

# Orthopedic Manifestations of Mucopolysaccharidoses and Perioperative Considerations: A Review of Literature

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## Article Info

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### Keywords

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## Abstract

**Aims:** This review investigates the musculoskeletal complications across all mucopolysaccharidosis types, highlighting those specific to each subtype and exploring perioperative concerns.

**Methods:** A comprehensive literature review was conducted using PubMed, Google Scholar, and Cochrane without restrictions on publication date, language, or article type. Search terms included: *mucopolysaccharidoses, MPS, Hurler, Hunter, Sanfilippo, Morquio, Maroteaux-Lamy, Sly, Natowicz, orthopedic, musculoskeletal, anesthesia and perioperative complications.*

**Conclusions:** MPS disorders are multifaceted conditions with diverse musculoskeletal involvement. Orthopedic management is crucial, as these abnormalities impair mobility, reduce quality of life, and pose unique perioperative challenges. Common findings include joint contractures, dysostosis multiplex, and spinal malformations, all of which increase operative risk. Limited joint and spine mobility, or cervical instability may complicate intubation and anesthesia.

Radiologic screening for cervical instability and early neurological evaluation are recommended before anesthesia. Orthopedic surgeons must recognize these manifestations and perioperative complications to ensure proper multidisciplinary management and improve surgical safety.

## Introduction

Mucopolysaccharidoses (MPS) are a group of inherited diseases caused by deficiencies in lysosomal enzymes required for glycosaminoglycan (GAG) degradation<sup>1</sup>. Accumulation of GAGs results in multisystem involvement, including the cardiac, respiratory, neurological, and musculoskeletal systems<sup>2</sup>. Within bone, cartilage and connective tissue, GAG accumulation triggers metabolic, inflammatory, and immune responses, producing musculoskeletal manifestations<sup>1</sup>. Skeletal involvement, collectively termed dysostosis multiplex, includes platyspondyly with anterior beaking of vertebral bodies, odontoid hypoplasia, thoracolumbar kyphosis (Gibbus deformity), oar-shaped ribs, short thickened clavicles, bullet shaped phalanges (Figure 1), an enlarged skull with thickened calvarium and J-shaped sella turcica<sup>4,9,10</sup>. A summary of manifestations and perioperative concerns is provided in Table 1.

Advances in allogeneic hematopoietic stem cell transplantation (HSCT) and enzyme replacement therapy (ERT) have improved life expectancy but may not halt the progression of orthopedic disease, making surgical intervention and perioperative management increasingly important<sup>12-14</sup>. Certain deformities, particularly spinal deformities that risk spinal cord compression, require timely surgical

**Table 1:** Summary of Orthopedic Manifestations and Perioperative Concerns in MPS

MPS Type	Orthopedic Features	Perioperative Concerns	Unique Notes
I (Hurler, Hurler-Scheie, Scheie)	Dysostosis multiplex, hip dysplasia (nearly universal), cervical myelopathy, thoracolumbar kyphosis (Gibbus), short stature, carpal tunnel, joint arthropathy	High surgical mortality (~4.2%), airway obstruction (“worst airway problem in pediatric anesthesia”), cervical instability	Severe skeletal burden, short stature <4 ft
II (Hunter)	Similar to MPS I: dysostosis multiplex, cervical stenosis, short stature, hip dysplasia (milder), joint contractures, trigger digits	Difficult intubation (20x normal risk), failed extubation in some, cardiac disease	Only <b>X-linked</b> MPS
III (Sanfilippo)	Mild: hip dysplasia, femoral head osteonecrosis, minimal spine involvement	Lowest anesthesia risk of all MPS; occasional airway obstruction, seizures	Primarily <b>neurologic disease</b> , near normal stature
IV (Morquio A/B)	Severe skeletal dysplasia, short stature, genu valgum, hip dysplasia, kyphosis, cervicothoracic stenosis, odontoid hypoplasia → atlantoaxial instability, joint hypermobility (unique)	Severe airway/cervical instability risk, ischemic cord injury in spine/hip surgery, valvular disease	Only MPS with joint hypermobility
VI (Maroteaux-Lamy)	Dysostosis multiplex, cervical stenosis, atlantoaxial instability, thoracolumbar kyphosis, short stature, hip dysplasia, genu valgum, carpal tunnel	Severe airway/cervical instability risk, lung disease, postoperative tongue swelling	Severe spinal disease; progressive phenotypes (rapid vs slow)
VII (Sly)	Similar to I/II: short stature, cervical stenosis, kyphosis, hip dysplasia, genu valgum, clawed hands	Limited data; anesthesia deaths reported, airway obstruction, cardiac disease	Associated with <b>non-immune hydrops fetalis</b>
IX (Natowicz)	Joint disease only: periarticular masses, effusions, polyarthropathy, acetabular erosions	Minimal data; likely lower risk	Extremely rare (only 4 cases reported)



**Figure 1:** Bullet-shaped phalanges and short metacarpals with proximal pointing (arrows) in MPS I.

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intervention regardless of life expectancy due to the associated morbidity. Careful pre-operative planning is essential to minimize intraoperative and postoperative complication<sup>15</sup>.

