MUCOPOLYSACCHARIDOSES (MPS) - PERIOPERATIVE MANAGEMENT - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- The mucopolysaccharidoses are characterised by the lysosomal accumulation of glycosaminoglycans in multiple tissues and multiple organ systems can be affected.
- Patients with mucopolysaccharidosis have an increased risk of complications in the perioperative period.
- With an elevated risk of difficult airway management, respiratory and cardiovascular complications, and spinal cord injury a consultant anaesthetist should be involved in every case.
- Preoperative preparation requires multidisciplinary assessment covering respiratory, cardiovascular, ENT, sleep and spinal cord status.
- Particular anaesthesia approaches to prioritise spinal cord protection should be considered. This may include intraoperative neuromonitoring, but should always involve consideration of measures to maintain spinal cord perfusion.

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CHANGE SUMMARY

- N/A – new guideline

READ ACKNOWLEDGEMENT

- Clinical teams working in anaesthetics, genetics/metabolics, spinal surgery, neurology department and radiology caring for patients with MPS are to read and acknowledge they have read and understood this guideline.

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Abbreviations and Acronyms in this Document

CPAP	Continuous Positive Airway Pressure
CVAD	Central Venous Access Device
ENT	Ear, Nose and Throat
ERT	Enzyme Replacement Therapy
GAGs	Glycosaminoglycans
HSCT	Haematopoietic Stem Cell Transplantation
IONM	Intraoperative Neuromonitoring
MEPs	Motor Evoked Potentials
MPS	Mucopolysaccharidosis
MRI	Magnetic Resonance Imaging
OSA	Obstructive Sleep Apnoea
RTI	Respiratory Tract Infections
SGA	Supraglottic Airway
SSEPs	Somatosensory Evoked Potentials

Introduction

For patients with a mucopolysaccharidosis (MPS), episodes of anaesthesia are both a feature of a comprehensive management plan to provide the best possible care, and a period of risk. With particular challenges evident in the anaesthetic care of these patients, it is important to draw on a comprehensive multidisciplinary assessment of the current clinical status of a patient, while applying a deep understanding of the perioperative journey, to develop a safe plan to manage admissions for surgery or medical imaging involving general anaesthesia. This document outlines a pragmatic approach to perioperative care of the MPS patient.

The following guidelines have been developed by a multidisciplinary team to aid anyone involved in the perioperative care of a patient with MPS. It covers the whole perioperative journey, including considerations when an emergency procedure is required.

1 Background Information

1.1 Some Background on the Mucopolysaccharidoses

All of the mucopolysaccharidoses are different forms of lysosomal storage disorders. The fundamental defect common to all of the MPS subtypes is a defect in the normal function of an enzyme responsible for one of the steps in degradation of glycoasminoglycans (GAGs). As GAGs are widely distributed in tissues, the problems created by an enzyme deficiency are inevitably multi-system in nature. The clinical phenotype of the disorder is a result of the degree of residual enzyme activity, and the distribution of the substrate as it builds up in the lysosomes in particular tissues.

Within the broader MPS diagnosis, there are individual subtypes, also known as eponymous syndromes:

- MPS-I - Hurler's Syndrome (most severe form), Hurler-Scheie Syndrome (intermediate severity); Scheie Syndrome (least severe form)
- MPS-II - Hunter's Syndrome
- MPS-III (subtypes A to D) - Sanfilippo Syndrome
- MPS-IV (subtypes A and B) - Morquio Syndrome
- MPS-VI - Maroteaux-Lamy Syndrome
- MPS-VII - Sly Syndrome
- MPS-IX - Natowicz Syndrome

***Note** that MPS-V and MPS-VIII are no longer recognised*.

Even allowing for the individual presentations, some broad organ systems are affected across all groups and of direct relevance to perioperative care. All of the subtypes involve musculoskeletal abnormalities, hepatosplenomegaly, vision and hearing dysfunction, cardiac complications and respiratory system ramifications. Some of the MPS groups also feature prominent neurological pathophysiology.

The table below highlights particularly prominent features of the subtypes. It should be noted that the spectrum of presentation within subtypes is broad and there is overlap in the pathophysiology seen between syndromes. The key message is that a comprehensive assessment of the presentation of the particular syndrome in each patient is required to understand how best to plan excellent perioperative care.

