REGULAR MONITORING FOR EARLY SYMPTOM MANAGEMENT

Help your patients navigate life with ASMD

ASMD (acid sphingomyelinase deficiency)—historically known as Niemann-Pick disease types A, A/B, and B—is caused by a deficiency in the enzyme acid sphingomyelinase (ASM). ASMD is a progressive, genetic disease that can lead to shortened lifespan in both children and adults.[1,2]

There are 3 subtypes of ASMD: type A, type A/B, and type B, which have variable onset, phenotype, and impacts on life expectancy. Regardless of the ASMD type, ASM deficiency can lead to lifelong, multisystemic complications, and patient uncertainty.[3,4]

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ASMD
ACID SPHINGOMYELINASE DEFICIENCY

PATIENTS WITH ASMD CAN EXPERIENCE SIGNIFICANT MORBIDITY AND EARLY MORTALITY

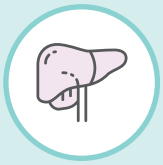
- ASMD symptoms can impact the liver, lungs, and spleen, as well as the hematologic system. Some types of ASMD can also affect the neurological system[3]
- Death is often premature in patients with ASMD type B. By the age of 35, patients with ASMD type B have ~30% reduced survival probability compared to the US general population[4,5]*

Multisystemic burden of disease

SPLENIC INVOLVEMENT

Splenomegaly seen in >90% of patients[6]

- Spleen volumes exceeding 20 times normal have been reported in pediatric and adult patients with certain types of ASMD[4]
- Increasing spleen volume correlated with worsening symptoms like[8]:
  - Increased liver volume, lung disease, bleeding and/or bruising, and triglyceride levels
  - Decreased high density lipoprotein cholesterol, and Z scores (in pediatric patients)



HEPATIC INVOLVEMENT

Hepatomegaly seen in >70% of patients[6]

- Liver failure was a leading cause of mortality (26.4%) in individuals with certain types of ASMD[7]
- Patients often experience liver volumes >1.5 times normal[7]

PULMONARY INVOLVEMENT

Interstitial lung disease seen in more than 80% of patients[6]

- Pulmonary dysfunction is a leading cause of death (32.1%) in patients with all types of ASMD[7]
- Abnormal DLCO (diffusing capacity for carbon monoxide) was recorded for 76% of patients[8†]
  - DLCO reflects the health and function of the alveolar-epithelial barrier, where gas exchange occurs[8]

HEMATOLOGIC INVOLVEMENT

Thrombocytopenia seen in >50% of patients[1]

- Hematologic symptoms, including thrombocytopenia, anemia, and leukopenia are common in patients with ASMD[8]
- Bleeding is the third most common cause of death in patients with ASMD type B[8]

GASTROINTESTINAL INVOLVEMENT

Seen in >75% of patients (all ASMD types)[6]

- Substrate accumulation in all ASMD types can lead to digestive system impacts, including: vomiting,[‡] feeding difficulty,[‡] cholestatic jaundice,[‡] diarrhea, and abdominal pain[6]

*Data extrapolated from a Kaplan-Meier curve generated in an 11-year natural history study that evaluated morbidity and mortality in 59 patients with ASMD type B. At entry, 30 patients were in the pediatric age group (<18 years of age), and 29 patients were adults (≥18 years of age). There were 9 deaths during the follow-up period. Reduction in survival probability is absolute, not relative. US General Population as of 2017.[3]

†In a natural history study of 59 adult and pediatric patients with ASMD type B.[3]

‡Common in ASMD type A.

REGULAR MONITORING IS CRITICAL FOR EARLY SYMPTOM MANAGEMENT

Reducing morbidity starts with monitoring and managing disease progression

Recommended symptom monitoring and schedule of assessments for people living with ASMD types A/B and B

This assessment overview is based on published recommendations developed by a group of physicians experienced with ASMD and the management of patients with ASMD. These recommendations are considered routine and appropriate to monitor multisystemic manifestations for most pediatric and adult patients with ASMD, and may potentially facilitate appropriate symptom management. They are not meant to replace clinical judgment of the healthcare team.

	Initial screening	Every 3-6 months	Annually Every 6-12 months	Periodically Every 2-4 years
GENERAL				
Physical exam, family history, vital signs, gastrointestinal symptoms, ophthalmology	●		●	
Screen for esophageal varices (veins connecting the esophagus to the stomach)	● As needed in patients with portal hypertension		●	
Vaccines	● As needed		● As needed	
SPLEEN				
Spleen size (MRI or CT)	●			
LIVER				
Liver panels (transaminases, GGT, coagulation, albumin)	●		●	
Liver size (MRI or CT)	●			
Portal pressure (blood pressure through liver)	● On an individual basis		●	
Liver fibrosis (elastrography)	●			
Monitor liver disease using the Child-Pugh classification	●			
Liver biopsy	● On an individual basis			
LUNGS				
Respiratory status	●	●		
Pulmonary function testing: DLCO, FVC, O_2 saturation, exercise tolerance	●		● Based on patient's condition	
Chest radiographs to monitor infiltrative lung disease	●			●

Types A/B and B ASMD Symptom Monitoring Recommendations (continued)

