Chapter 48

Hurler Syndrome

Kirk Lalwani and Erin Conner

Case Scenario

An 11-year-old girl with Hurler syndrome presents to the gastrointestinal suite for an aerodigestive evaluation including upper endoscopy and bronchoscopy. She has had two prior anesthetics. At the time of her first anesthetic for a Nissen fundoplication-gastrostomy tube placement at 3 years of age her airway was described as a Grade III view with a Wis-Hipple 1.5 blade utilizing direct laryngoscopy. She subsequently had another anesthetic at 8 years of age for open reduction of a supracondylar fracture, at which time a view was unobtainable on direct laryngoscopy with either a Miller 2 or Macintosh 2 blade. She required two-handed bag-mask ventilation; a laryngeal mask airway was ultimately placed, and the case proceeded without incident.

Echocardiography performed 6 months prior revealed the following:

- *Moderate-to-severe mitral regurgitation*
- *Dilated cardiomyopathy with mildly impaired ventricular function*

Key Objectives

- Discuss the pathogenesis of the mucopolysaccharidoses.
- Review the anesthetic considerations for patients with Hurler syndrome.
- Summarize hemodynamic goals for a patient with mitral regurgitation.
- Develop a plan to manage a known difficult airway in a patient with Hurler syndrome.
- Outline an anesthetic plan for aerodigestive evaluation.
- List potential airway management techniques.

Pathophysiology

What are the mucopolysaccharidoses?

The mucopolysaccharidoses (MPS) are a diverse group of lysosomal storage diseases caused by the genetic insufficiency of enzymes contributing to the degradation of glycosaminoglycans (GAGs). Glycosaminoglycans are then deposited in multiple organs of the body leading to widespread dysfunction, characteristic facies, and in some cases, early mortality. The constellation of signs and symptoms varies according to the specific enzyme deficiency.

These patients present multiple challenges to the anesthesiologist. Key features include difficult mask ventilation, difficult intubation, cardiac disease, coronary ischemia, obstructive sleep apnea (OSA), and skeletal abnormalities. Careful and thorough preoperative evaluation is crucial for safe management and anesthetic planning, and should be focused on airway management, as well as the cardiovascular, pulmonary, and neurologic systems. Cardiac valvulopathies and ventricular dysfunction are common and must be managed appropriately. Postoperatively, consideration should be given to caring for these patients in a high-acuity environment, depending on the type of surgery and severity of the disease.

What are GAGs?

Glycosaminoglycans are polysaccharides (dermatan, heparan, keratan, and chondroitin sulfates) that are degraded by lysosomal hydrolases. They have many functions in the body, including lubrication of joints, cell growth, regulation of proliferation, and adhesion to cell surfaces in molecules. When GAGs cannot be degraded, they accumulate and damage vital organs, bones, joints, and the central nervous system.

What is the classification system for MPS?

There are 7 types of MPS disorders (I, II, III, IV, VI, VII, and IX) and 11 subtypes. (See Table 48.1.)

What is the pathogenesis of Hurler syndrome, or MPS I?

Previously known as "gargoylism," MPS I is an autosomal recessive disorder caused by a deficiency of α-L-iduronidase, an enzyme required to break down dermatan sulfate and heparan sulfate, both of which accumulate

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

Table 48.1 Classification of Mucopolysaccharidoses

Type	Eponym	Defective Enzyme	Accumulated Product	Clinical Symptoms	Notes
IH IH/S IS	Hurler Hurler-Scheie Scheie	Alpha-L-iduronidase	Heparan sulfate, dermatan sulfate	Intellectual disability, micrognathia, coarse facial features, macroglossia, retinal degeneration, corneal clouding, cardiomyopathy, hepatosplenomegaly	The Hurlers form of type 1 is most severe, though all three may express these features
II	Hunter	Iduronate sulfatase	Heparan sulfate, dermatan sulfate	Intellectual disability, as well as the same symptoms as type I in more mild form	Only MPS that is X-linked recessive inheritance; all others are autosomal recessive
III A–D	Sanfilippo	A: Heparan sufamidase B: *N*-acetylglucosaminidase C: Heparan-α-glucosaminide, *N*-acetyltransferase D: *N*-acetylglucosamine 6-sulfatase	Heparan sulfate	Developmental delay, severe hyperactivity, spasticity, motor dysfunction	Most pronounced neurologic deficits of all MPS
IVA-B	Morquio	A: Galactose-6-sulfate sulfatase B: β-galactosidase	A: Keratan sulfate, chondroitin 6-sulfate B: Keratan sulfate	Severe skeletal dysplasia, short stature, motor dysfunction	
VI	Maroteaux-Lamy	*N*-acetylgalactosamine-4-sulfatase	Dermatan sulfate	Severe skeletal dysplasia, short stature, motor dysfunction, kyphosis, heart defects	
VII	Sly	β-glucuronidase	Heparan sulfate, dermatan sulfate, chondroitin 4,6-sulfate	Hepatomegaly, skeletal dysplasia, short stature, corneal clouding, developmental delay	
IX	Natowicz	Hyaluronidase	Hyaluronic acid	Nodular soft-tissue masses around joints with pain and swelling, short stature, normal intelligence	