Table 1: Prominent Features of MPS Subtypes

Organ Systems	***Subtype***					
	Skeletal Disease, Soft Tissue Storage, CNS			*Skeletal disease, soft tissue storage, no CNS*	*Skeletal, ligament, cartilage, no CNS.*	*Primary CNS; less skeletal and soft tissue*
	MPS-I	MPS-II	MPS-VII	MPS-VI	MPS-IV	MPS-III
Airway/ENT	Deposition in soft tissues, abnormal trachea, progressive obstruction.	Deposition in soft tissues, progressive airway obstruction.	Deposition similar to MPS-I in severe forms.	Deposition in soft tissues	Narrowed and floppy lower airways.	Deposition in soft tissues (tonsils, adenoids)around airway milder
Respiratory/Sleep	Frequent RTIs, OSA.	Frequent RTIs, OSA.	Frequent RTIs, OSA	Frequent RTIs, OSA	Restrictive effects of skeletal disease.	OSA may occur. Sleep apnoea may also be due to central cause.
Cardiac	Cardiomyopathy, endocardial fibroelastosis, valvular regurgitation.	Particularly valvular dysfunction.	Valvular abnormalities	Valvular dysfunction more common than cardiomyopathy and endocardial fibroelastosis.	Valvular heart disease.	Valvular, myocardial, and/or cardiac conduction system may be affected
Neurodevelopmental	Developmental delay.	Developmental delay.	Developmental delay, though some may be cognitively spared			Progressive CNS changes with cognitive impairment, developmental delay, behavioural challenges.
Spinal Cord	Odontoid dysplasia, C1-2 subluxation and cord compression.			Particular risk of spinal canal stenosis around upper C-spine.	Odontoid hypoplasia and atlantoaxial instability.	
Musculoskeletal	Arthropathy, joint stiffness, contractures. Short stature	Similar to MPS I, Short stature	Prominent features of arthropathy, joint stiffness and contractures.	Severe skeletal dysplasia. Short stature, degenerative joint disease.	Short stature with shortened neck and trunk pectus carinatum, joint laxity, kyphoscoliosis, genu valgum.	Less than other forms
Eyes/Ears	Corneal clouding. Combined conductive and sensorineural hearing loss.	Combined conductive and sensorineural hearing loss. no corneal clouding.		Combined conductive and sensorineural hearing loss. Corneal clouding.	Mild corneal clouding	Combined conductive & sensorineural hearing loss.
Specific Notes	Difficult airway management including intubation.		Attenuated forms may only have skeletal abnormalities.	Particular risks related to cord compression.	Particular risks of cord compromise.	

* MPS-IX has not been included in this table as it is particularly rare.

** For simplicity MPS-I has been described in a single grouping. Hurler-Scheie and Scheie syndromes generally present in a more attenuated form than Hurler syndrome. MPS-IV has two subtypes (A and B) based on specific enzyme defects but the clinical spectrum of presentation is similar. MPS-III has 4 subtypes on the basis of enzymes involved but clinical presentation is also similar.

1.2 Particular Perioperative Implications to Consider

Given this range of clinical features, further consideration of particular organ systems and their implications in the perioperative period is imperative.

Airway and ENT

Accumulation of GAGs in soft tissues can result in significant changes in both the upper and lower respiratory tract. This includes macroglossia, adenotonsillar hypertrophy and laryngeal soft tissue enlargement. For anaesthetists this translates to increased difficulty with airway management, particularly intubation. Difficult intubation has been reported in up to 86.7% of MPS patients[(1)]. Difficulties in airway management tend to increase with patient age. It should be noted that considerations related to the spinal cord and cervical spine may also complicate airway management.

From an ENT point of view, progressive airway obstruction can develop at multiple levels of the airway. This also means that ENT surgery such as adenotonsillectomy and laryngeal surgery are common indications for presentation to the perioperative suite.

Respiratory and Sleep

Issues with respiratory function and disordered sleep are interlinked with airway changes. Frequent respiratory tract infections are a feature of MPS, along with excessive secretions. Lower airways disease related to abnormalities of the tracheal cartilage, excess respiratory mucosa, inflammation and secretions can be associated with wheeze and airway reactivity. Restrictive lung disease can be related to skeletal involvement, a particular feature of MPS-IV.

Multilevel airway obstruction with deposition of GAGs can be associated with severe obstructive sleep apnoea and a large proportion of patients will require CPAP or other approaches to non-invasive monitoring.

In some patients with advanced disease, cord compression at high levels can be associated with central sleep apnoea.

Cardiovascular

The commoner features of cardiovascular disease may be related directly to GAG deposition, or secondary to chronic hypoxaemia leading to right heart failure. Valvular disease, particularly aortic and mitral insufficiency are commonest in MPS I, II and VI. Right-sided heart-valve insufficiency may also be seen. Some younger patients, particularly in MPS-I and MPS-VI, may present with cardiomyopathy or endocardial fibroelastosis.

Spinal Cord Compromise

Several different pathways lead to an elevated risk of spinal cord compromise in MPS patients:

- *Pachymeningitis cervicalis* - thickening and scarring of the meninges around the cervical spinal canal due to GAG deposition creates a sleeve around the spinal cord with alteration in CSF flow and cord compression.
- *Cervical spine disease* – odontoid dysplasia and ligamentous laxity predispose to C1-2 subluxation. This is particularly a feature of MPS-IV.

