Management of Malignant Hyperthermia versus Neuroleptic Malignant Syndrome in PICU setting:

Malignant Hyperthermia (MH)	Neuroleptic Malignant Syndrome (NMH)
Cause: Usually associated with use of potent halogenated inhalational anesthetic agents and succinylcholine	**Cause:** Usually associated with use of antipsychotic (neuroleptic) agents (e.g. haloperidol, chlorpromazine, risperidone, olanzapine) and antiemetic agents (e.g. metoclopramide, promethazine)
Non-pharmacological management: 1) Stop the causative agent 2) Consider cooling measures if temperature > 39°C	**Non-pharmacological management:** 1) Stop the causative agent 2) Consider cooling measures if temperature > 39°C
Pharmacological management of: **Malignant hypermetabolism:** **To call Paed Anaesthetist on call for MH kit** **IV Dantrolene**: Initial dose: 2.5mg/kg every 10-15 minutes via rapid infusion through a large-bore IV (if possible as drug is an irritant) until signs of hypermetabolism (acidosis, pyrexia, muscle rigidity) are resolving. **Post crisis management:** May repeat IV Dantrolene 1mg/kg/dose q4-6hourly or IV Dantrolene infusion 0.25mg/kg/hr for at least 24hours Note: doses >10mg/kg per course may be required for patients with persistent contractures or rigidity". **Refer table below for IV Dantrolene dilution:** Note: Do not delay dantrolene to insert a central line Monitor patient in CICU for at least 24hours (risk of recrudescence) **Arrythmia:** ***(AVOID calcium channel blockers they interact with Dantrolene)*** **IV Amiodarone:** Loading dose of 5mg/kg over 30-60mins (max=300mg/dose) followed by 5-15mcg/kg/min. Max 1.2g in 24 hours **IV Esmolol:** Loading dose of 100-500mcg/kg over 1 min followed by an infusion of 50mcg/kg/min over 4 mins; May re-load with 500mcg/kg if inadequate response and increase infusion by 50mcg/kg/min Repeat until effective or a maximum infusion of 200mcg/kg/min is reached. **IV MgSO4:** 0.1 to 0.2 mmol/kg (25-50mg/kg). Give slowly by IV injection over 10-20mins.Rapid infusion may cause hypotension	**Pharmacological management of:** **Mild NMH:** **IV/IM Lorazepam:** 0.05-0.1mg/kg/dose (max=2mg/dose) q4H-q6H **IV Diazepam:** 0.05-0.1mg/kg/dose (max=10mg/dose) q6-12H **Moderate NMH:** **PO Bromocriptine: Adult:** 2.5mg to 10mg/dose TDS. If there is no improvement after 24 hours: Titrate dose up to 20 mg orally 4 times per day (Max=45mg/day) Once symptoms are controlled, taper off slowly over 3 days **PO Amantadine (Non-form):** 100mg to 200mg q12H (Max=400mg/day) (note: doses above are based on adult studies) Consider the use of IV dantrolene in patients who are unable to swallow due to muscular rigidity unless patient has NGT **Severe NMH:** **To call Paed Anaesthetist on call for MH kit** **IV Dantrolene**: Initial dose: 1 to 2.5mg/kg every 10-15 minutes via rapid infusion through a large-bore IV (if possible as drug is an irritant) until signs of hypermetabolism (acidosis, pyrexia, muscle rigidity) are resolving. If inadequate response, may repeat IV Dantrolene 1mg/kg/dose q6H up to max cumulative dose of 10 mg/kg/DAY Once symptoms are controlled, consider switching to PO bromocriptine and taper off slowly to prevent relapse. **Refer table below for IV Dantrolene dilution:** Give an initial bolus of 3 to 7.5ml/kg of the Dantrolene solution (= 1 to 2.5mg/kg) Repeat further doses of 3 ml/kg (=1mg/kg) up to a maximum of 30ml/kg/day in total of Dantrolene.

