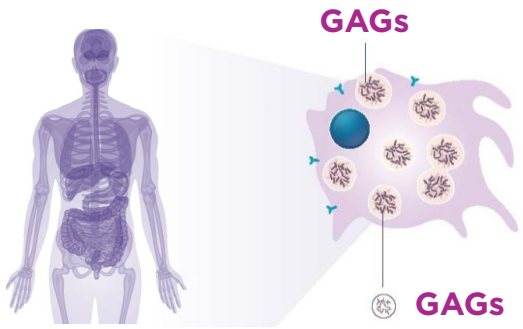
Mucopolysaccharidosis VII

Mucopolysaccharidosis VII (MPS VII), also known as Sly syndrome, is a progressive autosomal recessive metabolic disorder caused by variants in the *GUSB* gene resulting in a deficiency of the lysosomal enzyme β-glucuronidase.[1,2]



β–glucuronidase plays a key role in the breakdown of glycosaminoglycans (GAGs). GAGs are mucopolysaccharides (long chains of sugar molecules) that build up in lysosomes of organs and tissues in patients with MPS VII as a result of the body not being able to properly break down mucopolysaccharides.[1,2]

MPS VII is one of the 7 main types of mucopolysaccharidoses (MPSs),[3] a group of lysosomal storage disorders (LSDs) caused by a deficiency in lysosomal enzymes involved in glycosaminoglycan (GAG) catabolism.[4]

Subtypes of MPS[5]

Type	Common Name	Enzyme Deficiency	Gene Name	GAG Affected
MPS I	Hurler, Hurler-Scheie, Scheie syndromes	α-L-iduronidase	*IDUA*	DS, HS
MPS II	Hunter syndrome	Iduronate-2-sulfatase	*IDS*	DS, HS
MPS III	Sanfilippo A, B, C, D syndromes	A) Heparan N-sulfatase B) α-N-acetylglucosaminidase C) Acetyl CoA:α-glucosaminide acetyltransferase D) N-acetylglucosamine 6-sulfatase	*SGSH* *NAGLU* *HGSNAT* *GNS*	HS
MPS IV	Morquio A, B syndromes	A) N-acetylgalactosamine 6-sulfatase B) β-galactosidase	*GALNS* *GLB1*	KS, CS KS
MPS VI	Maroteaux-Lamy syndrome	N-acetylgalactosamine 4-sulfatase (arylsulfatase B)	*ARSB*	DS
MPS VII	Sly syndrome	β-glucuronidase	*GUSB*	DS, HS, CS
MPS IX	Hyaluronidase deficiency	Hyaluronoglucosaminidase-1	*HYAL1*	HA

Levels of the mucopolysaccharides (DS=dermatan sulfate, HS=heparan sulfate, CS=chondroitin sulfate, HA=hyaluronan, and KS=keratan sulfate) in the tissues and urine are increased in affected individuals.[5] The prevalence of MPS VII is estimated to be 1:300,000–1:2,000,000 and the MPS VII incidence is estimated to be 1:250,000 newborns.[1,2,4] Many patients may be unaccounted for due to early mortality, either in utero or in early infancy.[2]

Diagnosis of MPS VII

REFERRAL TO GENETICIST OR METABOLIC SPECIALIST

ENZYME DEFICIENCY TESTING

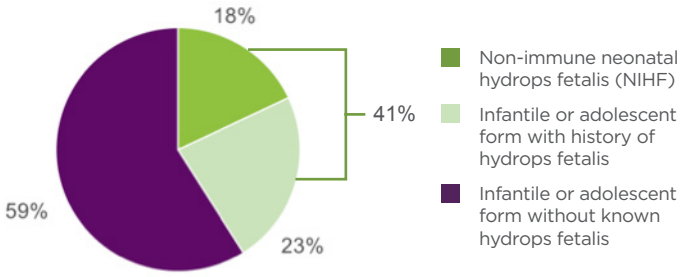
MOLECULAR TESTING IF NEEDED

CONFIRM DIAGNOSIS

MPS VII cannot be reliably diagnosed on clinical presentation alone.[5] Diagnosis may be confirmed by a combination of clinical evaluation, patient history, and laboratory tests which include:

- Urine GAG analysis
- β-glucuronidase enzyme activity testing
- Molecular testing for *GUSB* gene variants[1,5]