- *Other vertebral column disease* – a variety of ligamentous changes and altered morphology of the vertebral bodies can be associated with significant kyphoscoliosis. Evidence from cadaveric studies suggests that more severe degrees of kyphosis beyond 63 degrees may be associated with raised spinal intramedullary pressures which is thought to contribute to an elevated risk of cord ischaemia[(2)].

Given the significant pathophysiology resulting from all variants of MPS, an up to date and comprehensive understanding of the patient's condition is essential to planning for any procedure.

2 Preoperative Assessment and Preparation

2.1 Understanding the Patient's Present Condition

Patients with any MPS diagnosis are regularly reviewed by specialists from the Genetic Metabolic Disorders Service. A typical program includes baseline assessment and surveillance including:

- Regular clinic reviews.
    - Particular features on physical exam include assessment of change in musculoskeletal features and ENT exam.
- Regular cardiology assessment incorporating echocardiography. This will be guided by patient condition but is likely to be 2- 3 yearly. Holter monitoring may be indicated if there is any history of blackouts or falls.
- Respiratory assessment including spirometry once the child is over 5 years of age.
- Overnight sleep studies – both at around 2 years and then approximately 3-yearly unless there is evidence of need earlier than that.
- Regular imaging of the spinal cord, preferably with MRI. This is generally done on a yearly basis.
- Spinal imaging:
    - MRI full spine to assess for cord compromise.
    - Standing thoracolumbar radiographs to assess for kyphosis.
    - Flexion-extension cervical radiographs to assess for instability.
- Annual endurance testing.

Although patients with MPS will sometimes require emergency surgery, the majority of procedures requiring general anaesthesia in MPS children are elective and patients should be reviewed through the Pre-Anaesthetic Clinic process, either in person or utilising telemedicine options, well in advance of the surgery. Common indications for elective presentation include diagnostic imaging requiring general anaesthesia, orthopaedic and spinal surgery, ENT surgery, general surgical procedures and insertion of long term central venous access devices (CVADs).

It is particularly relevant to establish the following key information both before elective surgery and to help guide assessment in an emergency procedure setting:

1. **Is there information from a previous anaesthetic?**

   Specific information from any recent anaesthetic, particularly relating to management of the airway (including any difficulties with face-mask ventilation, supraglottic airway insertion, intubation or extubation), challenges or precautions with patient positioning, issues relating to vascular access, particular challenges with analgesia and postoperative course are highly useful in subsequent perioperative planning.

2. **When was the most recent specialist review?**

   In any elective situation, it is recommended that the patient should have had some form of review by the Genetic Metabolic team within the last 6 months. This review will help define whether updated subspecialty reviews are required.

3. **Do subspecialty reviews need repeating?**

   Prior to undergoing anaesthesia it is preferable to have summaries from the following subspecialty areas, as long as patient symptoms have not changed since that review:

   - Cardiology within the last 2 years.
   - Respiratory function within the last 2 years.
   - Sleep studies within the last 2 years.

   If any change in symptoms has occurred, it is preferable to repeat the review prior to proceeding to general anaesthesia.

4. **What is known about the spinal cord?**

   The results of the most recent spinal cord imaging should be checked to seek evidence of compression at any level, and the degree of any kyphosis. If spinal cord imaging is older than 12 months, this should prompt a discussion with the Genetic Metabolic Disorder Service regarding the potential for progression of any changes related to the cord and consideration of repeat imaging. This decision-making may be informed by whether there is prior documentation of the spinal manifestations being benign.

5. **What disease-specific treatment is the patient receiving?**

   - Historically the management of patients with MPS has been palliative with a focus on symptomatic treatment. Modern treatment options include haematopoietic stem cell transplantation (HSCT) for MPS I, II and VI. Enzyme replacement therapy (ERT) is available for patients with MPS I, MPS II, MPS IVA and MPS VI.
   - HSCT is performed before the age of 2, before developmental deterioration begins. It can preserve intellectual development, improve hearing, joint mobility, respiratory function, and cardiac function. It can also resolve upper airway obstruction including sleep apnoea, the facial features become less coarse and growth improves. Skeletal abnormalities do not respond to HSCT therefore patients post HSCT may still have limited neck mobility or mouth opening and will require multiple orthopedic and spinal procedures. In spite of this, several studies report lower incidences of airway complications in patients who received HSCT[1,3].

- Recombinant ERT is administered as a weekly infusion, and has proved to be safe, with minor allergic responses to the infusion being the main side effects. It is indicated as the primary treatment in MPS I (attenuated), MPS II, MPS IVA and MPS VI, or as an adjuvant to HSCT where it has been shown that administration prior to and after HSCT can improve engraftment. Although ERT produces a variable but often significant improvement in myocardial, airway and pulmonary complications, improved appearance and some quality of life parameters, the benefits to airway management are not as apparent compared to HSCT[1,3]. This is possibly related to it being received later in the patient's clinical course. Unfortunately ERT does not appear to significantly improve pre-existing neurocognitive dysfunction, skeletal abnormalities or cardiac valvular dysfunction.

