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

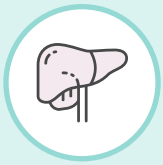
- ASMD symptoms can impact the liver, lungs, and spleen, as well as the hematologic system. Some types of ASMD can also affect the neurological system[3]
- Death is often premature in patients with ASMD type B. By the age of 35, patients with ASMD type B have ~30% reduced survival probability compared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

TYPES A/B AND B ASMD SYMPTOM MONITORING RECOMMENDATIONS[4]

This assessment overview is based on published recommendations developed by a group of physicians experienced with ASMD and the management of patients with ASMD. This is intended for monitoring pediatric and adult patients with ASMD types A/B and B, and may potentially facilitate appropriate symptom management.

	At baseline	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	● As needed in patients with portal hypertension		●	
Vaccines	● As needed		● As needed	
SPLENIC				
Spleen size	●			
HEPATIC				
Liver panels (transaminases, GGT, coagulation, albumin)	●		●	
Liver size	●			
Portal pressure	●		●	
Hepatic fibrosis	●			
Monitor liver disease using the Child-Pugh classification	●			
Liver biopsy	● On an individual basis			
PULMONARY				
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 (cont'd)

	At baseline	Every 3-6 months	Annually Every 6-12 months	Periodically Every 2-4 years
HEMATOLOGIC				
CBC	●		●	
Coagulation profile			●	
Hormone levels for delayed puberty	● Age dependent		●	
CARDIAC				
Auscultation		●	●	
Electrocardiogram			●	
Coronary artery status (HRCT with pulmonary assessment)				● In adults
Echocardiogram			●	
Lipid profile			●	
Coronary catheterization	● 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	● Patients with *Q292K* variant should be monitored more frequently once diagnosed		●	
Neuropsychology	●		●	

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.

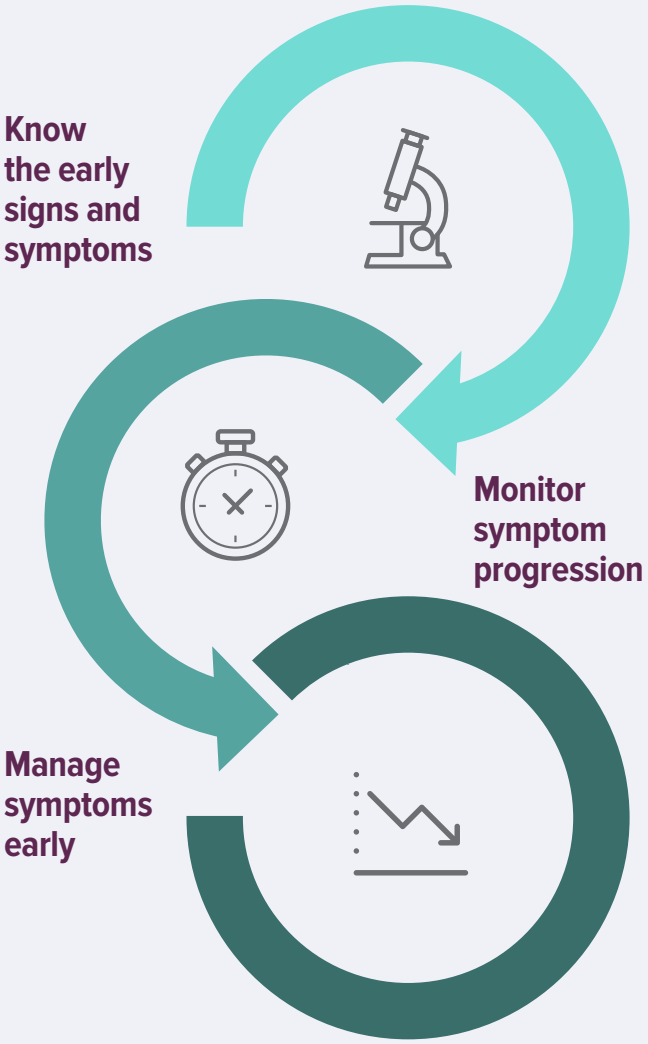
APRIL
Living with ASMD type B

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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