2 haut débit
- Boyau de sortie des gaz vierge
- Absorbeur de CO2 neuf
- Circuits neufs

Epidemiologie

- Incidence : Entre 1:10,000 et 1:250,000
- Incidence est plus grande chez les jeunes (18.3)
- Rare chez les nourrissons et chez les vieillards?
- Hommes plus que les femmes (2:1)
- Tous les groupes d’ethnie, partout dans le monde
- Anesthésies antérieures sans problème rapportées (typiquement ad 3)

Génétique

- Transmission autosomale dominante
- Hétérogène,>200 mutations sur 6 chromosomes

Présentation Clinique

- N’importe quel moment pendant l’anesthésie ad la période post-opératoire immédiate
- Tachycardie
- Augmentation de CO2, malgré augmentation de ventilation minute
- Rigidité musculaire, surtout post-succinylcholine
- Élévation de température corporelle, 1 à 2 C chaque 5 min
- État hypermétabolique

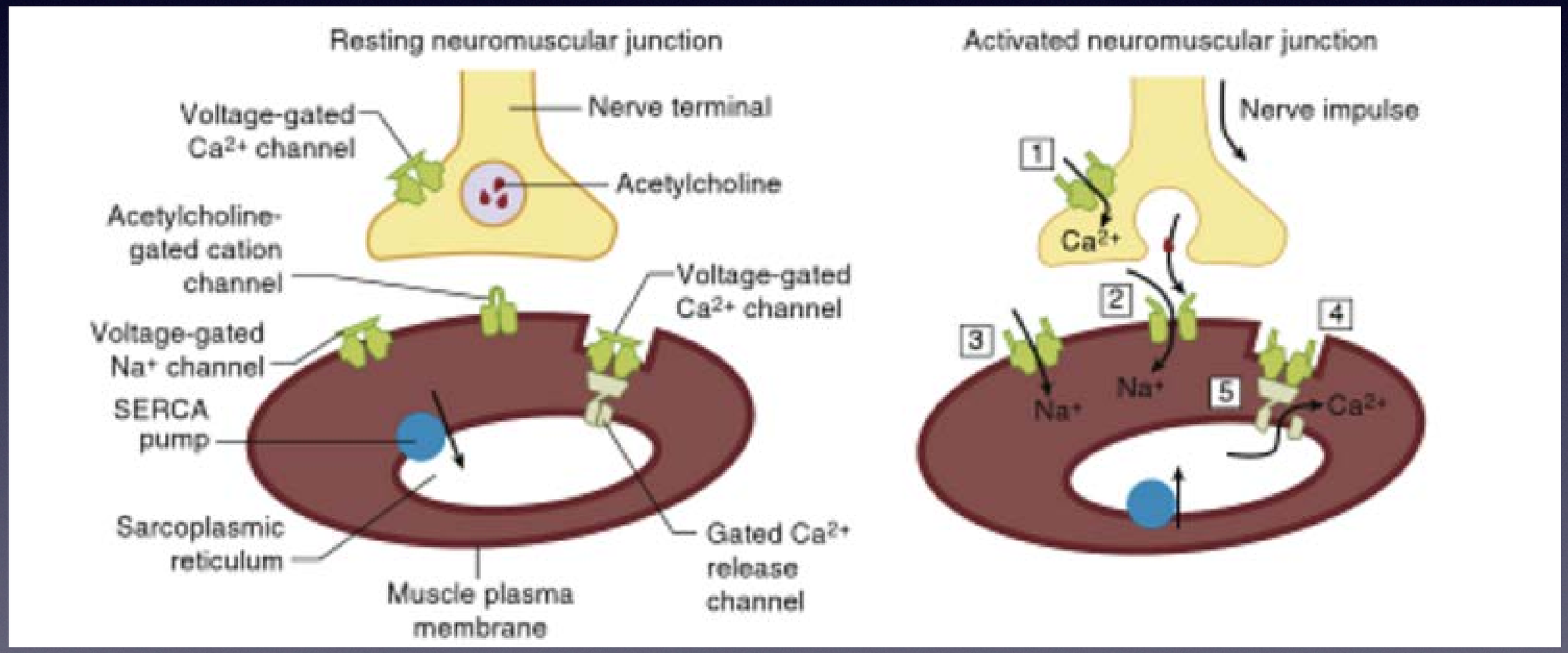
Physiologie Musculaire

- Influx nerveux: Acétylcholine libérée
- Activation du récepteur nicotinique
- Dépolarisation de la membrane
- Relâche de calcium
- Actine - Myosine - ATPase
- Cholinestérase et repolarisation
- Relaxation musculaire