2.2 Specific Consideration of Risk of Spinal Cord Injury

Patients with MPS are at risk of spinal cord injury in the perioperative period. It is therefore vital that the indication for the procedure is always weighed up against this risk. There are numerous case reports describing different patterns of spinal cord injury[4,5]. Some injuries described in the literature coincide with a location of maximal kyphosis, while others are distant to this location. They are reported in a variety of surgeries. Some are associated with hypotension intraoperatively, while others are not. Some seem to be associated with positioning during the procedure.

One approach to minimising the risk of spinal cord injury is to undertake intraoperative neuromonitoring (IONM) during procedures. Monitoring with both Somatosensory Evoked Potentials (SEPs) and Motor-Evoked Potentials (MEPs) may provide the operative team with a warning of impending cord compromise and thereby provide the opportunity to respond to try and optimise cord perfusion.

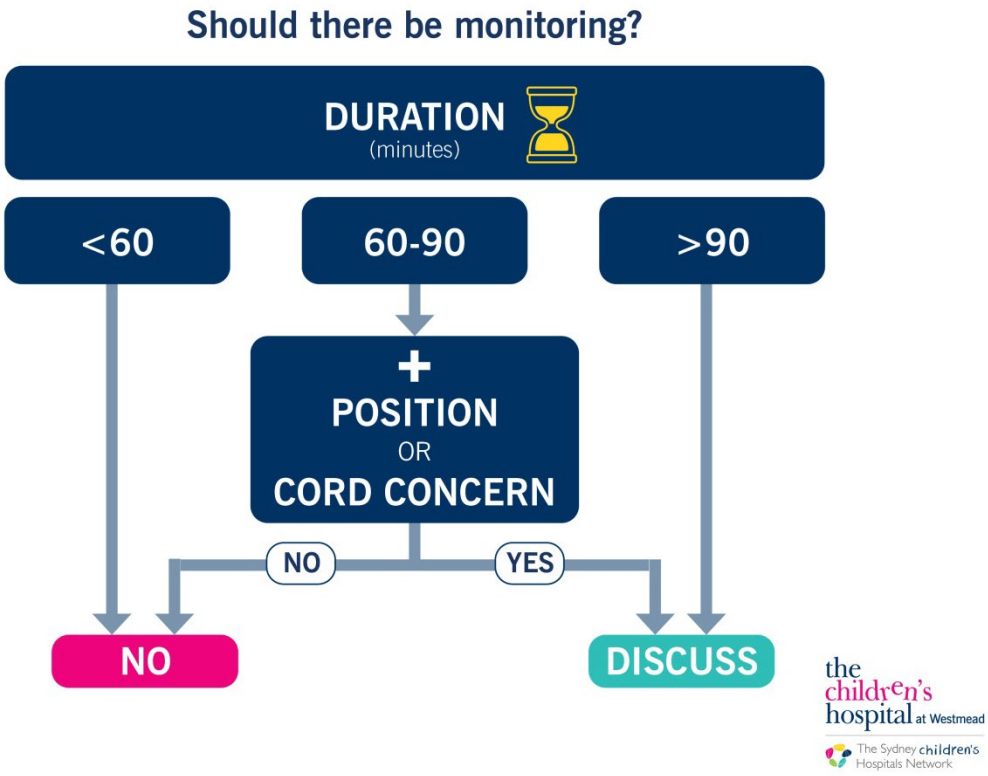
Utilisation of IONM imposes its own logistical challenges and prolongs the duration of surgery to establish baseline measurements. Increasing the duration of surgery may itself increase the possibility of perioperative complications.

As there are multiple factors contributing to the risk of spinal cord injury, it is sensible to consider more than any single factor when considering whether it is appropriate to arrange IONM.

At CHW, we suggest considering the following 3 elements:

- Total duration (anaesthetic plus surgery/procedure).
- Positioning required.
- Any known concerns about the cord.

Consideration of these elements is not expected to give a simple answer on every single occasion. As such any clinician is encouraged to consider the specific case they are dealing with and then, where indicated, initiate a discussion with senior colleagues from anaesthetics, the metabolic team and a spinal surgeon to weigh up the pros and cons and make a balanced decision. The following outline of the process highlights this.



The first question should always be about the duration. The duration includes consideration of the likely required anaesthetic time in addition to the set-up for the procedure and the procedure itself. In the context of considering IONM, it must be remembered that IONM requires time both for set-up and then establishment of baseline measurements. This may expand the time of the procedure itself and therefore influence the decision as to whether IONM is appropriate in the first instance.

If it is expected to be under 60 minutes, then there is likely to be no indication for spinal cord monitoring.