## MPS I

### Overview

MPS I results from a deficiency of α-L-iduronidase

(IDUA), leading to accumulation of heparan sulfate and dermatan sulfate. It presents as a spectrum comprising Hurler (I-H), Hurler/Scheie (I-H/S), and Scheie (I-S)<sup>2</sup>. Children with Hurler syndrome will typically develop symptoms by 1-2 years of age. Characteristic features, termed “gargoylism”, includes coarse facies, macrocephaly with frontal bossing, flattened nasal bridge, wide eyes and enlarged lips<sup>5</sup>.

Additional manifestations may involve the neurological, respiratory, cardiac, gastrointestinal, musculoskeletal, ocular, auditory, and integumentary systems. Multidisciplinary management, including physical therapy, is used to address and prevent comorbidities in Hurler syndrome<sup>5</sup>.

### Orthopedic Manifestations

Musculoskeletal manifestations of MPS I commonly include short stature, dysostosis multiplex, progressive joint arthropathy, carpal tunnel syndrome, and cervical myelopathy due to vertebral abnormalities<sup>5,6</sup>. Arthropathy produces stiff joints and restricted motion, genu valgum, coxa valga, and camptodactyly.

Nearly all children with MPS I have significant hip dysplasia characterized by a vertical acetabulum, increased femoral neck-shaft angle, and gradual femoral head deformation<sup>4,9</sup>. Additional spinal pathology includes spondylolisthesis, odontoid dysplasia, and vertebral body hypoplasia. Circumferential arthrodesis is recommended for angular kyphosis correction (Figure 2)<sup>4,50</sup>. In one study, surgical correction of thoracolumbar kyphosis significantly improved walking distance, suggesting gait

improvement (Figure 3). Indications for surgery included worsening kyphosis, stiffening or irreducible curvature, and threatened spinal cord compression, as outlined by international consensus guidelines<sup>48</sup>. This consensus also established that the overall treatment goal is maintaining or improving quality of life<sup>49</sup>. A review of the MPS I registry reported 321 orthopedic surgeries among 544 patients, most commonly tendon releases, followed by carpal tunnel release, lower extremity deformity correction, and spinal surgeries<sup>16</sup>.

### Perioperative Management

A subsequent review of the MPS I registry reported a 30-day perioperative all-cause mortality rate of 4.2%. Although many deaths were not thought to be directly

attributable to the surgery performed, overall surgical risk in this population is markedly higher than average and must be discussed with families and the surgical team before intervention<sup>17</sup>. In particular, Hurler syndrome has been called “the worst airway problem in pediatric anesthesia”<sup>15</sup>. A 2012 analysis found that airway obstruction or difficult intubation accounted for approximately 20% of surgery related deaths<sup>27</sup>.

In one case report, a 31 year-old male with MPS I had surgery postponed due to failed intubation. CT imaging revealed laryngeal deviation, stenosis and extreme narrowing at the glottis. To allow for general anesthesia for spinal surgery, a tracheostomy was performed, which was subsequently closed 16 days postoperatively<sup>40</sup>. Careful preoperative planning should emphasize airway management, potentially including endoscopy or CT imaging, as well as evaluation for cardiac abnormalities and spinal cord compression.

### MPS II

#### Overview

MPS II, or Hunter syndrome, results from a deficiency of iduronate-2-sulfatase (I2S), causing accumulation of dermatan sulfate and heparan sulfate. It is subdivided into two phenotypes, MPS IIA and MPS IIB<sup>2</sup>. Clinical features include developmental delay, intellectual disability, coarse or thickened facial features, growth delay, short neck, hearing loss, macroglossia, airway obstruction, hepatosplenomegaly, and hernias<sup>2</sup>. With the exception of corneal clouding, many features overlap with MPS I. Notably, Hunter Syndrome is the only X-linked recessive MPS type<sup>2</sup>.