Non-Immune Hydrops Fetalis



MPS VII is the most commonly diagnosed LSD in non-immune hydrops fetalis (NIHF).[5] In an MPS VII natural history study, more than 50% of patients with history of NIHF survived beyond infancy with a varied clinical course ranging from mild to intermediate.[2] Approximately 41% of MPS VII patients have a prenatal clinical history of NIHF,[2] defined as abnormal fluid collection in at least two areas of the fetus, including ascites, pleural effusions, pericardial effusions, and skin edema. The presence of NIHF was not predictive of the eventual severity of MPS VII.[2]

MPS VII Clinical Presentation

Characteristics of MPS VII

Common MPS VII characteristics have been established based on clinical information for 46 patients gathered from physician surveys.[2] Symptoms of MPS VII can present in the prenatal or postnatal period.[8]

Head and Neck

- Coarse facial features (87%)
- Increased head circumference (87%)
- Short neck (78%)
- Coarse hair (60%)

Musculoskeletal System

- Dysostosis multiplex (90%)
- Loss of joint range of motion (85%)
- Joint contracture (84%)
- Restricted mobility (78%)
- Stiffness (72%)
- Scoliosis (69%)
- Kyphosis (68%)
- Gibbus (63%)
- Knock knees (63%)
- Dysplastic hips (53%)
- Clawed hands (56%)
- Curved fingers (54%)

Pulmonary and Cardiovascular

- Decreased pulmonary function (71%)
- Obstructive airway disease (44%)
- Sleep apnea (35%)
- Chronic bronchitis (29%)
- Valvular heart disease (50%)
- Cardiomyopathy (37%)

Thoracolumbar and Abdominal

- Short trunk (88%)
- Pectus carinatum/excavatum (85%)
- Short stature (79%)
- Rib cage/chest deformities (78%)
- Hepatomegaly/splenomegaly (75%)
- Umbilical and/or inguinal hernia (61%)

Neurological

- Limited vocabulary (94%)
- Mental retardation (86%)

Ophthalmological

- Corneal clouding (63%)
- Heavy eyebrows (52%)
- Visual impairment (37%)
- Photosensitivity (30%)

Ear, Nose, Throat

- Respiratory infections (69%)
- Frequent otitis media (52%)
- Snoring (68%)
- Enlarged tongue (64%)
- Gingival hypertrophy (57%)
- Small and widely spaced teeth (57%)
- Abnormal dentition (50%)
- Sensorineural hearing loss (41%)

MPS VII Disease Progression

Some patients may develop spinal deformities requiring surgery

Some patients may lose the ability to walk due to hip dysplasia

Some patients may experience progressively worsening pulmonary function leading to oxygen dependence

Some patients may experience milder symptoms with fewer manifestations and skeletal abnormalities

Illustration of potential MPS VII disease progression over time.[1,2] Hip dysplasia and worsening pulmonary function are progressive symptoms commonly observed in patients with MPS VII. In general, the signs and symptoms of MPS VII become more severe with age.[1,7] In some cases, MPS VII patients may develop new signs and symptoms which may also progress over time.[1,2,4]

For more information please contact: medinfo@ultragenyx.com

References

1. National Institutes of Health. Genetic and Rare Diseases Information Center (GARD), Genetics Home Reference: Mucopolysaccharidosis type VII. 2016-2018. https://rarediseases.info.nih.gov/diseases/7065/mucopolysaccharidosis, http://ghr.nlm.nih.gov/condition/mucopolysaccharidosis-type-vii; 2. Montaño AM, et al. *J Med Genet*. 2016; 53: 403-18; 3. Muenzer. *Rheumatology* (Oxford). 2011;50(suppl 5):v4; 4. National MPS Society. A Guide to Understanding MPS VII: Sly Syndrome. 2008. https://mpssociety.org/cms/wp-content/uploads/2017/04/MPS_VII_2008.pdf; 5. Lehman TJA, et al. *Rheumatology*. 2011;50:v41-v48; 6. Gimovsky et al. *Am J Obstet Gynecol*. 2015;212:281; 7. NORD Guide for Patients and Families to Mucopolysaccharidosis Type VII, National Organization for Rare Disorders. 2017. https://rarediseases.org/rare-diseases/sly-syndrome/; 8. Zielonka M, et al. *Genet Med*. 2017; 19: 983-988.

ultragenyx medical affairs