If the patient is to have a procedure that is likely to fall between 60 and 90 minutes, then some consideration should be given to whether the position required for the procedure might put the cord at greater risk. Positions other than neutral may prompt this concern.

Alternatively it may be well known that the cord is of particular concern. This may be on the basis of assessment of the clinical picture and natural history of disease progression. It may be on the basis of known symptoms or signs in the particular patient. It may be on the basis of spinal cord imaging. Such concerns prompt an earlier consideration of a need for senior input to decision-making.

In instances where the procedure will last over 90 minutes, there is a stronger case that IONM should be arranged. However this still requires discussion amongst senior clinicians and then a decision to approach the IONM service to complete the decision-making process. It is not universally the case that every patient who might have a procedure that goes beyond 90 minutes will require IONM.

Note that spinal cord injury may still occur when using IONM. For each procedure, the risk of spinal cord injury should be discussed with the patient and family with discussion of the ways this risk is minimised.

It is also important to note that in circumstances where IONM is not feasible (e.g. MRI or an emergency out of hours case) this does not change the goals to provide perioperative care which optimises perfusion of the spinal cord.

A balanced decision is also required with consideration of these principles when it comes to decisions to combine procedures within a single anaesthetic, or indeed to undertake additional anaesthetics for procedures that could otherwise be completed with a single anaesthetic solely on the basis of keeping each anaesthetic duration under a specific cut-off time. Undertaking multiple general anaesthetics to undertake patient care while keeping duration under 60 minutes is not necessarily preferable to a single anaesthetic that extends just beyond 90 minutes.

Case Example

A 3 year old patient is scheduled for MRI brain and spine under general anaesthesia as part of their initial work-up with a diagnosis of MPS I. They have had one previous general anaesthetic which was uneventful. For completion of the scheduled sequences, the MRI itself may take 80 minutes of scanning time. With anaesthetic time this may mean the total procedural duration exceeds 90 minutes.

Staff from the Radiology Department note this and are aware of the Perioperative MPS guideline. They initiate a discussion between the Metabolic Team, Anaesthesia and the Radiology Department about whether the best approach is to book the brain and spine MRIs as separate investigations under GA.

The metabolic team are able to indicate that the likelihood of significant spinal cord concerns for this patient are low. The anaesthetics team assess that it is likely that minimal anaesthesia time will be required. The group agrees that they will proceed with a single MRI to undertake all sequences and discuss this plan with the child's parents. The total duration of the whole procedure ends up being 98 minutes.

3 Care at the Time of Anaesthesia

Patients with MPS are at increased risk of complications during anaesthesia. Examination of 753 patients in an MPS-I registry having at least one surgery during the sampling time showed that mortality within 30 days of surgery was 4.2% (or 0.7% per surgical procedure)[6]. This includes patients having HSCT but clearly highlights that MPS patients are vulnerable in the perioperative period. Recent reviews describe anaesthetic complication rates anywhere between 9% and 25.6%[7,8].

Anaesthesia should therefore involve an experienced anaesthetics team on all occasions.

3.1 Premedication

While some patients with MPS, particularly MPS II and III, may display challenging behaviours, any premedication needs to be considered carefully in the context of risk of airway obstruction.