	Initial screening	Every 3-6 months	Annually Every 6-12 months	Periodically Every 2-4 years
BLOOD				
CBC (complete blood count)	●		●	
Coagulation profile (blood clot screening)	●		●	
Hormone levels for delayed puberty	● Age dependent		● Age dependent	
HEART				
Stethoscope screening of heart/lungs	●	●		
Electrocardiogram	●		●	
Coronary artery status (HRCT with pulmonary assessment)	● In adults			● In adults
Echocardiogram	●			●
Lipid profile	●		●	
Coronary catheterization (blood circulation)	● On an individual basis			
SKELETAL				
Growth measurement/weight	● In children	●		
Bone density	● In adults		●	
Skeletal health	●			●
NEUROLOGICAL				
Neurological and developmental assessments	● Age appropriate	● In children	● In adults	
Peripheral neuropathy (damaged nerves)	● Patients with *Q292K* variant should be monitored more frequently once diagnosed		●	
Neuropsychology	● as needed			

CBC=complete blood count; DLCO= diffusing capacity of the lungs for carbon monoxide; FVC=forced vital capacity; GGT=gamma-glutamyl transferase; HRCT=high-resolution computed tomography.

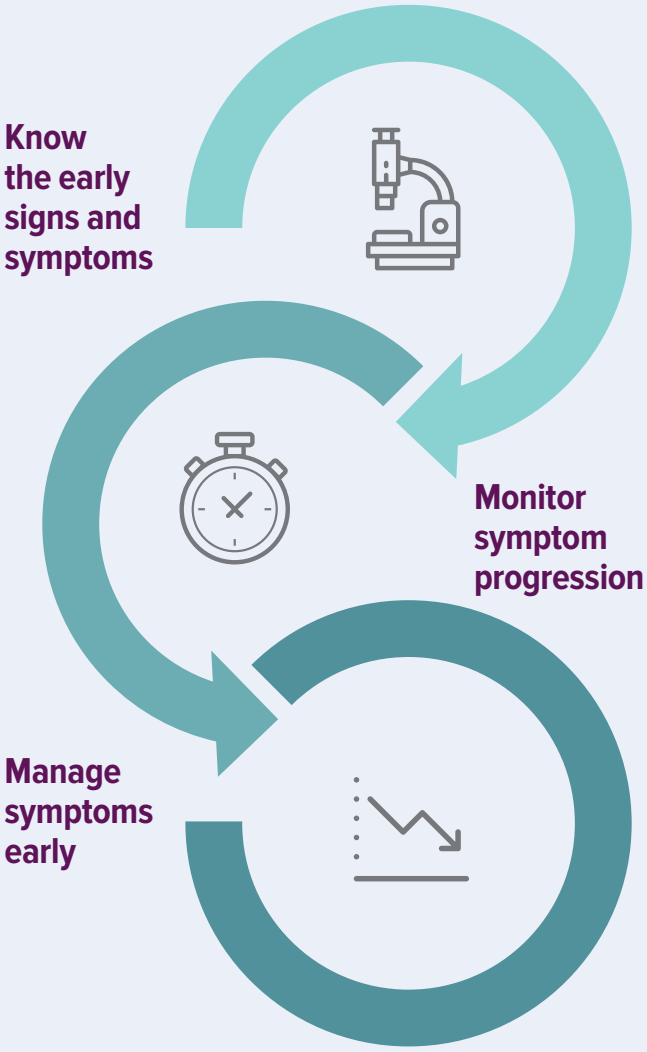
APRIL
Living with ASMD type B

Clinical assessment strategies may reduce the impact of **ASMD** symptoms before they become severe

MONITOR YOUR ASMD PATIENTS REGULARLY FOR NEW AND WORSENING SYMPTOMS

Multisystemic ASMD symptoms can result in severe damage over time. Regular monitoring can make a positive difference.

- ASMD affects multiple organs with significant clinical heterogeneity across the disease spectrum[4]
- Early monitoring by an interdisciplinary clinical team is required to assess symptom progression and enable appropriate symptom management



Register at **ASMDfacts.com/hcp** to stay up to date on ASMD.

References: 1. McGovern MM, Avetisyan R, Sanson B-J, Lidove O. *Orphanet J Rare Dis.* 2017;12(1):41. **2.** Faverio P, Stainer A, De Giacomi F, et al. *Int J Mol Sci.* 2019;20(2):327. **3.** McGovern MM, Dionisi-Vici C, Giugliani R, et al. *Genet Med.* 2017;19(9):967-974. **4.** Wasserstein MP, Dionisi-Vici C, Giugliani R, et al. *Mol Genet Metab.* 2019;126:98-105. **5.** Data on File, ASMD Mortality Claim. **6.** Cox GF, Clarke LA, Giugliani R, McGovern MM. *JIMD Rep.* 2018;41:119-129. **7.** Cassiman D, Packman S, Bembi B, et al. [Published correction appears in *Mol Genet Metab.* 2018;125(4):360]. *Mol Genet Metab.* 2016;118(3):206-213. doi:10.1016/j.ymgme.2016.05.001. **8.** McGovern MM, Wasserstein MP, Giugliani R, et al. *Pediatrics.* 2008;122:e341-e349.

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