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Hyperkalemia:
1) IV Insulin 0.1units/kg (**max 10 units**) with 5ml/kg **Dextrose 10%** or 1ml/kg/doseml D50% (Max =50mL D50%)
2) IV Calcium Chloride (CaCl2) : 0.2 ml/kg **OR**
~~**3)**~~ **IV Calcium Gluconate (10%):** 0.5- 1ml/kg
4) Salbutamol neb (0.5%):
<25kg: 0.5ml of 0.5% solution in 4ml NS Q1-2H
>25kg: 1ml of 0.5% solution in 4ml NS Q1-2H)
5) PO Resonium: 1g/kg (max 15 – 30g/DOSE) **OR**
PR Resonium: 1g/kg (max 30 – 60g/DOSE)

Metabolic acidosis
IV NaHCO3 0.5-1mmol/kg (0.5-1ml/kg) **(max 50mmol)**

Maintain Urine output (~~keep pu~~ at least 2 ml/kg/hr)
If required, use:
IV Mannitol 0.5 - 1.0 g/kg (2.5 – 5 ml/kg of 20% solution) and/or
IV Furosemide 1 mg/kg

Note: Do not delay dantrolene to insert a central line
Monitor patient in CICU for at least 24hours (risk of recrudescence)

Arrythmia:
(AVOID calcium channel blockers they interact with Dantrolene)
IV Amiodarone: Loading dose of 5mg/kg over 30-60mins (max=300mg/dose) followed by 5-15mcg/kg/min.
Max 2.2g in 24 hours
IV Esmolol: Loading dose of 100-500mcg/kg over 1 min followed by an infusion of 50mcg/kg/min over 4 mins; May re-load with 500mcg/kg if inadequate response and increase infusion by 50mcg/kg/min Repeat until effective or a maximum infusion of 200mcg/kg/min is reached.
IV MgSO4 (49.3%): 0.1 to 0.2 mmol/kg (25-50mg/kg, **max 2g/dose**). Give slowly by IV injection over 10-20mins.Rapid infusion may cause hypotension

Hyperkalemia:
1) IV Insulin 0.1units/kg with 5ml/kg **Dextrose 10%** or 0.5ml **D50%**
Adults: Give 10 units **insulin** with 50 ml **Dextrose 50%**
2) IV Calcium Chloride (CaCl2) : 0.2 ml/kg OR
3) IV Calcium Gluconate (10%): 0.5- 1ml/kg
4) Salbutamol neb:
<25kg: 0.5ml of 0.5% solution in 4ml NS Q1-2H
>25kg: 1ml of 0.5% solution in 4ml NS Q1-2H)
5) PR/PO resonium: 1g/kg

DRUG	VIAL SIZE	RECONSTITUTION		ROUTE	SUITABLE DILUENT	CONCEN-TRATION	RATE	Comments
		Dilute with (WFI)	Final Con-centration					
DANTROLENE (Dantrium®)	20 mg	60 mL	0.33 mg/mL	IV Bolus	No further dilution	0.33 mg/mL	Therapeutic / emergency: Rapid IV push	May cause tissue necrosis if extravasated (vesicant) The reconstituted solution should be protected from direct light and used within 6 hours after reconstitution. Avoid glass bottles for IV infusion due to potential for precipitate formation
				IV Intermittent	No further dilution		Prophylaxis: 1 hour	

* Please refer to the **PAEDIATRIC PARENTERAL ADMINISTRATION CHART: DRUGS under Drug Information Service on Infopedia for updated information**

Note: There are supplied of Dantrolene kept in Malignant Hyperthermia Kits in the following locations: MOT/DSOT/OT20/IVF OT/DDII
Extra supplies also kept in Pharmacy Store. There are barcode labelled stocks in PS-OT: in the event more Dantrolene is required, these stocks can be used, pls inform PS to bring in more stocks.

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References:

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2. An Approach to the Pharmacotherapy of Neuroleptic Malignant Syndrome. Article in Psychopharmacology bulletin. 2019; 49(1): 1-8
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