#### Orthopedic Manifestations

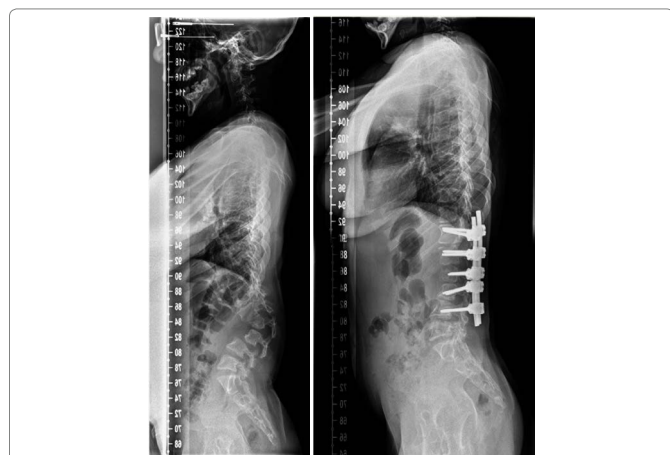
MPS II shares many musculoskeletal manifestations with other MPS types, including dysostosis multiplex, short stature, joint contractures, atlanto-axial instability, genu valgum, and trigger digits<sup>3</sup>. A 2024 study using 15 years of Hunter Outcome Survey data on 245 patients reported skeletal deformity in 90.2% of patients: 76.7% had upper body stiffness, 61.2% had lower body stiffness, and 63.7% had three or more joint manifestations<sup>35</sup>. MPS II, along with MPS I and VI, has a high prevalence of carpal tunnel syndrome<sup>4</sup>. Surgical release was performed in 18.2% of 527 patients in the 2009 Hunter Outcome Survey and in 20% of patients in the 2024 study, often requiring repeat procedures<sup>18,35</sup>. Hip dysplasia tends to be milder in MPS II than in MPS I, but has similar morphology and progression<sup>4</sup>.

HSCT can improve somatic and skeletal symptoms in MPS II, with greater efficacy when performed early, though not commonly used in the United States<sup>12</sup>. ERT with intravenous idursulfase can reduce mobility limitations



**Figure 2:** A 12 year-old with MPS I and thoracolumbar kyphosis. (a) Preoperative x-ray, (b) Preoperative CT, (c) Postoperative anterior fusion with tricortical bone graft and instrumented posterior fusion.

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**Figure 3:** Patient with MPS I and high lumbar kyphosis. A: Preoperative. B: Postoperative after correction.

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and other somatic manifestations, but does not cross the blood-brain barrier and therefore is not expected to improve cognitive function<sup>35</sup>. ERT showed improvement in shoulder joint range of motion but had little effect on other joints, and no effect on skeletal deformities. However, early initiation of ERT may provide some benefit in growth outcomes<sup>13</sup>.

### Perioperative Management

Data from the 2009 Hunter Outcome Survey showed that over 80% of patients required surgical intervention, often before the age of 10 years and frequently before MPS II was formally diagnosed<sup>18</sup>. The same study reported intubation difficulties in 22.0% of 428 patients, with 3.7% unable to be extubated. The study did not specify the duration of intubation or whether tracheostomies were performed in these cases<sup>18</sup>. A systematic review of tracheostomy placement in MPS patients found that nearly half of cases involved the MPS II subtype<sup>42</sup>. Thickened soft tissues, macroglossia, mandibular enlargement, short immobile neck, and restricted cervical spine and temporomandibular joint mobility make laryngoscopy challenging. As a result, difficult intubation is reported to be 20 times more common in children with MPS II compared to children of a similar age or weight<sup>19</sup>.

ERT has not been shown to reduce tonsillar or adenoidal hypertrophy or to significantly modify bronchial or tracheal stenosis or malacia<sup>13</sup>. MPS II is also associated with increased prevalence of cardiac hypertrophy, aortic dilatation, and valvular disease, indicating the importance of thorough cardiac screening and evaluation prior to surgery<sup>22</sup>.

### MPS III

#### Overview

MPS III, or Sanfilippo syndrome, comprises of four types, IIIA, IIIB, IIIC, and IIID, caused by deficiencies in heparan-N-sulfatase (SGHS),  $\alpha$ -N-acetylglucosaminidase (NAGLU),  $\alpha$ -glucosaminidase acetyltransferase (HGSNAT), and N-acetylglucosamine 6-sulfatase (GNS), respectively. This leads to an accumulation of heparan sulfate<sup>2</sup>. Although there is variation among subtypes, the primary manifestation is central nervous system dysfunction, progressing in three phases<sup>2</sup>. These include speech deterioration, behavioral problems such as hyperactivity, anxiety, autistic-like behavior, and aggression, followed by motor function decline, severe dementia, spasticity, and dysphagia<sup>2</sup>. While neurological features are dominant, peripheral manifestations may include facial dysmorphism, macroglossia, tonsil hyperplasia, short neck, organomegaly, obstructive lung disease, and cardiac pathologies<sup>28</sup>.