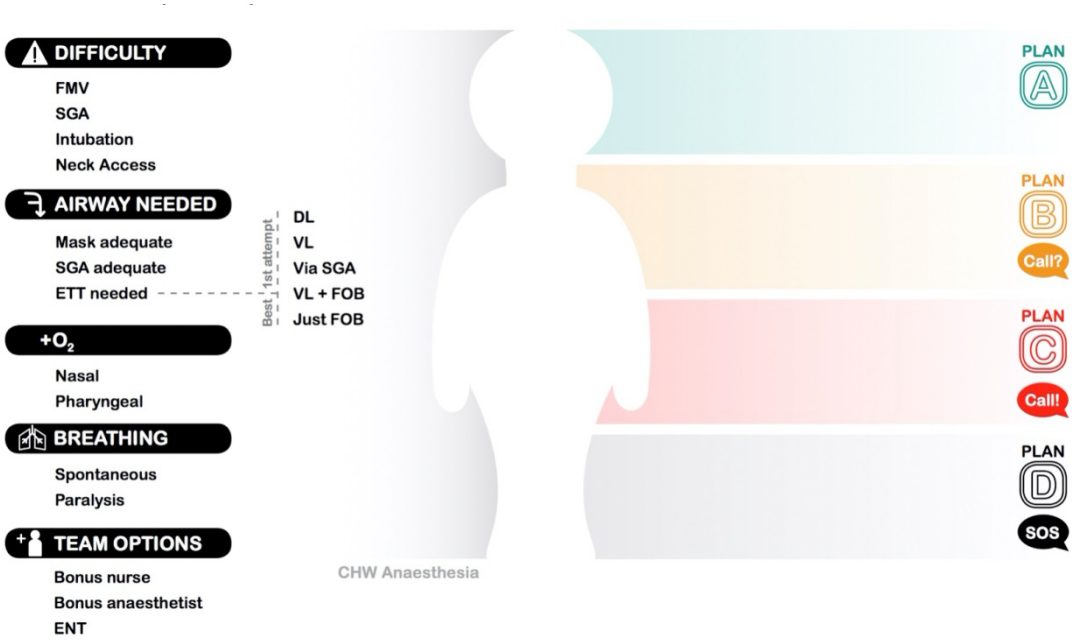
3.2 Considerations Around Induction

The total duration of the anaesthetic may be a critical factor in minimising risk. Given the potential for difficult airway management consideration should be given to utilising the operating room for induction rather than the anaesthetic bay. This offers greater all-round access to the patient for airway management. For cooperative patients it also offers the opportunity to position the patient for surgery with their cooperation while able to advise that they are comfortable. Time may be saved by avoiding the need to transfer the patient into the room.

3.3 Airway Management

All elements of airway management may be difficult in MPS patients. The one subtype where this does not apply is MPS III. A recent retrospective review examined 86 anaesthetics for 34 patients[9]. There were only 2 episodes of difficulty with laryngoscopic view, 1 failed intubation and 0 cases of difficulty with mask ventilation.

For all patients a comprehensive airway strategy should be prepared and fully briefed with the involved team. The Airway Decision and Planning Tool developed by the Department of Anaesthesia at CHW is one framework for making such a plan:



Specific points derived from the published literature may help inform decision-making by the team:

- Most published literature recommends maintenance of spontaneous ventilation until the airway has been secured, noting that administration of muscle relaxants may be associated with airway obstruction[10].
- A history of sleeping in a specific position may suggest that certain postures may help prevent or alleviate airway obstruction during induction of anaesthesia through the period of securing the airway, including the option of lateral positioning[10].
- Face-mask ventilation is generally successful with low rates of failed mask ventilation[11].
- Supraglottic airway insertion is likewise generally successful and therefore provides a good option for maintaining oxygenation[8,11].
- However, a recent retrospective review incorporating 67 patients with MPS (63) and mucolipidoses (4) indicated that SGA was associated with a need for conversion to another airway approach in 10.7% of cases, and was associated with a 14.4% rate of airway complications.
- The same paper examined success and complication rates with different approaches to intubation. The most consistently successful approach was intubation with a fibreoptic bronchoscope via SGA with 0 failures over 59 intubations and 0 episodes of needing conversion. This compared favourably with direct laryngoscopy (47.8% with airway problems and 24.4% conversion rate), videolaryngoscopy (10.1% with airway problems and 12.5% conversion rate).
- Limitations to neck movement should be considered as part of the approach to securing the airway.
- Choose a small-sized paediatric cuffed endotracheal tube. [3]

Note that patients with MPS also represent a challenge at the time of extubation. Preparation for extubation should include administration of intravenous steroids intraoperatively, reversal of muscle relaxants if used, consideration of utilisation of an airway adjunct to help maintain a patent airway after extubation (e.g. nasopharyngeal airway), and a defined plan for delivery of ongoing respiratory support after extubation (e.g. post-procedural CPAP or humidified high flow nasal cannulae amongst other options). A plan for reintubation should be prepared.

3.4 Patient Position

Many surgeries will require specific positioning to facilitate surgery. Where feasible checking with the patient that this position is comfortable may be useful, both because pain can be a significant issue for MPS patients and as neck positioning may create issues (see section 3.5).

On some occasions previously, maintenance of a consistent position has been assured by utilising the orthotics service to create a brace to maintain head and neck position during the operation, or even for afterwards in the recovery phase.

3.5 Spinal Cord Precautions

As outlined above, patients with MPS are at significant risk of spinal cord injury in the perioperative period.

General approaches to try and provide protection of spinal cord perfusion include:

- Maintain mean arterial blood pressure within 20% of the patient's baseline blood pressure. Consider invasive arterial blood pressure monitoring to help with haemodynamic monitoring.
- Maintain normocarbia.
- Ensure Hb is >80 g/L.
- Careful positioning with avoidance of flexion, extension or rotation of the spine.
- Where intraoperative neuromonitoring is used, maintaining normothermia prevents changes in SSEP latency related to temperature.

It should be standard practice to document a neurological examination prior to surgery, and again afterwards.

