International Niemann-Pick Disease Registry (INPDR)

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Acid Sphingomyelinase Deficiency (ASMD)

Acid Sphingomyelinase Deficiency (ASMD; alternatively known as Niemann–Pick Disease Types A, B and A/B,) is a rare multisystem genetic disorder caused by pathogenic variants of the SMPD1 gene. The rarity of the disease and the scarcity of expertise contribute to misdiagnosis, delayed diagnosis and barriers to adequate care. This may lead to inadequate or inappropriate care and patients' and families' loss of confidence in healthcare systems, even though ASMD is compatible with improved quality of life if a diagnosis is made promptly and appropriate disease modifying and supportive management is instituted.

The consensus clinical management guidelines for ASMD have been developed by an group of international experts and are freely available online. A brief summary of key aspects of the guidelines are below.

Signs and Symptoms
ASMD can be divided into:

- Infantile neurovisceral (Type A)
- Chronic neurovisceral (Type A/B)
- Chronic visceral (Type B)

Clinical features, time of onset and disease severity can vary greatly among the ASMD subtypes (Table 1)

Diagnosis:

- ASM enzyme activity assay should be performed for suspected ASMD patients. The diagnosis is established by deficient or very significantly diminished ASM activity in leucocytes or fibroblasts.

- *SMPD1* gene testing should be performed to confirm diagnosis in subjects with reduced ASM activity

Management and Treatment

- Key assessments should take place at the time of diagnosis or symptom onset and at regular intervals for optimal symptom control and maintain functional capacity (Table 2)

- Olipudase Alfa is a disease modifying therapy for patents with ASMD. ASMD patients with non-Central Nervous System (CNS) manifestations could be considered for olipudase alfa therapy on an individual basis

- Monitoring of treatment efficacy should be undertaken for treated patients

To assess the full guidelines, please scan the QR code.

Disease Feature	Infantile neurovisceral (Type A)	Chronic neurovisceral (Type A/B)	Chronic visceral (Type B)
Onset	Early infancy (<1 years)	Infancy to childhood	Childhood to adulthood
Hepatosplenomegaly	+	+	+
Proatherogenic lipid profile	+	+	+
Delayed growth and puberty	N/A	+	+
Thrombocytopenia	+	+	+
Interstitial lung disease	+	+	+
Skeletal involvement	+	+	+
Liver disease	+	+	+
Cherry red macula	+	Some patients	Some patients
Hypotonia	+	Some patient	-
Neurodegeneration	Rapidly progressive	Slowly progressive	-
Life expectancy	<3 years of age	Childhood to mid-adulthood	Childhood to late adulthood

Table 1. ASMD Disease features by subtype

Recommended assessment	Frequency
Baseline history	At diagnosis
Interval history	Each visit
Physical examination	At diagnosis then each visit
Pulmonary assessment, including pumonary function testing	At diagnosis then annually
Neurologic assessment	At diagnosis then annually
Blood investigations	At diagnosis then annually
Imaging studies, including liver, spleen and chest imaging assessments	At diagnosis then as indicated

Table 2. Recommended assessments for ASMD patients

Geberhiwot T, Wasserstein M, Wanninayake S, Bolton SC, Dardis A, Lehman A, et al. Consensus Clinical Management Guidelines for acid sphingomyelinase deficiency (Niemann–pick disease types A, B and A/B). Orphanet Journal of Rare Diseases. 2023;18(1). doi:10.1186/s13023-023-02686-6