

Maroteaux-Lamy Syndrome

Authored by
mohammad looti

October 1, 2025

RECOMMENDED CITATION

mohammad looti (2025). *Maroteaux-Lamy Syndrome*. PSYCHOLOGICAL SCALES.
Retrieved from <https://scales.arabpsychology.com/?p=32153>

Maroteaux-Lamy Syndrome

Primary Disciplinary Field(s): Genetics, Pediatrics, Lysosomal Storage Disorders, Metabolic Diseases

1. Core Definition

Maroteaux-Lamy syndrome, formally known as Mucopolysaccharidosis Type VI (MPS VI), is a rare, inherited lysosomal storage disorder characterized by the body's inability to properly break down specific complex sugar molecules called **glycosaminoglycans (GAGs)**. These GAGs, specifically dermatan sulfate, accumulate within cells and tissues throughout the body, leading to progressive cellular damage and a wide range of debilitating symptoms. The condition is also referred to as arylsulfatase-B deficiency or polydystrophic dwarfism, names that reflect its underlying biochemical defect and some of its prominent physical characteristics. It is a congenital disorder, meaning it is present from birth, although its clinical manifestations often become apparent in early childhood, progressing in severity over time.

The fundamental cause of Maroteaux-Lamy syndrome lies in a deficiency of the enzyme **N-acetylgalactosamine-4-sulfatase**, commonly known as **arylsulfatase B (ASRB)**. This enzyme is crucial for the lysosomal degradation pathway of dermatan sulfate, a type of GAG that is an essential component of connective tissues, bones, cartilage, and other structures. Without sufficient functional ASRB, dermatan sulfate cannot be broken down and recycled effectively. Instead, it accumulates in the lysosomes--the "recycling centers" of the cells--causing them to swell and ultimately disrupting normal cellular function. This widespread cellular dysfunction affects multiple organ systems, resulting in the diverse and complex clinical presentation of the syndrome.

The syndrome's classification as a lysosomal storage disorder places it within a broader group of metabolic diseases characterized by the accumulation of undigested or partially digested macromolecules within lysosomes. While all MPS disorders involve GAG accumulation, MPS VI is distinct due to the specific enzyme deficiency and the particular GAGs that accumulate. The severity of Maroteaux-Lamy syndrome varies significantly among affected individuals, ranging from rapidly progressive forms presenting with severe symptoms in early childhood to more attenuated forms with a slower progression and a later onset of noticeable clinical signs. This variability is often linked to the specific genetic mutations affecting the ARSB enzyme, influencing its residual activity.

2. Etymology and Historical Development

The syndrome bears the names of Dr. Pierre Maroteaux and Dr. Maurice Lamy, two French physicians who played a pivotal role in its initial description and classification. In 1963, Maroteaux

and Lamy, working at the Hôpital des Enfants Malades in Paris, identified a distinct type of mucopolysaccharidosis characterized by skeletal abnormalities, corneal clouding, and urinary excretion of dermatan sulfate, but notably without intellectual disability, which differentiated it from other known MPS types like Hurler syndrome (MPS I). Their meticulous clinical observations and biochemical analysis were instrumental in distinguishing this unique form of lysosomal storage disease, leading to its designation as Maroteaux-Lamy syndrome.

Prior to Maroteaux and Lamy's work, various forms of mucopolysaccharidoses were often grouped together or misdiagnosed due to overlapping symptoms. The mid-20th century saw significant advancements in understanding these complex genetic disorders, moving from purely clinical descriptions to identification of specific biochemical defects. The recognition of MPS VI as a distinct entity was a crucial step in this process, enabling more accurate diagnosis, prognosis, and eventually, the development of targeted therapies. The identification of the specific enzyme deficiency, arylsulfatase B, by subsequent researchers solidified the biochemical basis of the syndrome and further clarified its pathogenesis.

The ongoing research into mucopolysaccharidoses has led to a deeper understanding of the genetic basis and molecular mechanisms underlying these conditions. The journey from initial clinical description to the identification of the causative gene and the development of enzyme replacement therapies highlights the transformative progress in rare disease research. Maroteaux-Lamy syndrome, therefore, represents not only a specific medical condition but also a testament to the scientific process of discovery, classification, and the relentless pursuit of effective treatments for complex genetic disorders. Its historical development parallels the broader evolution of medical genetics and metabolic disease research.

3. Genetic Basis and Pathophysiology

Maroteaux-Lamy syndrome is inherited in an **autosomal recessive** pattern. This means that an individual must inherit two copies of the defective gene, one from each parent, to develop the condition. Parents who carry one copy of the mutated gene are typically unaffected but are carriers of the disease and have a 25% chance of having an affected child with each pregnancy. The specific gene responsible for MPS VI is the **ARSB gene**, located on chromosome 5. Mutations in this gene lead to the production of a non-functional or deficient arylsulfatase B enzyme. Over 100 different mutations have been identified in the ARSB gene, and the specific mutation an individual carries can influence the residual enzyme activity and, consequently, the clinical phenotype, explaining the wide spectrum of disease severity.