Use of Intraoperative Neuromonitoring

In some cases intraoperative neuromonitoring (IONM) may be appropriate (see section 2.2) and this must be organised in advance. While IONM can be booked with the aid of the perioperative CNS2 team, the program for IONM (and in particular where being used for non-scoliosis surgery) is overseen by the Department of Neurology. The process for first considering the role of IONM and then arranging for not just the appropriate equipment but the appropriate technical team with clinician support is as follows:

1. The particular case is referred to a senior clinician group:
    - This group requires a member of the genetics metabolic service, an anaesthetist and one of the spinal surgeons to inform an assessment of risk to the spinal cord. The group may need to consult other specialists to inform their assessment (e.g. the surgeon for the intended surgery to understand requirements of the procedure and likely duration).
2. This senior group then assesses the potential role for IONM as described in the guideline on a case-by-case basis.
3. If the senior clinician group reaches a conclusion that IONM would enhance patient safety they will then forward on information to the Specialist Neurologist overseeing the neurophysiology service including the following information:
    - Patient demographics.
    - Nature of intended surgery.
    - Date of intended surgery.
    - Criteria on which IONM has been recommended by the senior clinician group.

The Specialist Neurologist will then provide final approval to support IONM on the day of the intended procedure.

Final arrangements for the specific date of surgery will then need to consider:

- Availability of the technician support to manage IONM.
- Availability of an appropriate clinician to support IONM interpretation. IONM requires expertise in interpretation so the clinician support for the technician team is essential. For scoliosis surgery this role is undertaken by the surgeon. On previous occasions during other types of surgery one of these surgeons has also attended to provide this support. For other indications it is likely that an experienced neurologist will be the most appropriate clinician to provide this vital input for the team.

Final negotiation of the date of surgery will therefore require communication between the proceduralist, the neurology team, anaesthesia, the Waitlist Manager and the Surgical CNCs who manage equipment bookings.

Technical Aspects of Use of IONM

To establish reliable IONM and make the use of the additional information it provides, certain technical considerations are vital:

- TIVA anaesthesia may be preferable to facilitate IONM.
- On rare occasions it may be worth considering whether it is appropriate (and also feasible) to establish IONM baseline measurements prior to manipulation or instrumentation of the airway where there are concerns related to neck movement.
- Measures with a focus of maintaining spinal cord perfusion are appropriate:
    - Maintain mean arterial blood pressure within 20% of the patient's baseline blood pressure.
    - Maintain normocarbia.
    - Maintain haemoglobin > 80 g/L.
    - Maintenance of temperature helps support IONM.

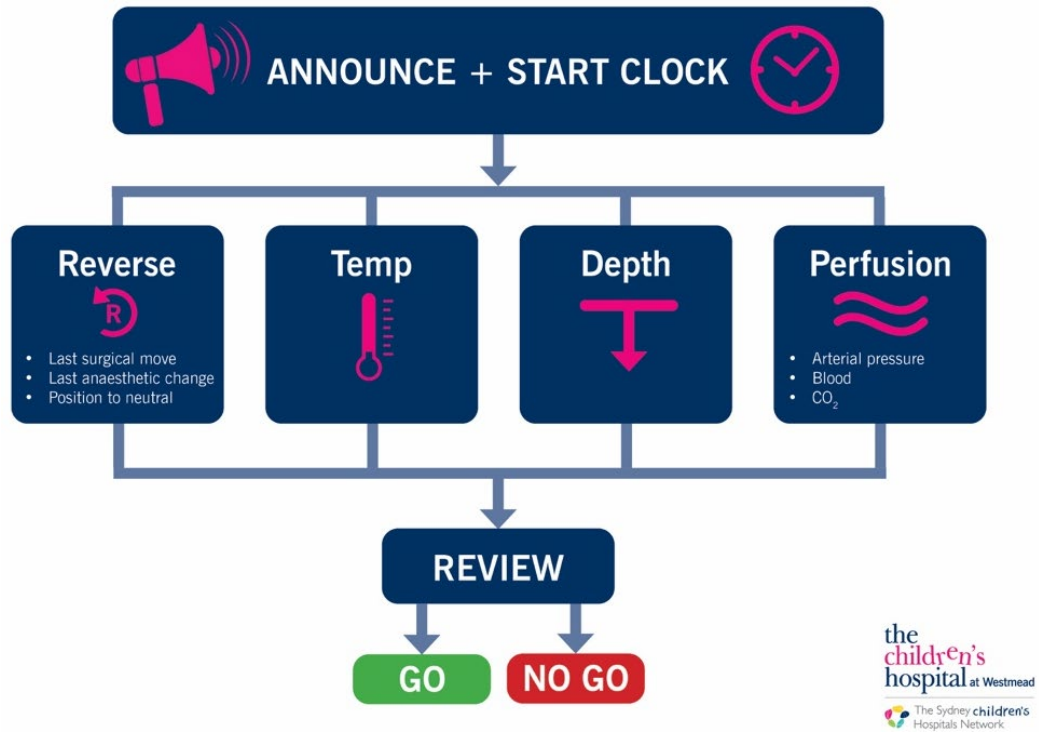
Responses to Changes in Monitoring Signals

Before commencing the operation, as part of the team huddle an agreed approach to responding to changes in IONM signals should be discussed.

For SSEPs, a significant change is a decrease in amplitude of > 50% or an increase in latency of > 10% from baseline.