**Figure 4:** Osteonecrosis of bilateral femoral heads in an 8-year-old with MPS IIIA.

Adapted from Breyer SR, et al.<sup>44</sup> Licensed under CC BY 4.0 (<http://creativecommons.org/licenses/by/4.0/>).

### Orthopedic Manifestations

Orthopedic manifestations of MPS III are generally milder than in other MPS types<sup>8</sup>. Findings may include costovertebral malformations and joint contractures, though overall stature is often near normal<sup>4,10</sup>.

Proximal femoral epiphyseal dysplasia and osteonecrosis of the femoral head are common (Figure 4), whereas genu valgum is rare<sup>8</sup>. Hip deformities differ from other MPS types in that the acetabulum is typically normal; instead, increased femoral neck-shaft angle and femoral head deformities drive complications<sup>4</sup>. Surgical management of hip pathology remains controversial due to the risk of femoral head osteonecrosis and collapse<sup>9</sup>. Manifestations frequently observed in other MPS types, such as cervical stenosis, occipito-cervical instability, thoracolumbar kyphosis, and carpal tunnel syndrome, are uncommon in MPS III<sup>8</sup>.

### Perioperative Management

Retrospective studies report few, if any, cases of difficult intubation in MPS III, even when children underwent multiple procedures at different ages<sup>27</sup>. One study noted upper airway obstruction and desaturations during general anesthesia with a native airway, though these resolved without intervention<sup>31</sup>. A recent retrospective analysis of MPS patients from 2002-2018 found that MPS III carried the lowest risk and event rate for anesthesia related complications compared with other MPS types. Nevertheless, macroglossia, sleep apnea, and airway obstruction raise concern for difficult airway management<sup>28</sup>. When complications occurred, they were primarily respiratory (respiratory insufficiency, hypoxemia, airway obstructions), cardiocirculatory (bradycardia, tachycardia, heart failure), difficult airway management, or seizures<sup>28</sup>. Importantly, complication rates remained very low overall.

## MPS IV

### Overview

MPS IV, or Morquio syndrome, has two subtypes of differing severity. MPS IVA, the more severe phenotype, results from deficiency of N-acetylglucosamine-6-sulfate sulfatase, leading to accumulation of keratan sulfate and chondroitin-6-sulfate<sup>21</sup>. MPS IVB is caused by  $\beta$ -galactosidase deficiency, resulting in accumulation of only keratan sulfate and a milder phenotype<sup>2</sup>. These substrates primarily accumulate in bone, cartilage, heart valves, and cornea, producing skeletal abnormalities within the first few years of life<sup>21</sup>. Common features include corneal clouding, hearing loss, respiratory obstruction, sleep apnea, and only mild cognitive impairment compared with other types<sup>2</sup>. ERT with elosulfase alfa can improve pulmonary function tests, endurance, and quality of life but has limited effect on skeletal disease<sup>36,37,39</sup>.

