



## PAEDIATRIC ANAESTHETIC EMERGENCIES Part 2

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### INTRODUCTION

- Laryngospasm
- Suxamethonium Apnoea
- Malignant Hyperthermia (MH)
- Anaphylaxis

Part one of this tutorial pair covered laryngospasm and suxamethonium apnoea. This tutorial aims to provide a better understanding of the presentation, immediate treatment and subsequent management of MH and anaphylaxis.

### MALIGNANT HYPERTHERMIA

Malignant hyperthermia (MH) is a pharmaco-genetic disorder of skeletal muscle induced by exposure to certain triggering anaesthetic agents. It is inherited in an autosomal dominant fashion, with around 60% of MH families having mutations in the RYR1 gene located on chromosome 19q. The incidence of MH in the general population is thought to be 1:10,000 – 15,000. It affects all races and both sexes (but is more common in some populations such as the Maori people in New Zealand). It most commonly presents in children or young adults having minor surgery because of the anaesthetic techniques commonly used for such procedures and the fact that most people have their first exposure to anaesthesia during their childhood years. Mortality rates have fallen dramatically from 75% to 2-3% of all cases because of increased awareness and better treatment. <sup>1</sup>

## Mechanism

In around 60% of cases, malignant hyperthermia is due to a mutation of the ryanodine receptor (type 1), located on the sarcoplasmic reticulum (SR), the organelle within skeletal muscle cells that stores calcium. Normally, RYR1 opens in response to increases in intracellular  $Ca^{2+}$  level mediated by L-type calcium channels, thereby resulting in a drastic increase in intracellular calcium levels and muscle contraction. In MH patients, the end result of this mutation is greatly increased & uncontrolled  $Ca^{2+}$  release. The process of reabsorbing this excess  $Ca^{2+}$  consumes large amounts of adenosine triphosphate (ATP), the main cellular energy carrier, and generates the excessive heat that is the hallmark of the disease. The muscle cell is damaged by the depletion of ATP (and possibly the high temperatures) and cellular constituents "leak" into the circulation, including potassium, myoglobin, creatine, phosphate and creatinine kinase.

The two most common triggering anaesthetic agents are:

- Suxamethonium
- Volatile anaesthetic gases e.g. Halothane, Isoflurane, Desflurane & Sevoflurane

## Clinical Presentation

The clinical presentation can be varied and therefore, difficult to recognise, hence the need for a high index of suspicion. A case of MH can have a rapid and florid onset, becoming life threatening within a short time frame, or a slower more insidious onset.

### *Muscle signs*

- Generalised muscle rigidity
- Masseter spasm
- Hyperkalaemia
- Increased CK levels
- Myoglobinuria
- Acute renal failure

### *Signs of increased metabolism*

- Tachycardia
- Pyrexia
- Increased end tidal  $CO_2$  levels despite adequate ventilation
- Cardiac arrhythmias
- Metabolic acidosis
- Disseminated intravascular coagulopathy (DIC)

## Management

The management plan is based on recommendations from the Association of Anaesthetists of Great Britain & Ireland (AAGBI).<sup>2</sup> The aims of treatment are broadly to remove the trigger agent, administer Dantrolene, support the patient and prevent complications.

The guidelines are broken into 4 sections:

Recognition, Immediate Management, Monitoring & Treatment and Follow Up.

### *Recognition*

Unexplained increase in  $ETCO_2$  AND unexplained increase in Heart Rate AND unexplained increase in oxygen requirements. Temperature changes are a late sign.

### *Immediate Management*

- REMOVE all triggering agents
- CALL FOR HELP, arrange clean breathing circuit
- HYPERventilate with 100% OXYGEN
- ABANDON/FINISH surgery as soon as possible.

### *Monitoring and Treatment*

- Give DANTROLENE 2.5mg/kg IV bolus & repeat 1mg/kg boluses as required to max 10mg/kg,
- Start ACTIVE COOLING,
- Check for & manage likely complications (hyperkalaemia, arrhythmias, metabolic acidosis & myoglobinaemia).
- Initiate/maintain full AAGBI monitoring plus invasive central and arterial lines
- Send blood samples for FBC, U&Es, plasma Creatinine Kinase (CK), coagulation studies & arterial blood gases

### *Follow up*

Transfer to ICU, monitor for acute renal failure & compartment syndrome

### *Subsequent Management*

All patients and families should be offered counselling after the event.

Ideally, all cases of suspected MH should be referred to, and investigated by, a specialist unit. In the UK all testing occurs in Leeds. Testing involves invasive muscle biopsies and may not be appropriate for young children.

The muscle biopsy is taken from the thigh under LA and undergoes caffeine-halothane contracture testing. This involves bathing the muscle in solutions of caffeine or halothane and observing for contracture. It has a very high sensitivity (97%) and high specificity (78%). Results are MH negative, MH susceptible or equivocal (these patients are regarded as positive for safety).<sup>3</sup>

In developing countries specialist investigations are unlikely to be available. In such cases all patients and their families should therefore be regarded as MH susceptible should a further general anaesthetic be required.