in body tissues. Diagnosed at an average age of 9 months, MPS I is the most severe form of MPS. Without treatment, death occurs within the first decade of life. The manifestations grow progressively worse as the child gets older, and these patients have been described as some of the most challenging in all of pediatric anesthesia.

Clinical Pearl

Mucopolysaccharidosis I is the most severe form of MPS, with an average age at diagnosis of 9 months. Without treatment, death occurs within the first decade of life.

Are there any variants of MPS I?

Hurler–Scheie and Scheie syndromes are often referred to as the intermediate and mild forms of MPS I, respectively. Cognitive impairment is mild in Hurler–Scheie, but physical manifestations including growth retardation are severe. Scheie syndrome patients have near-normal intelligence and close to normal life expectancy. Since physical manifestations are milder, these patients are often diagnosed later in life.

What are the characteristic features of Hurler Syndrome (MPS I)?

Patients with Hurler syndrome have characteristic coarse facies, macrocephaly, umbilical and inguinal hernias, angular thoracolumbar kyphosis (gibbus deformity), joint stiffness, progressive skeletal dysplasia (dysostosis multiplex), and growth retardation. They may also have ocular abnormalities, progressive neurologic disease, hydrocephalus, developmental delay, and hepatosplenomegaly. Cardiac and respiratory issues include macroglossia, airway compromise, obstructive sleep apnea (OSA), chronic and recurrent respiratory infections, restrictive lung disease, cardiac valvular disease, coronary artery disease (CAD), and cardiomyopathy.

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

What treatments are available for MPS?

Hematopoietic stem cell transplantation is effective at prolonging survival, preserving cognitive function, and reducing hepatosplenomegaly and sleep apnea. Weekly enzyme replacement infusion therapy with laronidase has also been effective at reducing liver volume, urinary GAG excretion, functional capacity, sleep apnea, joint flexion, visual acuity, and left ventricular (LV) hypertrophy. Enzyme replacement therapy allows minimal improvement in cognitive, skeletal, ocular, and heart valve function. However, most patients develop antibodies to laronidase that limit enzyme cell uptake.

What cardiac defects are commonly associated with MPS?

Cardiac defects are common in MPS, occurring in 60%–100% of patients. They are more common in syndromes where dermatan sulfate breakdown is affected (MPS I, II, and VI). Clinical signs and symptoms are uncommon despite the early development of cardiac lesions in severe forms of the disease, such as MPS I. Left-sided valvular lesions are more common as a result of thickened leaflets leading to regurgitation or stenosis. Progressive valvular disease ultimately leads to ventricular hypertrophy, overload, and dysfunction. Diffuse coronary artery narrowing or occlusion is most common in MPS I and II. Apical aneurysms have also been described along with diffuse narrowing of the great vessels, dilation of the aorta, and associated hypertension. Conduction defects are often seen in some types of MPS as well. Acute cardiomyopathy associated with endocardial fibroelastosis has been a presenting condition in some infants with MPS I at <1 year of age.

Clinical Pearl

Patients with MPS should have a full cardiovascular evaluation at time of diagnosis followed by regular monitoring (every 1–2 years for types I and VI and every 2–3 years for type II) as well as evaluation before any major surgical intervention. Full evaluation should include right arm and leg blood pressure measurements, careful auscultation, transthoracic echocardiogram, and 12-lead electrocardiogram.

Anesthetic Implications

What are the specific preoperative assessment concerns in a patient with MPS?