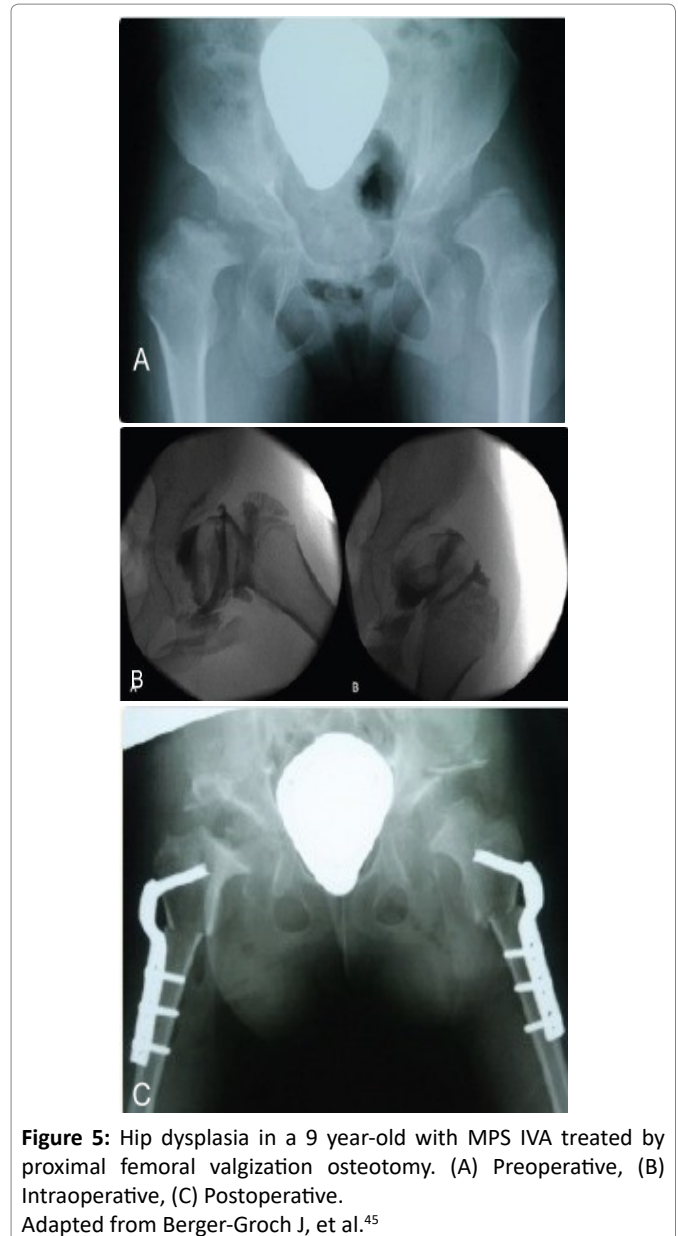
### Orthopedic Manifestations

Skeletal dysplasia is typically the earliest manifestation of MPS IV, appearing between ages 1-3 years<sup>2</sup>. After the first year of life, growth progressively declines, leading to the severe short stature seen in "classic" Morquio A syndrome<sup>29</sup>. Other common features include coxa valga, pectus carinatum, ankle valgus, waddling gait, and rib flaring<sup>21</sup>.

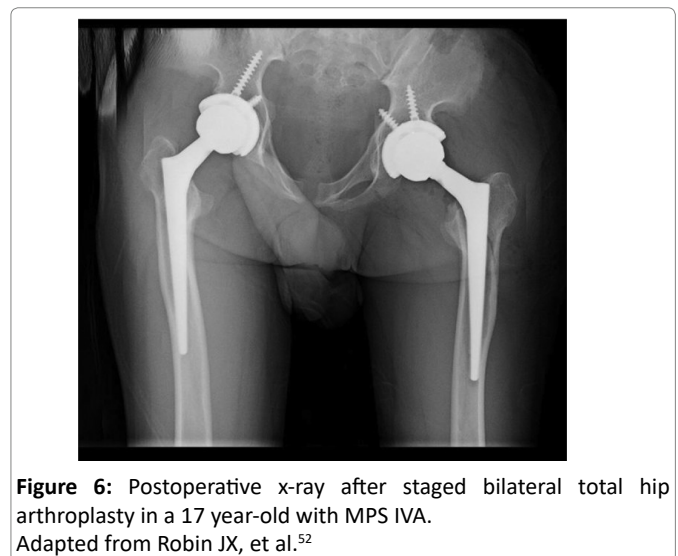
Unlike most other MPS types, which present with joint contractures, MPS IV is characterized by joint hypermobility, seen in approximately two-thirds of patients. The wrists are most commonly affected due to metaphyseal deformities, bone hypoplasia, and connective tissue degradation near the joint, resulting in weak grip strength and difficulty with activities of daily living<sup>20</sup>.

Lower extremity involvement is common in MPS IV. A 2012 retrospective review reported 61 hip, 78 knee, and 20 ankle procedures performed in just 20 patients<sup>30</sup>. Proximal femoral epiphyseal dysplasia and a small, shallow acetabulum is frequently seen (Figure 5), leading to hip subluxation and progression to degenerative arthritis if untreated<sup>29</sup>. In a case report of staged bilateral total hip arthroplasty in a 17 year-old with MPS IVA, the authors recommended full-length standing films, CT evaluation of severity, and careful consideration of hip flexion contractures to optimize cup position (Figure 6)<sup>52</sup>. Hip arthritis may be accelerated by genu valgum, which affects nearly all MPS IV children and often progresses to surgical severity due to underlying ligamentous laxity in these patients<sup>8,9</sup>. In patients with adequate growth potential, effective correction can be achieved with guided growth using tension band plate hemiepiphysiodesis (Figure 7)<sup>29,53</sup>.