Pathophysiologie

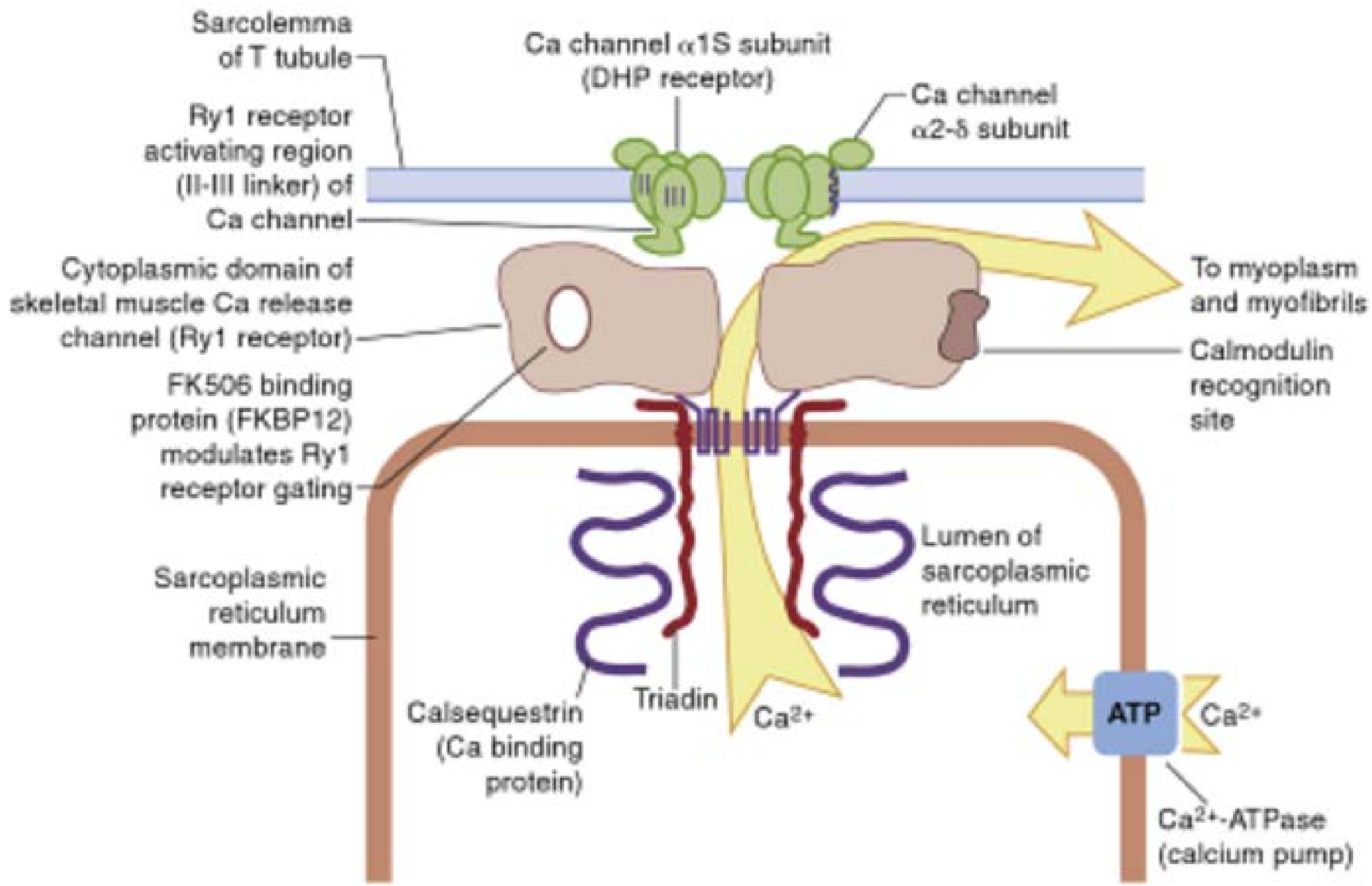
- Relâche soutenue de calcium
- Surcharge de mécanismes de compensation
- Absence de relaxation
- Hypermétabolisme
- Lyse des cellules musculaires
- Hperkaliémie, myoglobinémie…