Cardiac: If the patient has MPS subtype I, II, or VI, a focused cardiovascular history and physical must be performed. Many of these children will not overtly manifest significant cardiac clinical signs and symptoms (in part due to inactivity and communication difficulties), and therefore require additional evaluation by their cardiologist. A recent echocardiogram (within 6 months) should be considered a necessity. While not yet routine in MPS patients, a dobutamine-stress induced echocardiogram to assess LV function and areas of under-perfused myocardium should be considered. This may lead to evaluation for CAD, which can commonly exist in MPS patients. Unfortunately, MPS patients usually develop diffuse coronary disease, which is less easily detected but still carries significant risk.

Airway: Obstructive sleep apnea occurs in >80% of patients with MPS I and II. Details of polysomnography, previous airway surgeries or the use of continuous positive airway pressure (CPAP) should be investigated in detail. Severe OSA with chronic hypoxemia can also result in pulmonary hypertension; if suspected, pulmonary hypertension should also be assessed by echocardiography.

Pulmonary: While many MPS patients have restrictive lung disease and may have had pulmonary function testing done, these tests can be difficult to interpret given the lack of standardized data in patients who often have significantly shortened stature and skeletal abnormalities. Therefore, these results should be taken into consideration, but not solely relied on. Treatment for chronic infections, and optimization of any reactive airway disease or chronic bronchospasm should be noted. Consultation with a pulmonologist may be required.

Neurologic: A neurologic exam focusing on hyperreflexia or other signs of neurologic compromise from cervical spine stenosis should be done in patients with MPS type I, II, IV, and VI. Flexion/extension imaging studies may be indicated.

Which MPS variants are associated with a difficult airway? What features make their airway management difficult?

Most serious anesthetic complications in patients with MPS are airway related: these can include obstruction, difficulty with oxygenation and ventilation, and difficulties with advanced airway device placement. Airway-related difficulties can also lead to possible cardiopulmonary compromise, which is particularly concerning in patients who may also have cardiovascular involvement depending on their MPS subtype. Difficulty with airway obstruction and intubation are most pronounced in patients with MPS

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

I and II, though the overall difficult airway incidence for all subtypes of MPS is >75%.

- ***Upper airway obstruction*** may be obvious on induction, with sternal and intercostal retractions and a poor capnography trace. A precordial stethoscope is useful, simple, and easy to use for early detection of compromised breath sounds.
- ***Bag-mask ventilation*** may also be more difficult due to a flattened nasal bridge, midface hypoplasia, mandibular abnormalities, and/or a short, thick neck.
- ***Tracheostomy*** can be technically difficult due to a short, thick neck. In an emergency securing a surgical airway in these patients may take longer than anticipated, so if there is significant concern about the airway, having a surgeon and necessary surgical equipment available at induction may be prudent.
- ***The internal upper airway*** may be further obstructed due to narrowing caused by the accumulation of GAGs, resulting in macroglossia, adenotonsillar hypertrophy, and thickened pharyngeal tissues.
- ***Laryngeal and tracheal*** accumulations of GAGs may also occur, causing distortion of normal structures and making identification of the glottis difficult. Given their airway narrowing, these patients may not be able to accommodate the expected age-appropriate endotracheal tube (ETT) size. Multiple sizes should be available, and the first intubation attempt should be with a full size smaller cuffed ETT than the patient's age would predict.
- ***Excessive and thick secretions*** can affect visualization of the glottis, particularly with fiberoptic intubation. Treatment with an antisialagogue preoperatively is useful.
- ***Cervical spine abnormalities*** may be seen in patients with MPS type I, II, IV, and VI. Spinal canal narrowing can lead to spinal cord compression with even minor neck manipulation. Both MPS type IV and VI may have associated atlantoaxial instability due to odontoid hypoplasia. This must always be considered and included in the plan for airway management and positioning. Manual in-line stabilization during airway management should be planned for all MPS patients.

The degree of obstruction on induction and intubation portends difficulty with ventilation post-extubation and should alert the provider to consider having CPAP available postoperatively, or even electively keeping the patient intubated overnight or longer in the intensive care unit (ICU) depending on the difficulty of intubation, length of surgery, and the patient's respiratory reserve.

Clinical Pearl

All MPS patients should be considered a difficult airway until proven otherwise. Difficulty with airway obstruction and intubation are most pronounced in patients with MPS I and II. In an emergency securing a surgical airway in these patients may take longer than anticipated, so if there is significant concern about the airway, having a surgeon and necessary surgical equipment available at induction may be prudent.

What factors have been associated with pediatric airway complications?