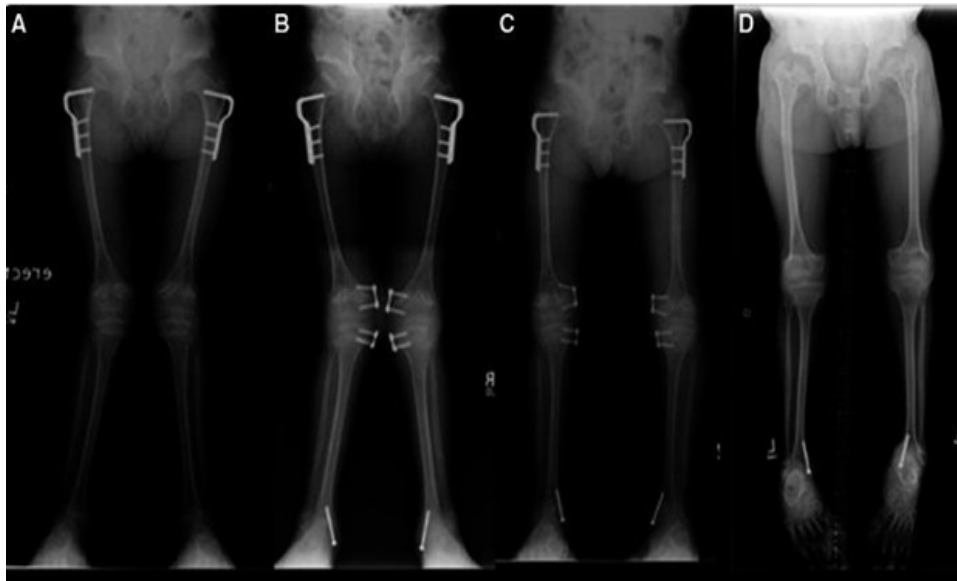
Kyphosis and cervicothoracic stenosis are common in MPS IV patients and are associated with spinal



**Figure 5:** Hip dysplasia in a 9 year-old with MPS IVA treated by proximal femoral valgization osteotomy. (A) Preoperative, (B) Intraoperative, (C) Postoperative. Adapted from Berger-Groch J, et al.<sup>45</sup>



**Figure 6:** Postoperative x-ray after staged bilateral total hip arthroplasty in a 17 year-old with MPS IVA. Adapted from Robin JX, et al.<sup>52</sup>



**Figure 7:** Genu valgum in a 9 year-old with MPS IVA at (a) age 9 years, (b) age 10 years, (c) age 12 years (slight over-correction, tension band plates removed) and (d) age 16 years (skeletally mature). Adapted from White KK, et al.<sup>29</sup>

cord compression and neurological sequelae. These complications are considered the leading cause of premature death in Morquio syndrome, highlighting the importance of surgical intervention<sup>4,8</sup>. Patients with MPS IV also have the highest risk of odontoid hypoplasia, predisposing them to atlantoaxial instability<sup>10</sup>. C1/C2 subluxation may cause myelopathy, spastic quadriparesis, or even death<sup>9,24</sup>. Given the high incidence and risk, prophylactic fusion, often with decompression, has been recommended for these patients<sup>9</sup>.

### Perioperative Management

Patients with MPS IV face high anesthetic risk due to cervical instability, myelopathy, compromised respiratory function, and cardiac disease<sup>29</sup>. Airway obstruction further complicates intubation<sup>15</sup>. A 2016 case series reported tracheal narrowing in 67% of patients, which worsened over time<sup>27</sup>. Theroux et al. recommended use of a Glidescope and manual anterior tongue displacement during intubation. Increased caution is required with intubation maneuvers because their short and stiff cervical spine predisposes to instability and stenosis<sup>4</sup>. Preoperative extension and flexion films may aid in planning, but manual in-line stabilization during airway management should still be done to minimize atlantoaxial subluxation risk previously discussed<sup>15</sup>. Flexion films themselves carry risk and must be performed cautiously with preoperative assessment by surgeons.

Surgical operations in MPS I and MPS IV can carry devastating risks. Thoracic spinal cord ischemia has been increasingly reported in both spinal and lower extremity surgeries, in both prone and supine positioning, and

under both general and epidural anesthesia<sup>24</sup>. To minimize these risks, careful positioning, minimal neck manipulation, and continuous electrophysiological monitoring are recommended<sup>29</sup>. Williams et al. further advocated perioperative immobilization with a halo-body orthosis in MPS IVA patients undergoing occiput to cervical fusion.

Valvular disease is more prevalent in MPS patients and is known to contribute to increased perioperative mortality in non-MPS populations. Providers should maintain high suspicion for cardiac pathology in all MPS patients<sup>15,41</sup>. For MPS IV patients, recommendations include preoperative otolaryngology, pulmonary and cardiac consultations, avoidance of epidural anesthesia, and combining procedures when able to reduce anesthetic exposures<sup>24,41</sup>.

### MPS VI

#### Overview

MPS VI, or Maroteaux-Lamy syndrome, is caused by deficiency of N-acetylgalactosamine 4-sulfatase, impairing degradation of dermatan sulfate and chondroitin 4-sulfate<sup>23</sup>. Common features include coarse facial features, macroglossia, impaired hearing and vision, hernias, hirsutism, and cardiac and pulmonary disease<sup>2</sup>. Patients with rapidly progressing MPS VI exhibit shorter stature and typically die before the second decade of life due to cardiac and pulmonary complications<sup>23</sup>. The slowly progressing phenotype presents with fewer symptoms and height >140cm, but still often requires surgery in advanced disease stages and is associated with reduced life expectancy<sup>23</sup>.

