Review Article

Joint contractures in the absence of inflammation may indicate mucopolysaccharidosis[1]

Cimaz R, Coppa GV, Koné-Paut I, *et al. Pediatric Rheumatology* 2009, 7:18 doi:10.1186/1546-0096-7-18.

Background

Mucopolysaccharidosis type I (MPS I) is one of the more common mucopolysaccharidoses, a family of seven inherited metabolic diseases caused by deficient activity of various lysosomal enzymes, resulting in the inability to metabolise certain glycosaminoglycans.[1]

Patients with attenuated MPS I may have no obvious physical abnormalities.[1]

Diagnostic delays are common for patients with attenuated MPS I, who can suffer for years, sometimes decades, from this progressive and debilitating disease before it is finally recognised.[1]

Prominently affected organ systems include airways, heart, viscera, skeleton, and (in the most severe cases), the central nervous system.[1]

Undiagnosed patients with the attenuated form of mucopolysaccharidosis type I often have joint symptoms in childhood that prompt referral to a rheumatologist.[1]

An international working group has formulated a rheumatology-based diagnostic algorithm, which applies to all MPS disorders with musculoskeletal manifestations.[1]

About MPS I

Common early clinical features include joint pain and stiffness, corneal clouding, umbilical and/or inguinal hernia, carpal tunnel syndrome, hearing loss, frequent ear, nose and throat infections, and "noisy" breathing.[1]

Musculoskeletal abnormalities that can occur later in the disease course include progressive arthropathy, hip dysplasia, dysostosis multiplex, spine deformities and spinal cord compression.[1]

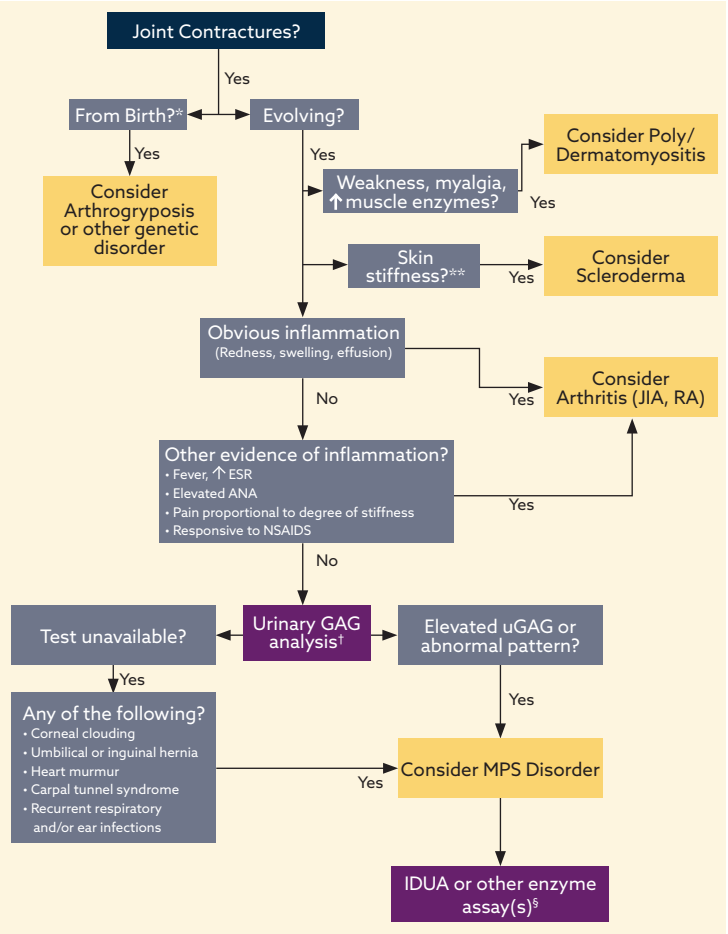
Corneal clouding is an early and almost universal sign of MPS I in both severe and attenuated phenotypes.[1]

Joint symptoms in MPS I

Joint symptoms in MPS I patients are almost universal and, in the case of attenuated disease, are often the first symptom that brings a child to medical attention.[1]

Presentation of the hypothesis

- To aid in the differential diagnosis of MPS I and other MPS disorders, a diagnostic algorithm is proposed (Figure 1).[1]
- The algorithm applies to all MPS disorders with musculoskeletal manifestations.[1]
- Joint contractures were chosen as a starting point in the algorithm because they are an early and almost universal symptom among MPS patients with attenuated disease.[1]



Adapted from Cimaz R, *et al.* 2009[1]

Joint pain and joint contractures in the absence of systemic and local signs of inflammation should always raise the suspicion of an MPS disorder, especially in concert with any other common sign or symptom of MPS.[1]

MPS patients typically have:[1]

- No swelling or local inflammation of any joints
- No morning stiffness
- No laboratory indicators of inflammation (erythrocyte sedimentation rate, C-reactive protein and white blood cell counts are not elevated)
- No response to steroids or nonsteroidal anti-inflammatory drugs
- No radiographic evidence of erosive bone lesions

Figure 1
Diagnostic Algorithm for Attenuated Mucopolysaccharidoses. *Newborn infants with the most severe form of MPS I (Hurler syndrome), although normal appearing, often have radiologic evidence of bone and joint abnormalities. **Note that overall skin texture in patients with MPS I can be thickened and rough. MPS II and rarely MPS I can be associated with a distinctive skin lesion consisting of white "pebbly" papules 2-10 mm in diameter, sometimes coalescing in ridges. †We recommend both quantitative and qualitative (GAG profile) analysis in a reputable laboratory. False negatives can occur with spot screening. §See Table 1 for listing of enzyme deficiencies.
Abbreviations: IDUA: α-L-iduronidase; uGAG: urinary glycosaminoglycan; JIA: juvenile idiopathic arthritis; RA: rheumatoid arthritis.

Note: The algorithm applies to all MPS disorders with musculoskeletal manifestations.[1]

When MPS I or other MPS disorder is suspected, a urinary glycosaminoglycan (uGAG) analysis (both quantitative and qualitative) should be performed.[1]

An elevated uGAG level and/or an abnormal uGAG pattern confirms the presence of an MPS disorder and specific enzyme testing will determine the MPS type.[1] See Table 1.

- A definitive diagnosis of MPS I is based on deficient α-L-iduronidase activity in fibroblasts, leukocytes, serum or blood spots.[1]

Table 1: MPS Disorders Likely to be Encountered by a Rheumatologist or Orthopaedist

	MPS I (Hurler, Hurler-Scheie, Scheie)	MPS II (Hunter)	MPS IV (Morquio)	MPS VI (Maroteaux-Lamy)	MPS VII (Sly syndrome)
Deficient lysosomal enzyme	α-L-iduronidase	Iduronate sulfatase	Galactose 6-sulfatase or β-galactosidase	Arylsulfatase B	β-Glucuronidase

Adapted from Cimaz R, *et al.* 2009[1]

Treatment

Patients with confirmed MPS should be referred to a geneticist or metabolic specialist for further evaluation and treatment.[1]

Reference: 1. Cimaz R, Coppa GV, Koné-Paut I, *et al.* Joint contractures in the absence of inflammation may indicate mucopolysaccharidosis. *Pediatric Rheumatology* 2009, 7:18 doi:10.1186/1546-0096-7-18.

sanofi-aventis south africa (pty) ltd., Reg. no.: 1996/010381/07, Floor 5, Building I, Hertford Office Park, 90 Bekker Road, Midrand, 2196. Tel: (011) 256 3700.
MAT-ZA-2100867-2.0-02/2023

For Medical Information Enquiries kindly contact ZA.Medinfo@sanofi.com