In a prospective multicenter study from the Pediatric Difficult Intubation (PeDI) Registry, several factors were associated with any complication (severe or nonsevere):

- Multiple (>2) tracheal intubation attempts
- Weight <10 kg
- Short thyromental distance
- Abnormal airway physical examination
- Persistent direct laryngoscopy (DL) attempts, with an incremental increase in the occurrence of complications with each additional intubation attempt

The success rate of first intubation attempts was lowest for DL (3%), and similar for video laryngoscopy (55%) and fiberoptic bronchoscopy (54%). Early transition to a non-DL method (after the first or second DL attempt) was also associated with fewer complications than cases with late transition (>2 DL attempts). Hypoxemia was the most common nonsevere complication that occurred (9% of intubation attempts). Interestingly, only 10% of practitioners provided supplemental oxygen during intubation attempts, which could have contributed to interrupted attempts and additional attempts, thus increasing the incidence of complications. The incidence of cardiac arrest in children with difficult intubation in this study was 1:68, which is substantially higher than in the general pediatric population of 1–2 in 10,000, and hypoxemia was no doubt a contributory factor in most of these arrests.

In another PeDI Registry multicenter study investigators found that on the first intubation attempt fiberoptic intubation via a supraglottic airway was more successful than video laryngoscopy in children <1 year old. They also noted that the incidence of hypoxemia was lower when continuous ventilation through the supraglottic airway was used throughout the intubation attempt.

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

What strategies from the PeDI Registry can prove useful for optimizing airway management in MPS patients?

Three strategies can be utilized from these studies to improve the management of difficult intubation and reduce complications:

1. In a known difficult intubation, consider video laryngoscopy or fiberoptic bronchoscopy instead of DL on the first intubation attempt.
2. If DL is used initially, transition early (after two attempts) to an alternate method.
3. Insufflate oxygen continuously into the airway at a sufficient flow rate for passive oxygenation to occur during all intubation attempts to reduce hypoxemia and the number of interrupted intubation attempts.

Clinical Pearl

Use or transition early to methods other than DL for endotracheal intubation and insufflate oxygen continuously during intubation attempt(s).

What are the anesthetic considerations for patients with mitral regurgitation?

The regurgitant volume in mitral regurgitation (MR) depends on the size of the mitral valve orifice, the heart rate (HR) and the left ventricle–left atrial (LV–LA) pressure gradient. Major hemodynamic goals for anesthetic management of patients with MR include maintenance of relative tachycardia, reduced afterload, and avoidance of significant increases in preload. When HR is decreased the increased diastolic time allows the LV to overfill, further distending the valve annulus and worsening regurgitation. Caution must also be taken with volume administration, as excessive fluid administration can also worsen left ventricular dilation. Increased afterload increases the LV–LA pressure gradient, causing more regurgitant flow. (See Table 48.2.)

Clinical Pearl

Major hemodynamic goals for anesthetic management of patients with MR include maintenance of relative tachycardia, reduced afterload, and avoidance of significant increases in preload.

Table 48.2 Common Valvulopathies and Hemodynamic Goals

Lesion	Preload/ Volume	Afterload/ SVR	Heart Rate
Aortic stenosis	Increase	Increase	Decrease
Aortic regurgitation	Decrease	Decrease	Increase
Mitral stenosis	Increase	Maintain or Increase	Decrease
Mitral regurgitation	Maintain	Decrease	Increase

What other anesthetic concerns exist for patients with MPS?

Given the potential for difficult airway management in the setting of spinal pathology, it is worth considering whether a patient would benefit from spinal cord neuromonitoring with evoked potentials. While this would be expected in spinal surgery, it should also be considered in cases that require any significant head movement, or in particularly long cases requiring nonneutral head positions.

Patients with MPS often develop restrictive pulmonary disease secondary to thoracic cage abnormalities or compromised excursion of the diaphragm secondary to hepatosplenomegaly. Respiratory therapies to address possible elevations in inspiratory pressures and/or bronchospasm should be readily available.

Excessive secretions and gastroesophageal reflux disease (GERD) should be expected in all MPS patients. While a rapid sequence intubation would not be advisable for a patient with a difficult airway, these patients should be considered high-risk for aspiration and precautions to minimize this risk should be taken.

When is intraoperative neuromonitoring useful or required when caring for patients with MPS?