## Orthopedic Manifestations

MPS VI demonstrates musculoskeletal changes common to many MPS types, including dysostosis multiplex, scoliosis, joint stiffness and contractures, and pectus carinatum<sup>2</sup>. Discordant short stature, with reduced trunk-to-limb ratio is also characteristic, especially in the rapidly progressing form<sup>4</sup>. As stated above, MPS VI has a higher prevalence of carpal tunnel syndrome compared to most other forms of MPS. In early infancy, deformity of the femoral head and lateral migration of the hip can already be detected, although the role of early surgical intervention remains unclear<sup>4</sup>. Progressive genu valgum deformity can become severe enough to warrant surgery<sup>9</sup>.

Spinal pathology is particularly prominent in MPS VI. Multiple level cervical stenosis and atlanto-axial instability are common, which can result in spinal cord compression, myelopathy, and spastic quadriparesis (Figure 8)<sup>9</sup>. One study found cervical cord compression on MRI in 75% of patients, with cases identified as early as 2 years of age<sup>25</sup>. Similar to MPS I and IV, patients with MPS VI can develop progressive angular thoracolumbar kyphosis due to vertebral wedge deformity, which may lead to canal compromise and neurologic injury. Surgical correction is generally indicated when kyphotic angles exceed 40 degrees. Osteopenia is more frequently observed in patients with types VI and VII of MPS<sup>1</sup>.

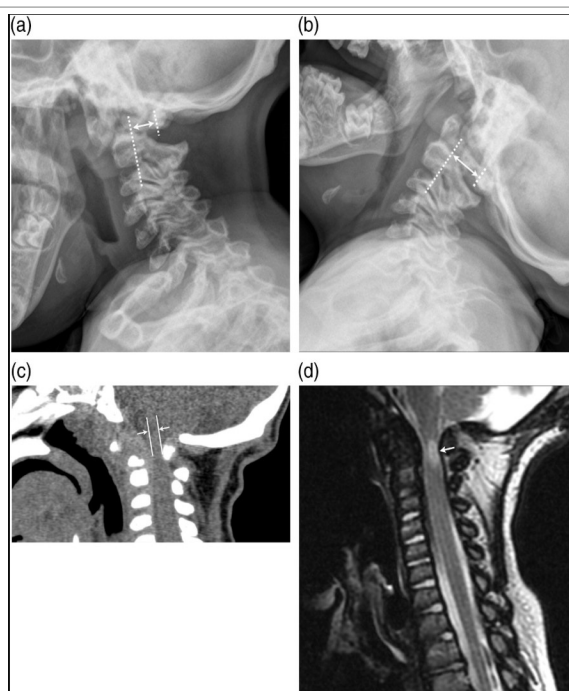
## Perioperative Management

Anesthetic risks in MPS VI include hypopharyngeal and tracheal narrowing, cervical pathology, macroglossia, limited mouth opening, cardiac disease, and restrictive or obstructive lung disease<sup>26</sup>. Severe odontoid hypoplasia and cervical instability, common in MPS IV and VI, complicate endotracheal intubation and increase the risk of paralysis during anesthesia<sup>1,27</sup>. Strict stabilization of the head and neck during management is essential to reduce the risk of C1/C2 sublaxation<sup>15</sup>. Cervical instability should be addressed surgically when feasible before other procedures. It is recommended that intubation be performed by anesthesiologists experienced in flexible bronchoscopy-assisted intubation<sup>43</sup>. Additionally, postoperative mucosal and tongue swelling may occur in MPS IV and VI patients, particularly after prolonged prone positioning<sup>26</sup>.

## MPS VII

### Overview

MPS VII, or Sly syndrome, is a rare MPS type caused by deficiency of  $\beta$ -D-glucuronidase, leading to accumulation of dermatan sulfate, heparan sulfate, chondroitin-4-sulfate, and chondroitin-6-sulfate<sup>2</sup>. Clinical features resemble those of MPS I and II, including short stature, coarse facial features, corneal clouding, cognitive impairment, hydrocephalus, pulmonary involvement and cardiac disease. A distinguishing feature of severe MPS VII is non-immune hydrops fetalis, where excessive fluid accumulates



**Figure 8:** A 3 year-old with MPS VI (a-b) flexion and extension radiographs with atlanto-axial instability. (c) CT showing severe spinal stenosis with space available to the cord measured at 5 mm in the antero-posterior plane (double arrow). (d) MRI showing stenosis at C1, cervical cord compression and myelomalacia (arrow).