For MEPs, a significant change in polyphasic morphology or a decrease in amplitude of > 50% compared to baseline is considered to be a significant change.

The response to a significant change involves some simple things being done by the team simultaneously as shown in the following diagram.



The aim should be to take steps to address the items above and reach the review point as promptly as possible for the team to then discuss and agree on whether to proceed with surgery if the IONM has improved or bring the procedure rapidly to a finish.

If signals do not return acceptably towards baseline the procedure should be terminated. Even if the signals do return acceptably towards baseline, efforts should be made to expedite completion of the procedure.

Decision-Making Where IONM Baseline Cannot Be Established

On some occasions it may not be possible to establish useful monitoring signals. This possibility should be acknowledged prior to the procedure and discussed with the patient and family where there is a plan to utilise IONM.

In the event of not being able to establish baseline monitoring signals, the same checks and responses as required when there is a change in signal are appropriate. Check any reversible factors, make sure the patient is warm, review anaesthetic depth and take steps to maintain cord perfusion. If it is still not possible to establish baseline readings, this suggests that there will not be any ability to offer IONM as an adjunct to patient monitoring.

If the surgery is elective it is reasonable to consider not proceeding. However in this patient group it is likely that the surgery is necessary and that steps have already been taken to minimise duration of the procedure. As a return visit to the operating theatre is not likely to change whether or not IONM can be used, it is reasonable to proceed with the procedure while maintaining the same focus on spinal cord perfusion. This possibility should be part of the discussion with the patient and family when discussing the procedure as part of informed consent.

3.6 End of Procedure

Depending on the nature of the procedure, it may be appropriate to consider leaving the patient intubated, though there are advantages to early extubation and neurological assessment.

As noted above extubation may be a key point of risk for patients. Patients should be extubated after administration of IV steroids, fully reversed where muscle relaxants have been used, and with the patient awake.

A plan for ongoing respiratory support should be prepared. This may involve use of the patient's own non-invasive respiratory support, institution of new support or humidified high flow nasal cannula oxygen.

3.7 Postoperative Care

Patients with MPS and a need for non-invasive respiratory support should be considered for management in a high acuity setting. In the postoperative period, ongoing neurological observations for the first postoperative night should be continued where patients are admitted.

3.8 Analgesia

Analgesia can be challenging in patients with MPS. Opioids may be associated with drowsiness or respiratory depression. Neuraxial techniques may be associated with increased risk in MPS patients. Although there are reports of successful use of epidural anaesthesia, observed cases of spinal cord infarction following lower extremity surgeries seem to indicate an elevated risk of complications[12,13]. There is no evidence that regional analgesia techniques involving plane blocks or peripheral nerves are associated with elevated risk.

It is therefore reasonable to consider:

- Use of ERAS-style pathways wherever possible.
- Multimodal approaches with minimal use of opioids wherever possible. This may include:
    - Simple analgesics such as paracetamol.
    - Non-steroidal anti-inflammatory drugs.
    - Regional analgesic approaches, such as peripheral nerve blockade, plane blocks or wound catheters. Ongoing infusions of local anaesthetic can be considered.
    - Other opioid-sparing options (e.g. alpha-2-agonists, gabapentinoids) though noting these may also be associated with sedation in some patients at some doses.

4 Emergency Procedures

Wherever possible surgery for MPS patients should be undertaken on an elective basis with time for planning and preparation. An MPS patient may present with a need for emergency surgery that cannot be delayed. This should be established at the time of referral.

Therefore whenever a booking for an emergency case is received, it is vital to establish if the patient's clinical condition would allow for the operation to happen in daylight hours, with an experienced anaesthetics team. If the patient's condition allows planning of the surgery in daylight hours, it may allow consideration of the potential role for IONM. However, IONM may not always be immediately available.

If the patient's condition requires that they proceed immediately to surgery then planning should proceed following similar principles to those for elective surgery. The only major difference is that emergency IONM is not feasible. Planning should therefore include:

- Preparation for difficult airway management.
- Maintenance of a neutral position of the head and neck throughout, if compatible with the procedure.
- Optimisation of spinal cord perfusion.
- Postoperative disposition should be planned with an appropriate postoperative bed arranged in advance.

5 Ongoing Monitoring of Outcomes

Ongoing monitoring of perioperative outcomes in MPS patients is a requirement of a comprehensive approach to managing these challenging patients. 6-monthly review of all cases should be undertaken by a multidisciplinary team involving anaesthesia, the pain service, the genetic metabolic service, and neurology/neurophysiology.

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Appendix 1

Recommendation to Neurology for Intraoperative Neuromonitoring

Demographics	Relevant Clinical Background
Name *DOB* *MRN*	

Intended Surgery

Criteria for Recommendation of IONM

Appendix 2

Responding to a Change in Intraoperative Neuromonitoring