Mucopolysaccharidosis patients often suffer from angular thoracolumbar kyphosis/gibbus deformity, which may predispose their spinal cord to intraoperative injury. There are multiple case reports of MPS patients presenting with postsurgical neurologic deficits after nonspinal surgery, leading several institutions to employ somatosensory evoked potential and transcranial motor evoked potential monitoring intraoperatively for these patients. While there are no defined guidelines, expert opinion and available evidence suggest the use of intraoperative neuromonitoring (IONM) for MPS patients who meet the following criteria: significant

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

kyphoscoliosis (>60 degrees), anticipated procedural duration >90 minutes, and/or expectation of extensive blood loss or hemodynamic fluctuations. In a recent report by Kandil et al. from Cincinnati Children's Hospital Medical Center, when these criteria were utilized to risk stratify patients, no new postoperative neurologic deficits were noted in patients who did not meet criteria for IONM, and when IONM was used for patients meeting criteria, 14% had significant changes detected with IONM which necessitated intervention.

Clinical Pearl

As the use of volatile anesthetic agents can significantly impact the reliability of IONM, total intravenous anesthesia (TIVA) with propofol and/or dexmedetomidine is the preferred anesthetic technique as these agents have the least effect on IONM signals.

What are the anesthetic considerations for these procedures?

Combined esophagogastroduodenoscopy (EGD) and bronchoscopy procedures are becoming more common as otolaryngology, gastroenterology, and pulmonology providers coordinate to simultaneously evaluate the anatomy of the upper airway, digestive, and respiratory systems in patients with complex issues during one anesthetic episode. Airway management may also require multidisciplinary coordination. However, if the patient is not having an airway evaluation and simply a combined bronchoscopy and EGD, these procedures could be performed with a natural airway, depending on the patient's anatomy and degree of airway obstruction. However, in a patient with likely obstructive airway disease and the potential for difficult intubation, this may not be an ideal way to ensure adequate ventilation.

Clinical Pearl

A preoperative discussion should be held with all proceduralists involved in a planned aerodigestive evaluation, focusing on the sequence of procedures, the airway management plan, and the management of potential complications.

Should this case be performed in a location that is remote from the general operating rooms?

Where an aerodigestive evaluation occurs is often dependent on the institution and the available resources. As patients with MPS are likely to have complex upper airway anatomy, OSA or other pathologies resulting in more challenging airway management and ventilation, deciding whether this case can safely be performed in a gastrointestinal suite depends on the proximity of the equipment needed for difficult airway management as well as the support personnel able to respond in case of difficult/impossible ventilation and/or intubation. The size and setup of the room in a possible emergent situation is also an important consideration.

How could induction and maintenance of anesthesia be managed in this patient?

Given the likelihood of difficult bag-mask ventilation and intubation, this patient should have an intravenous line (IV) placed preoperatively. Premedication such as oral midazolam can be given to facilitate IV placement, though caution should be taken with dosing to avoid significant respiratory depression and it may be advisable to reduce the premedication dose by 20%–30%. Cardiorespiratory monitoring should be established and maintained once medication has been administered. Induction agents should be chosen that meet the goals of maintaining both spontaneous ventilation and appropriate hemodynamics in a patient with MR and potentially reduced ventricular function. Ketamine will allow maintenance of spontaneous ventilation and hemodynamics, though an antisialagogue such as glycopyrrolate should be given to avoid increasing secretions. Dexmedetomidine may be considered but may induce excessive bradycardia; pretreatment with glycopyrrolate may assist in adequately maintaining HR. Dexmedetomidine may also prolong emergence in these patients. The use of a muscle relaxant in an unproven airway should be withheld if at all possible and is usually not necessary for a fiberoptic intubation or laryngeal mask airway (LMA) placement. The use of neuromuscular blocking agents is acceptable for MPS patients as indicated by their surgical procedure requirements once they are intubated.

Anesthesia may be maintained with inhalational agents but patients with moderate to severe MR may be very sensitive to volatile agents. A balanced technique allowing volatile agent to be used at a lower MAC is generally preferable. Continuous infusions such as remifentanil and/or ketamine and/or propofol can also be used to achieve anesthetic goals without hemodynamic compromise.

Can this case be performed without endotracheal intubation? Could these procedures be done with an LMA?

Both EGD and bronchoscopy can be performed with a natural airway and spontaneous ventilation. However, in an MPS patient, this decision should not be made lightly.

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press

After induction, if the patient is able to maintain adequate ventilation and oxygenation while receiving TIVA with supplemental oxygen via nasal cannula, it may be safe to proceed with a natural airway. While the bronchoscopy portion of the procedure could be completed through the lumen of an LMA, the risk of LMA displacement with EGD exists. However, one could consider using an intubating LMA during bronchoscopy and placing an ETT for the endoscopy portion of the procedure if appropriate.