Reproduced from Solanki GA, et al.<sup>47</sup> with permission from Elsevier.

within fetal extravascular compartments and body cavity<sup>2</sup>. A 2015 study reported a history of hydrops fetalis in 41% of patients with MPS VII, however, its presence does not reliably predict disease severity<sup>32</sup>. Like other MPS types, MPS VII symptoms present along a spectrum, with onset ranging from infancy to childhood, and typically a shorter life expectancy, with heart disease and airway obstruction being major causes of death<sup>2</sup>.

### Orthopedic Manifestations

Musculoskeletal manifestations of MPS VII resemble those of MPS I and II and include dysostosis multiplex, disproportionate short stature, joint contractures with reduced range of motion, odontoid hypoplasia, atlantoaxial instability (less common than in MPS IV), acetabular dysplasia, and pectus carinatum<sup>10</sup>. Additional frequent findings include genu valgum, claw hand deformity, and curved fingers.

Spine involvement is prominent in MPS VII, with scoliosis, kyphosis and thoracolumbar kyphosis among the common deformities<sup>32</sup>. With age, gradual progression of spine and chest deformities develop, often accompanied by pain from hip dysplasia, leading to wheelchair dependence as early as age 10<sup>32</sup>.

### Perioperative Management

Atlantoaxial instability, though less common, has been reported in MPS VII and poses a risk of cervical dislocation during intubation. One case report described the death of a 12 year-old with MPS VII during anesthesia for a dental procedure<sup>32</sup>. While anesthetic concerns specific to MPS VII remain underreported, risks can be inferred from other MPS types. Anatomical variations such as short neck and macroglossia increase the likelihood of difficult intubation. In addition, decreased pulmonary function, obstructive airway disease, sleep apnea, cardiac valve disease and cardiomyopathy, place these patients at elevated risk for perioperative pulmonary and cardiovascular complications<sup>32</sup>.

## MPS IX

### Overview

MPS IX, or Natowicz syndrome, is an incredibly rare MPS subtype caused by deficiency of hyaluronidase, resulting in accumulation of hyaluronan, which is involved in cartilage composition and acts as joint lubrication<sup>2</sup>. To date, only 4 patients with MPS IX have been reported. The first, described in 1996, presented with generalized cutaneous swelling, flat nasal bridge, bifid uvula, submucosal cleft palate, and recurrent otitis media<sup>33</sup>. In 2011, three siblings with a deletion in the *HYAL1* gene were identified, though they did not share the same clinical features as the index case<sup>33</sup>. Integral clinical features remain to be established

pending further discovery and evaluation of MPS IX patients.

### Orthopedic Manifestations

The first reported patient exhibited short stature, multiple periarticular soft-tissue masses, popliteal cysts, joint effusions, and acetabular erosions. The three subsequently reported patients demonstrated isolated joint disease. They developed polyarthropathy of large joints, with MRI revealing unusual proliferative synovitis and effusions but no erosions at that time<sup>33</sup>. Initially, they were thought to have Juvenile Idiopathic Arthritis (JIA) until the familial pattern of joint disease became apparent. MPS IX may be distinguished from JIA by its familial presentation, lack of response to standard therapies, widespread synovial changes on MRI, and pathologic synovial biopsy findings. However, because MRI and biopsy are not routinely included in JIA evaluations, additional undiagnosed MPS IX cases may exist.<sup>33</sup> A subsequent study screening for MPS IX in 108 Turkish patients with JIA found no evidence of hyaluronidase deficiency, suggesting the disorder is exceedingly rare<sup>34</sup>.

### Perioperative Management

Due to the rarity of MPS IX, limited data is available regarding perioperative risks<sup>27</sup>. However, since MPS IX appears largely confined to joint disease at this time, perioperative complications are presumed to be less frequent compared with other MPS subtypes.

### Conclusion

Mucopolysaccharidosis disorders affect multiple systems, including cardiovascular, neurological, and musculoskeletal. Musculoskeletal involvement often necessitates orthopedic intervention.

Whether it be limited mobility of the cervical spine, cervical instability, joint contractures, anatomic variations of the airway or cardiopulmonary comorbidities, mucopolysaccharidoses are at increased risk for perioperative challenges. These risks increase with age as GAGs continue to accumulate in tissues. Preoperative cervical imaging and preparedness for difficult airway management, including availability of adjuncts, are essential for anesthesiologists. Intraoperative neurological monitoring during lower extremity surgeries has been done to monitor real-time spinal cord function, allowing for surgical plan adjustments or aborting the procedure if needed<sup>38</sup>. This review highlights the orthopedic manifestations and perioperative complications of MPS, underscoring the importance of multidisciplinary management to optimize patient safety and outcomes.

### Conflict of Interest

The authors have no relevant conflict of interest to disclose.

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