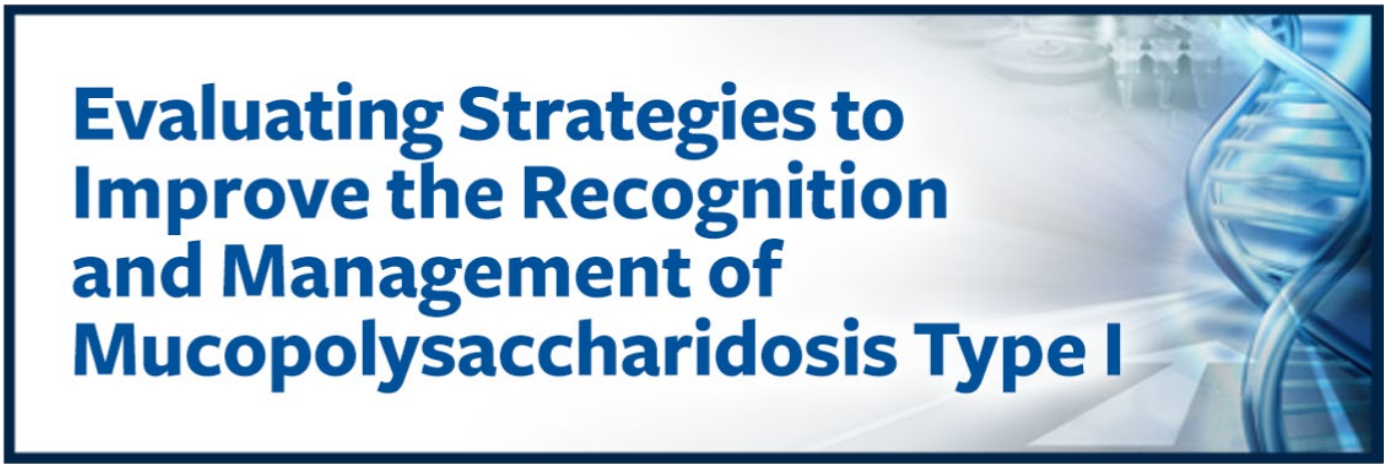

FAQs

Q: Especially for non-geneticists, what is the most effective test to make a diagnosis of mucopolysaccharidosis Type 1 (MPS I)? And should they be ordering more than one test?

A: Commonly, a non-geneticist would order a urine glycosaminoglycan (GAG) determination or fractionated urine GAG if they are thinking of MPS I, and that is a fine place to start. If this is negative and you are very suspicious of MPS I, don't stop there because false negatives are possible. An enzyme analysis panel can be done off blood and can help rule out other MPS and lysosomal storage disorders (LSDs) that clinically overlap. If the results are all negative and the patient still has something significant clinically, a referral to a medical geneticist can help to make an accurate diagnosis and direct further testing.

Q: Is a different sample needed from a patient for each test?

A: Not necessarily, because labs often run different tests using the same sample. There may be enough sample to do several tests. Talk to your testing lab because it could avoid the need to bring your patient in for different or more samples. For example, a lab may run a urine GAG analysis with the same sample it uses to run a urine oligosaccharide screen for MPS and other LSDs, which might need to be ordered later. If you are considering multiple diagnoses, contact your testing lab to see if there are ways to consolidate samples or tests to avoid needless patient visits.

Q: How many testing labs in the U.S. are routinely still using the traditional dimethymethyleneblue dye-binding (DMB) assay for urine total GAG analysis, which is more susceptible to false negatives?

A: Several large reference labs still use the DMB assay. But more and more specialty labs are doing the newer liquid chromatography tandem mass spectrometry (LC-MS/MS) assay. This has a higher sensitivity for all MPSs and leads to fewer false negatives. It's always good to check the method your testing lab uses for GAG analysis and consider analytical limitations that exist with the assay method used.

Q: Are urine GAGs higher in patients with severe MPS I when compared to those with attenuated MPS I? In other words, can you use GAG levels as a biomarker to predict disease severity?

A: Generally speaking, it has not been possible to distinguish between severe and attenuated MPS I using urine GAG analysis. However, there are studies coming out to show that some ability to predict severe or mild disease with the newer methods of GAG analysis may be possible. The evidence is still building around this.

Q: When a patient has a positive newborn screen (NBS) for MPS I, does it need to be confirmed?

A: Following positive newborn screening results, enzyme deficiency and substrate accumulation must both be shown to confirm a diagnosis of MPS I. GAG elevation is typical confirmed in urine, but it could also be done on dried blood spots. Genotyping with molecular testing can help. An important point is that iduronidase enzyme activity on dried blood spots does not predict disease severity. The diagnosis must first be confirmed, which can include genetic testing. If the genotype is not clearly predictive of either the severe or attenuated pheotype, carefully look for phenotypic features. Sometimes a skeletal survey can identify clinical features, because skeletal findings can present very early. You can repeat these every few months. If nothing emerges over time, the patient likely does not have the severe phenotype.

Q: Is there a sense of how many patients with MPS I have been diagnosed in the U.S. by NBS?

A: The exact number is currently unknown, but it may be around 30 or more. As of October 2020, 23 U.S. states screen all babies for MPS I. A majority of babies identified through NBS have the severe form of MPS I, so they can then get treatment and be considered for a transplant. Hopefully, the outcomes for these children will be better because they were found to have MPS I at such young ages.