Clinical Pearl

Consider early use of an LMA in MPS patients who do not require endotracheal intubation, or in MPS patients with difficult or failed intubation attempts.

What are the considerations for extubation and postoperative management of these patients?

While early extubation is preferred to avoid significant airway swelling associated with ETT placement, this must be done cautiously. Patients should be fully awake, coughing vigorously, breathing adequately, and moving deliberately before they are extubated. All equipment should be available and ready for reintubation. Depending on the level of difficulty of initial intubation consideration can be given to leaving a tube exchanger in place. Transitioning the patient immediately post-extubation to CPAP is generally prudent. If extubation is delayed for any reason, the patient may benefit from a fiberoptic airway evaluation for swelling, debris, or bleeding prior to extubation. At the time of extubation the same precautions regarding available equipment and personnel should be followed even if the patient is no longer in the OR setting.

In some MPS patients with severe lung disease and/or challenging airway management it may be safer to keep the ETT in place and allow the effects of the anesthetic drugs and any iatrogenic airway edema to dissipate overnight in the ICU. This scenario is more likely with prolonged surgery and this decision should be made on a case-by-case basis.

If extubation occurs in the OR, the patient should be transitioned to CPAP immediately, and consideration should be made to continuing this in the ICU setting until the patient has fully emerged from anesthesia.

Should laryngospasm occur, how should it be managed?

The best cure for laryngospasm is prevention. Ensuring that the patient is wide awake (grimacing and making purposeful movements) and has a dry oropharynx (via suction and antisialagogue administration) makes laryngospasm less likely following extubation. The placement of an oral airway soon after extubation can also precipitate laryngospasm. Waking patients up following placement of an appropriately sized nasopharyngeal airway is extremely useful to avoid post-extubation obstruction and is far less likely to cause laryngospasm. Applying a jaw thrust in the "laryngospasm notch" may also be useful. If laryngospasm does occur, the use of CPAP and small doses of propofol may be sufficient to break the spasm without resultant apnea. If these measures are insufficient, administration of succinylcholine may be required, generally in a much smaller dose than needed for full paralysis.

If reintubation is required, serious consideration should be given to leaving the patient intubated overnight for the reasons mentioned earlier.

Suggested Reading

Braunlin E. A., Harmatz P. R., Scarpa M., et al. Cardiac disease in patients with mucopolysaccharidosis: presentation, diagnosis and management. *J Inherit Metab Dis* 2011; **34**: 1183–97.

Burjek N. E., Nishisaki A., Fiadjoe J. E., et al. Videolaryngoscopy versus fiber-optic intubation through a supraglottic airway in children with a difficult airway: an analysis from the multicenter Pediatric Difficult Intubation Registry. *Anesthesiology* 2017; **127**: 432–40.

Donaldson M. D. C., Pennock C. A., Berry P. J., et al. Hurler syndrome with cardiomyopathy in infancy. *J Pediatr* 1989; **114**: 430–2.

Fiadjoe J. E., Nishisaki A., Jagannathan N., et al. Airway management complications in children with difficult tracheal intubation from the Pediatric Difficult Intubation (PeDI) registry: a prospective cohort analysis. *Lancet Respir Med* 2016; **4**: 37–48.

Kandil A. I., Petit C. S., Berry L. N., et al. Tertiary pediatric academic institution's experience with intraoperative neuromonitoring for nonspinal surgery in children with mucopolysaccharidosis, based on a novel evidence-based care algorithm. *Anesth Analg* 2019: DOI: 10.1213/ANE.0000000000004215, PMID: 31082970.

Osthaus W. A., Harendza T., Witt L. H., et al. Paediatric airway management in mucopolysaccharidosis 1: a retrospective case review. *Eur J Anaesthesiol* 2012; **29**: 204–7.

Sawamoto K., Stapleton M., Almeciga-Diaz C. J., et al. Therapeutic options for mucopolysaccharidoses: current and emerging treatments. *Drugs* 2019; **79**: 1103–34.

Stapleton M., Arunkumar N., Kubaski F., et al. Clinical presentation and diagnosis of mucopolysaccharidoses. *Mol Genet Metab* 2018; **125**: 4–17.

Walker R., Belani K. G., Braunlin E. A., et al. Anesthesia and airway management in mucopolysaccharidosis. *J Inherit Metab Dis* 2013; **36**: 211–19.

https://doi.org/10.1017/9781108657341.049 Published online by Cambridge University Press