The primary pathophysiological consequence of deficient arylsulfatase B activity is the progressive accumulation of **dermatan sulfate** within the lysosomes of virtually every cell type in the body. Lysosomes are organelles responsible for breaking down cellular waste products; when this

process is impaired, particularly for GAGs, the lysosomes become engorged. This engorgement disrupts normal cellular processes, leading to cellular dysfunction, tissue damage, and ultimately organ pathology. The accumulation is progressive, meaning symptoms worsen over time as more and more GAGs build up. The widespread nature of dermatan sulfate in connective tissues, cartilage, and bone explains the multisystemic involvement seen in MPS VI patients.

The cellular dysfunction extends beyond simple lysosomal swelling. The accumulation of GAGs can interfere with other cellular pathways, including protein trafficking, signal transduction, and autophagy. This chronic cellular stress contributes to inflammation, fibrosis, and ultimately organ failure in advanced stages of the disease. For instance, in the heart, GAG accumulation can lead to valvular thickening and dysfunction; in the bones, it can disrupt normal bone remodeling, leading to skeletal dysplasias; and in the eyes, it can cause corneal opacification. Understanding these intricate cellular and molecular mechanisms is crucial for developing therapies that can not only reduce GAG accumulation but also mitigate the downstream cellular damage.

4. Key Clinical Manifestations

The clinical presentation of Maroteaux-Lamy syndrome is highly variable but generally involves a progressive multisystemic decline, with symptoms often becoming apparent in early childhood. One of the most common and prominent features is **skeletal malformations**, often referred to as dysostosis multiplex. This includes short stature, typically noticeable by school age, and various bone deformities affecting the spine (e.g., gibbus deformity, kyphoscoliosis), long bones, and joints, leading to restricted joint mobility. Patients may develop a characteristic coarse facial appearance, which can become more pronounced with age, often accompanied by macrocephaly (enlarged head) and sometimes hydrocephalus (excess fluid in the brain), which can lead to neurological complications.

Cardiac involvement is a significant concern and a major cause of morbidity and mortality in MPS VI. Patients frequently develop **heart valve disease**, particularly thickening and insufficiency of the mitral and aortic valves, which can lead to progressive heart failure. Other cardiac issues include cardiomyopathy and coronary artery disease. Respiratory complications are also common due to skeletal abnormalities affecting the rib cage, compromised lung mechanics from GAG accumulation in airways, sleep apnea, and recurrent respiratory infections. These factors can lead to reduced pulmonary function and chronic respiratory compromise, further exacerbated by frequent sinus and ear infections.

Ocular manifestations are another hallmark of the syndrome. **Clouding of the cornea**, caused by GAG accumulation, is very common and can progressively impair vision. Other symptoms include an enlarged liver and spleen (hepatosplenomegaly) due to visceral GAG accumulation, which can cause abdominal distension and discomfort. Patients may also experience gastrointestinal

problems, including chronic constipation or diarrhea, and umbilical or inguinal hernias. Neurological symptoms, while not involving primary intellectual disability as in some other MPS types, can include spinal cord compression due to skeletal deformities in the cervical spine, leading to impaired mobility, weakness, and neurological deficits. Carpal tunnel syndrome, caused by GAG deposition compressing nerves in the wrist, is also frequently observed.

As patients age, the progressive nature of the disease often leads to significantly impaired mobility by 10 years old, with many requiring wheelchairs. Delayed or absent puberty is also common, along with reduced growth velocity. The cumulative effect of these systemic issues places patients at significant risk for severe complications, including heart failure by 20 to 30 years old, if left untreated. The wide variability in the manifestation and progression of symptoms underscores the importance of individualized patient care and monitoring, as the impact on different organ systems can vary greatly from one patient to another, even within the same family.

5. Diagnosis

The diagnosis of Maroteaux-Lamy syndrome typically begins with the recognition of characteristic clinical symptoms, particularly in early childhood. However, given the variability and overlap with other conditions, definitive diagnosis requires biochemical and genetic confirmation. The initial diagnostic step often involves screening for elevated levels of **urinary glycosaminoglycans (GAGs)**. While elevated GAGs in urine can indicate an MPS disorder, further specific tests are needed to differentiate MPS VI from other types. In MPS VI, specifically, dermatan sulfate levels are disproportionately elevated.

The most definitive biochemical test is the measurement of **arylsulfatase B (ARSB) enzyme activity** in white blood cells (leukocytes), fibroblasts (skin cells), or dried blood spots. A significantly reduced or absent enzyme activity confirms the diagnosis of Maroteaux-Lamy syndrome. It is crucial to perform this enzyme assay carefully, as some carriers of the gene mutation may have slightly reduced enzyme activity, but not low enough to cause the disease. This specific enzyme assay helps distinguish MPS VI from other MPS disorders, which involve deficiencies in different lysosomal enzymes.