Physiologie Musculaire



Mutation

- Majorité gène de RyR1, 50% 80% des patients et des familles. Plus que 200 mutations, in vitro tests + (IVCTs).
- Récemment retrouvé 3 mutations dans CACNA1S gène


Sarcolemma of T tubule
Ry1 receptor activating region (II-III linker) of Ca channel
Cytoplasmic domain of skeletal muscle Ca release channel (Ry1 receptor)
FK506 binding protein (FKBP12) modulates Ry1 receptor gating
Sarcoplasmic reticulum membrane
Ca channel α1S subunit (DHP receptor)
Ca channel α2-δ subunit
II
III
To myoplasm and myofibrils
Calmodulin recognition site
Lumen of sarcoplasmic reticulum
Calsequestrin (Ca binding protein)
Triadin
Ca2+
ATP
Ca2+
Ca2+-ATPase (calcium pump)

In Vitro Test De Contracture NAMHR

- Exposition à halothane 3%, test + si contracture >0.5g
- Exposition à des concentrations incréments de caféine(0.5,1,2,4,8…), test + si contracture >0.3g avec caféine 2mM

Sensibilité & Spécifités

	NAMHR CHCT	EMHG IVCT
Sensitivity	0.97	0.99
(95% CI)	(0.84-1.00)	(0.97-1.00)
Specificity	0.78	0.936
(95% CI)	(0.71-0.85)	(0.89-0.97)

Criteria used in the clinical Grading scale for MH

- I: Rigidité
- II: Lyse Musculaire
- III: Acidose Respiratoire
- IV: Hyperthermie
- V: Cardiaque
- VI: Histoire Familiale
- Autres

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DEPARTMENT OF ANAESTHESIA
FACULTY OF MEDICINE
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Malignant Hyperthermia Clinical Grading Scale

Patient Name:

I: Rigidity	15	Generalized muscular rigidity (in absence of shivering due to hypothermia, or during or immediately following emergence from inhalational general anesthesia)
	15	Masseter spasm shortly following succinylcholine administration
II. Muscle Breakdown	15	Elevated creatine kinase >20,000 IU after anesthetic with succinylcholine
	15	Elevated creatine kinase >10,000 IU after anesthetic without succinylcholine
	10	Cola colored urine in perioperative period
	5	Myoglobin in urine > 60ug/L
	5	Myoglobin in serum >170ug/L
	3	Blood/plasma/serum K+>6mEq/L (in absence of renal failure)
III. Respiratory Acidosis	15	PETCO2>55mmHg with appropriately controlled ventilation
	15	Arterial PaCO2>60mmHg with appropriately controlled ventilation
	15	PETCO2>60mmHg with spontaneous ventilation
	15	Inappropriate hypercarbia (in anesthesiologist's judgment)
	10	Inappropriate tachypnea
IV. Temperature Increase	15	Inappropriately rapid increase in temperature (in anesthesiologist's judgment)
	10	Inappropriately increased temperature >38.8°C (101.8°F) in the perioperative

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V. Cardiac Involvement	3	Inappropriate sinus tachycardia
	3	Ventricular tachycardia or ventricular fibrillation
VI. Family History (used to determine MH susceptibility only)	*15*	*Positive MH family history in relative of first degree*
	5	*Positive MH family history in relative not of first degree*
Other indicators that are not part of a single Process	10	Arterial base excess more negative than -8mEq/L, in absence of circulatory arrest
	10	Arterial pH<7.25, in absence of circulatory arrest
	5	Rapid reversal of MH signs of metabolic and/or respiratory acidosis with IV dantrolene
	10	*Positive MH family history together with another indicator from the patient's own anesthetic experience other than elevated resting serum creatine kinase*
	10	*Resting elevated serum creatine kinase (in patient with a family history of MH)*

Score	Rank	
0	1	Almost never
3 - 9	2	Unlikely
10-19	3	Somewhat less than likely
20-34	4	Somewhat greater than likely
35-49	5	Very likely
50+	6	Almost certain