### *Important points for anaesthesia involving known MH susceptible patients*

- MH susceptibility is not an absolute contraindication to general anaesthesia
- An MH safe technique should be used, avoiding suxamethonium and all volatile agents. All local anaesthetics are safe, as is total intravenous anaesthesia (TIVA).
- Few hospitals have a 'volatile free' anaesthetic machine because of resource limitations and checking/maintenance issues. In such cases remove all vaporisers and breathing circuits from a machine and flush with high flow oxygen for 30 minutes before use.
- Use new breathing circuits and airway devices such as laryngeal mask airways and endotracheal tubes.
- Minimum monitoring: non-invasive blood pressure, electrocardiogram, pulse oximetry, airway gas sampling & airway pressure monitors and continuous core temperature should be monitored during the peri-operative period.  
N.B. Not all cases present on exposure to first anaesthetic. A previous, uneventful GA does not exclude MH as a diagnosis should any of the signs occur.

## **ANAPHYLAXIS**

Anaphylaxis is a life threatening allergic reaction mediated by the release of histamine and other substances from mast cells after exposure to certain antigens. There is a lack of consistent clinical manifestations and hence there is a wide range of possible clinical presentations. In addition, the timing of the reaction in relation to exposure to the triggering agent can vary. Both these facts mean diagnosis can be difficult and a high index of suspicion is required.

Common triggering agents in anaesthesia include:

- Muscle relaxants
- Latex
- Antibiotics
- Colloids

More commonly in children, anaphylaxis is caused by penicillin, contrast media or nuts.

## Recognition

As stated above the clinical presentation of an anaphylactic reaction is varied. The most common presentations include:

- Cardiovascular collapse (88%)
- Erythema (48%)
- Bronchospasm (40%)
- Angioedema (24%)
- Cutaneous rash (13%)
- Urticaria (8%)

The incidence in anaesthesia is estimated at 1 in 10-20,000 and the overall mortality (across all age groups) is 5%. It has been classified clinically into 5 grades:

- I. Cutaneous reaction only: urticaria, erythema, angio-oedema
- II. As above but also hypotension, tachycardia or bronchospasm
- III. As II but more severe: collapse, arrhythmias
- IV. Cardiac and/or respiratory arrest
- V. Death

## Immediate management <sup>7</sup>

- STOP triggering agent (if known or suspected)
- Call for HELP
- Deliver 100% OXYGEN
- Exclude airway or breathing circuit obstruction, intubate trachea if not already done
- Give ADRENALINE (epinephrine), either intravenously (IV) or intramuscularly (IM). IM adrenaline is less likely to provoke potentially life-threatening arrhythmias, but may be poorly absorbed if perfusion is compromised, such that the dose may be ineffective. IV adrenaline should be carefully titrated to effect and only administered by anaesthetists familiar with its use.
- For information on which route to use and doses of both IV and IM adrenaline see Table 1. • Give a FLUID bolus of 20ml/kg of crystalloid.

## Subsequent management

Once stable consider:

- IV Chlorphenamine
- IV Hydrocortisone
- Bronchodilators such as salbutamol if persistent wheeze

**Table 1:** Drug doses in anaphylaxis

| Age            | IV adrenaline<br>(1:10 000)<br>Suggested<br>increments | IM adrenaline<br>(1:1000) | Chlorpheniramine<br>(IM or slow IV) | Hydrocortisone<br>(IM or slow IV) |
|----------------|--|---------------------------|-------------------------------------|-----------------------------------|
| < 6 mths       | 5mcg (0.05ml)  | 150mcg (0.15ml)           | 250mcg/kg                           | 25mg                              |
| 6 mths – 6 yrs | 10mcg (0.10ml)   | 150mcg (0.15ml)           | 2.5mg if over 1 year                | 50mg if over 1 year               |
| 6 – 12 yrs     | 25mcg (0.25ml)   | 300mcg (0.3ml)            | 5mg                                 | 100mg                             |
| > 12 yrs       | 50mcg (0.50ml)   | 500mcg (0.5ml)            | 10mg                                | 200mg                             |

NB: 10mcg/kg = 0.1ml/kg 1:10,000

### Intramuscular versus intravenous route for adrenaline

The IM route is the most appropriate way of administering adrenaline for most healthcare professionals treating anaphylaxis, in both adults and children. There is a greater margin of safety, it does not require intravenous access and is easier to learn.

Doses are administered in 150/300/500mcg boluses (depending on age), which can be repeated at 5 minute intervals according to the patient's response.

IV Adrenaline is reserved for specialist use only. Only those trained in paediatrics and skilled in the use of IV adrenaline should consider this route of administration.

There is no evidence on which to base a dose recommendation. Some children may respond to a bolus as small as 1mcg/kg. Doses should be given, monitored and titrated to response. Table 1 gives suggested incremental doses of IV adrenaline with a total dose target of 10mcg/kg. In small children, further dilution of the solution may be required. Extra care should be taken when calculating doses in these circumstances.

### Post anaphylaxis investigations

Any patient who has had a suspected anaphylactic reaction under anaesthesia should be fully investigated if possible. The patient should be made aware of the trigger agent and any hospital records should be clearly labelled with an alert.

Investigations post-operatively should include standard tests to inform any required treatment or care: FBC/Electrolytes/ABG/ECG/CXR

Specific investigations to assist diagnosis and identify the trigger for the reaction include:

- Mast Cell Tryptase (SST tube – yellow top in the UK) to be taken:
  - As soon as possible (but not at the expense of therapeutic measures)
  - 1–2hrs (peak)
  - 24hrs (baseline)
- Skin prick testing once the patient has recovered fully.

## REFERENCES and FURTHER READING

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