Genetic testing provides further confirmation by identifying specific **mutations in the ARSB gene**. This is particularly useful for carrier identification, prenatal diagnosis, and in cases where biochemical results are equivocal. Genetic testing can also help in predicting the severity of the disease in some cases, as certain mutations are associated with more severe or attenuated phenotypes. A comprehensive diagnostic approach combines clinical assessment, urinary GAG analysis, enzyme activity measurement, and genetic sequencing to ensure an accurate and timely diagnosis, which is critical for initiating appropriate management and treatment strategies.

6. Treatment and Management

The treatment of Maroteaux-Lamy syndrome is primarily directed at managing specific symptoms and, more recently, at addressing the underlying enzyme deficiency. A multidisciplinary approach involving pediatricians, geneticists, cardiologists, ophthalmologists, orthopedic surgeons, neurologists, and other specialists is essential to provide comprehensive care. Symptom-directed therapy aims to alleviate pain, improve function, and prevent complications. This can include surgical interventions for skeletal deformities, hydrocephalus shunting, carpal tunnel release, and valve replacement for severe heart valve disease. Physical and occupational therapy are vital to maintain mobility and improve daily living activities, especially given the progressive joint stiffness and skeletal issues.

A significant breakthrough in the treatment of MPS VI came with the development of **enzyme replacement therapy (ERT)**. This therapy involves intravenously administering a genetically engineered version of the missing arylsulfatase B enzyme. The recombinant enzyme, known as galsulfase (marketed as Naglazyme), is designed to be taken up by cells, particularly those with GAG accumulation, where it can then enter the lysosomes and facilitate the breakdown of dermatan sulfate. ERT has been shown to reduce urinary GAG levels, improve growth, enhance walking capacity, improve pulmonary function, reduce hepatosplenomegaly, and in some cases, lessen joint stiffness and improve cardiac function. Early initiation of ERT is generally associated with better outcomes, as it can help prevent or slow the progression of irreversible organ damage.

While ERT is effective in many aspects, it has limitations. The enzyme, being a large protein, has difficulty crossing the blood-brain barrier, meaning it has limited impact on neurological symptoms such as hydrocephalus or spinal cord compression. Regular infusions, typically weekly, are required for life. Other supportive treatments include aggressive management of respiratory infections, hearing aids for hearing loss, and corneal transplants or other ocular interventions for severe corneal clouding, though these may require careful consideration in patients with systemic disease. Dietary management does not correct the underlying metabolic defect but can be part of a holistic approach to address gastrointestinal issues. Ongoing research is exploring other therapeutic avenues, including gene therapy and chaperone therapies, to potentially offer more comprehensive and curative solutions for MPS VI.

7. Prognosis and Variability

The prognosis for individuals with Maroteaux-Lamy syndrome has significantly improved with the advent of enzyme replacement therapy and comprehensive supportive care. Historically, individuals with severe forms of the disease often faced a significantly shortened lifespan, with many succumbing to cardiac or respiratory complications in early adulthood. With current treatments, particularly early and consistent ERT, many patients can experience an improved

quality of life and a prolonged life expectancy, often reaching adulthood and beyond. However, the prognosis remains highly variable, heavily dependent on the specific genetic mutations, the severity of the disease at diagnosis, the timeliness of treatment initiation, and the individual's response to therapy.

Patients with attenuated forms of MPS VI may have a slower progression of symptoms and a longer natural lifespan, even without ERT, although they still benefit from therapy to prevent long-term complications. Conversely, those with severe forms, characterized by very low or absent enzyme activity, typically present with more rapid and aggressive disease progression and require intensive medical management from a young age. Even with ERT, complications such as spinal cord compression, severe heart valve disease, and progressive joint damage can require ongoing surgical interventions and lead to significant disability. Therefore, lifelong monitoring by a multidisciplinary team is crucial to address emerging symptoms and optimize patient outcomes.

Research into the long-term efficacy of ERT and the exploration of novel therapeutic strategies continue to refine the understanding of MPS VI prognosis. The goal is not only to extend life but also to improve the overall quality of life by mitigating the progressive organ damage and functional limitations associated with the syndrome. The variability of the disease phenotype necessitates personalized treatment plans, with a focus on comprehensive care that adapts to the individual's evolving needs and challenges throughout their life. Genetic counseling is also important for affected families to understand the inheritance pattern and risks for future pregnancies.

Further Reading

[Mucopolysaccharidosis Type VI - Wikipedia](#)

[Maroteaux-Lamy Syndrome - National Institute of Neurological Disorders and Stroke \(NINDS\)](#)

[Mucopolysaccharidosis Type VI \(MPS VI\) - National Organization for Rare Disorders \(NORD\)](#)

[Mucopolysaccharidosis Type VI - GeneReviews®](#)