PHYSICIAN GUIDE
Sanfilippo Syndrome (MPS III)
Disease Information & Screening Options

WHAT IS SANFILIPPO
Sanfilippo syndrome, also known as mucopolysaccharidosis Type III (MPS III), is a progressive neurometabolic disease.

There are four subtypes of Sanfilippo - A, B, C, and D. Each caused by autosomal recessive genetic mutations that encode the enzymes needed to break down the glycosaminoglycan (GAG) heparan sulfate. Missing or poorly-functioning enzymes lead to excessive build up of heparan sulfate. This is especially damaging to the nervous system.

Each subtype has similar signs and symptoms, which progress at varying speeds. Features of classic Sanfilippo subtype A (the most common), typically appear early in life and progress more rapidly. Most children with this form do not live into adulthood.

HOW COMMON IS SANFILIPPO
Sanfilippo is one of the most-common types of MPS. The estimated combined incidence of all four subtypes is 1 in 70,000 newborns.

SIGNS & SYMPTOMS
Signs of Sanfilippo can be present in the newborn period. However, most symptoms begin to be recognized between 1-6 years of age when the child shows signs of developmental delay.

Early Features
- Transient Tachypnea of Newborn*
- Coarse Facial Features*
- Prominent, thick eyebrows*
- Persistent Hirsutism*
- Macrocephaly*
- Speech & Developmental Delays+
- Hearing Loss+
- Recurrent Ear/Sinus Infections
- Chronic Upper Respiratory Congestion
- Challenging Behaviors
- Features of Autism
- Sleep Disturbances
- Diarrhea/Chronic Loose Stools
- Umbilical/Inguinal Hernia
- Enlarged Liver/Spleen

Later Features
- Continued Coarsening of Facial Features
- Development of features of Autism
- Progressive Intellectual Disability with Brain Atrophy
- Seizures/Movement Disorders
- Behavioral problems
- Hyperactivity
- Impulsivity
- Loss of Ambulation
- Loss of Oral Feeding
- Enlarged Liver/Spleen
- Hearing Loss
- Early Death

*The most-specific indicators of Sanfilippo syndrome in infants, as reported in Escolar C, Bradshaw J, Byers V, et. al, 2020, Development of a Clinical Algorithm for the Early Diagnosis of Mucopolysaccharidosis III. Journal of Inborn Errors of Metabolism & Screening. 2020, Volume 8: e20200002.
+Early neurological features of Sanfilippo.
Progression of Coarse Facial Features in Sanfilippo

HOW TO SCREEN FOR SANFILIPPO

The American Academy of Pediatrics suggests considering evaluation of inborn errors of metabolism (including MPS disorders) in children with neuromotor and global developmental delays.

The American College of Medical Genetics and Genomics strongly recommends exome and genome sequencing as a first or second-tier test for children with congenital anomalies that onset by age 1, as well as those with developmental delay or intellectual disability that occurs by age 18.

Initial Testing Options for Sanfilippo:

Urine MPS (glycosaminoglycans) Test | A sterile specimen is not required. Test details: CureSFF.org/UrineTest

Gene Panel Testing | Freely available for suspicion of lysosomal storage disorders. Physicians can request the free genetic testing kit at Invitae.com/en/detectLSDs.

Follow-Up Testing to Confirm Sanfilippo:

Enzyme Activity Test | If suspicion remains after a negative urine test or if the above tests are positive, the diagnosis should be confirmed with a blood MPS enzyme panel. Learn more at: CureSFF.org/BloodEnzymeTest

Work to develop and test newborn screening strategies is underway and, once implemented, will likely reflect a higher incidence than previously recognized, particularly for milder disease phenotypes.

PROGNOSIS

Sanfilippo is a severely life-limiting disease at present.

Medical research has achieved promising breakthroughs in the development of therapies under clinical investigation in recent years. Go to ClinicalTrials.gov and/or contact the Foundation for assistance and information about current clinical trials and emerging research.

FOR MORE INFORMATION
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