



Have you seen Maroteaux-Lamy?

Early diagnosis is key

Maroteaux-Lamy syndrome, also known as mucopolysaccharidosis type VI (MPS VI), is one of more than 40 lysosomal storage disorders (LSDs). As a group, LSDs occur in approximately 1 in 5,000 live births, making this a disease category that you are likely to see in your practice. Wide variability in the clinical presentation of LSDs creates a diagnostic challenge, and as a result, diagnosis is often delayed. However, early diagnosis is crucial to prevent irreversible damage and is even more urgent now that new disease-specific therapies are becoming available.¹⁻³

A progressive disease with a broad clinical spectrum

As a result of an inherited enzyme deficiency, individuals with MPS VI are unable to degrade dermatan sulfate, a glycosaminoglycan (GAG) found in connective tissues throughout the body. The resulting GAG accumulation leads to multisystemic abnormalities.¹

MPS VI is a progressive disease. As excess GAGs accumulate, the clinical manifestations worsen. The extent of organ involvement and rate of disease progression varies widely among affected individuals. Rapidly advancing disease appears early in life with marked signs and symptoms, often matching the hallmark features described in textbooks. Due to genetic mutations that allow a small amount of enzyme activity, some affected individuals display slowly advancing disease and may not present signs and symptoms until adolescence. Regardless of the rate of progression, MPS VI is a serious disease that leads to severe disability and a shortened life span in virtually all cases.¹

Signs and symptoms

It is critical to diagnose MPS VI and other LSDs as early as possible, before irreversible complications occur. Proactive assessment and appropriate intervention can prevent or ameliorate some of the most severe complications of MPS VI.^{1,2}

Photos courtesy of The National MPS Society, Inc. (right 3)



Rapidly Advancing ← → Slowly Advancing

Early signs of MPS VI may be subtle. These 4 affected individuals illustrate the spectrum of disease severity in MPS VI.

Unfortunately, although symptoms often emerge during the first few years of life, diagnosis is frequently delayed. The initial symptoms of MPS VI may be subtle, especially in patients with slowly advancing disease. Furthermore, initial signs and symptoms often represent common pediatric complaints, such as recurrent otitis media, recurrent sinopulmonary infections, slow growth, and umbilical or inguinal hernia.¹

Common clinical manifestations of MPS VI are listed in the table below. The broad range of clinical presentations and the subtlety of initial symptoms require a high index of suspicion to ensure prompt referral to a medical genetics clinic and early diagnosis.

Clinical Manifestations of MPS VI^{1,4-6}

Appearance and General Symptoms	Coarse facial features Macrocephaly Short stature Reduced endurance
Eyes, Ears, Nose, Throat	Impaired vision Corneal clouding Glaucoma Optic nerve disease Impaired hearing Recurrent otitis media Recurrent sinusitis
Mouth, Teeth	Enlarged tongue Abnormal teeth
Airways, Respiration	Obstructive airway disease Restrictive airway disease Sleep apnea Reduced pulmonary function Recurrent pulmonary infections
Heart	Valvular disease Cardiomyopathy Cardiac arrhythmia Pulmonary hypertension
Abdomen	Hepatosplenomegaly Umbilical and inguinal hernias
Bones, Joints	Joint stiffness and contractures Skeletal abnormalities (dysostosis multiplex) Hip dysplasia
Brain, Nerves	Cervical spinal cord compression Communicating hydrocephalus Carpal tunnel syndrome Normal intelligence

Suspect— then refer for diagnosis

The key to early diagnosis of MPS VI (Maroteaux-Lamy syndrome) is rapid recognition of a cluster of suggestive signs and symptoms. (See list of manifestations.)

Although the severe features of MPS VI may take time to develop, even mild facial coarsening or joint stiffening should provoke suspicion of an MPS disorder and prompt referral to a medical geneticist for evaluation and testing. Diagnosis of MPS VI requires a specialized biochemical laboratory.

An elevated urinary GAG assay level establishes the probable presence of an MPS disorder and may be helpful in determining which enzyme assay(s) should be done. An abnormally low level of arylsulfatase B activity on the enzyme assay provides a definitive diagnosis of MPS VI, distinguishing it from other MPS disorders.¹


There is more reason than ever to diagnose MPS early

Clinical management of MPS has traditionally been symptom based, aimed at treating complications as they occur.¹

The ideal approach would be to treat the underlying pathology of MPS, by replacing the deficient enzyme and reversing the GAG accumulation that causes so many deleterious effects. Hematopoietic stem cell transplantation (HSCT) may accomplish this in selected patients, but difficulties with tissue matching and high morbidity and mortality rates mean that HSCT is an option for only a few patients.¹

A different therapeutic approach called enzyme replacement therapy (ERT) has shown positive clinical results in lysosomal storage diseases, including Gaucher disease, Fabry disease, and MPS I. ERT may benefit a much wider range of patients.⁷⁻¹¹

The future availability of ERT will increase the urgency of diagnosing MPS disorders early, in order to optimize the potential benefits of treatment.



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Visual Clues of MPS VI



Photo courtesy of The National MPS Society, Inc. (right).

Short Stature and Flexed-Knee Stance. Seen with coarse facies, shortened neck, and protruding abdomen in a patient with advanced disease (left). A patient with slowly advancing disease (right) does not show the marked facial coarsening or flexed-knee stance.¹

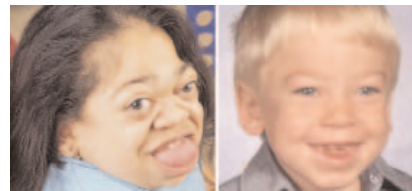
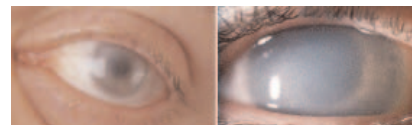


Photo courtesy of The National MPS Society, Inc. (right).

Coarse Facial Features. Broad nose, flat nasal bridge, and enlarged tongue and lips occur with macrocephaly and shortened neck in an individual with rapidly advancing disease (left). An individual with slowly advancing disease presents with subtle coarsening of facial features with flat nasal bridge (right).¹



Corneal Clouding. Ocular GAG accumulation reduces visual acuity.¹

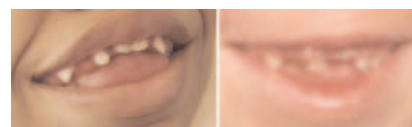


Photo courtesy of The National MPS Society, Inc. (right).

Small, Irregular, Widely Spaced Teeth. With enlarged tongue and lips, and hyperplastic gums in an advanced-stage patient (left). A patient with earlier-stage disease exhibits more mild manifestations (right).^{1,6}

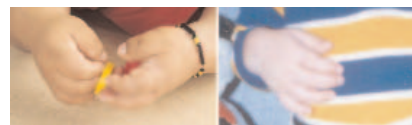


Photo courtesy of The National MPS Society, Inc. (right).

Claw Hand Deformity. Short fingers with fixed flexion and poor dexterity, seen in a 16-year-old with rapidly advancing disease (left). A 5-year-old earlier in the course of the disease exhibits less severe finger flexion (right).¹

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