Date coded: _____ by _____

Rang HM et probabilité qualitative

Score	Description of Likelihood	Rang
0	Almost never	1
3-9	Unlikely	2
10-19	Somewhat less than likely	3
2-34	Somewhat grater than likely	4
35-49	Very likely	5
50+	Almost certain	6

Morbidité et Mortalité

- Sans Dantrolène, mortalité >90%
- Arrêt cardiaque (hperkaliémie)
- Rhabdomyolyse
- Insuffisance rénale
- Coagulopathie
- SDRA
- Coma

Laboratoire

- Acidose métabolique et respiratoire: Gaz A/v
- CK élevés (stat, et q 6h)
- Myoglobinémie / Myoglobinurie
- Hyperkaliémie / Hypercalcémie

Diagnostic Différentiel

- Choc septique
- Crise thyroïdienne
- Phéochromocytome
- Syndrome neuroleptique malin
- Anaphylaxie
- Fièvre d’origine ?
- Etc…..

Traitement D’urgence

- Cesser l’administration d’agents déclenchants
- Hyperventilation, avec O2 à haut débit
- Appeler de l’aide et le chariot d’urgence HM
- Administrer Dantrolène

Crise HM

- Diagnostic précoce
- Dantrolène à dose appropriée
- RX de réanimation
- Éducation (patient et famille)
- Investigation

MH au CANADA

- Étude par Sheila Riazi, Anesth Analg 2014)
- 1992-2011, Canadiens référés pour test Dx
- 129 + parmi les 373
- Hommes jeunes prédominent
- 13.2% ont déjà eu des AG sans problèmes
- Volatiles et succinylcholine, seul ou ensemble
- 6.2% de ces manifestations sont apparues au PACU
- Pas de réaction après congé de SR

MH au CANADA

- Hyperthermie chez 66.7%
- Tachycardie chez 62.0%
- Hypercarbie chez 51.9%
- 20% des patients ont eu des complications
- Complication la + fréquente étant dysfonction rénale
- Taux de complications étaient >30% si un délai d’applications de Dantrolène, 20min ou plus

DANTROLENE

- 20 mg / bouteille à dissoudre avec EAU STÉRILE (60 ml)
- 2.5 mg/kg caque 5 min, peut aller jusqu’à 10 mg/kg
- Pourra néccesiter plusieurs personnes pour dissoudre
- Être prêts à répéter q4-6h de 1mg/kg ad 24h

Administration du Dantrolène

- Minimum de 36 bouteilles de Dantrolène par hôpital
- SO, accès immédiat par les cliniciens
- Réunir l’eau stérile pour injection
- Former l’équipe et pratiquer!

Réanimation I

- IV gros calibre
- Salin froid pour diurèse >2ml/kg/h
- Accès central et artériell
- Contrôle de la température corporelle
- Correction de l’acidose, $NaHCO_3$ 1-2 mEq/kg

Réanimation II

- Tx de l’hyperkaliémie PRN
- Tx des arythmies ventriculaires
- Tests sanguins et urinaires
- Monitorage du débit urinaire

MHAUS

- Poster du traitement d’urgence
- EN CAS D’URGENCE:
- 1-800-MH-HYPER (1-800-644-9737)
- ou 1-315-464-7079
- Site Web: www.MHAUS.orgss

MH Hotline
1-800-644-9737
Outside the US:
1-315-464-7079

Effective May 2008

EMERGENCY THERAPY FOR MALIGNANT HYPERTHERMIA

DIAGNOSIS vs. ASSOCIATED PROBLEMS

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 12 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. Prewarming (not to exceed 39° C.) the sterile water may expidite solublization of dantrolene. However, to date, there is no evidence that such warming improves clinical outcome.
- Repeat until signs of MH are reversed.
- Sometimes more than 10 mg/kg (up to 30 mg/kg) is necessary.
- Each 20 mg bottle has 3 gm mannitol for isotonicity. The pH of the solution is 9.

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 **<u>except calcium channel blockers, which may cause hyperkalemia or cardiac arrest in the presence of dantrolene.</u>**

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 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. 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.mhaus.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

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Dedicated to Patient Safety

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

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