Splenomegaly?
Hepatomegaly?
Thrombocytopenia?
Pulmonary involvement?

YOUR DIFFERENTIAL

could make all the difference.

If you see any combination of these symptoms – think ASMD.

ASMD, also known as Niemann-Pick disease types A, A/B, and B, is a progressive and often life-threatening genetic disease.[1]

Show your patients the way to an early ASMD diagnosis.

SANOFI GENZYME

ASMD
ACID SPHINGOMYELINASE DEFICIENCY

APRIL
Living with
ASMD type B

ASMD: PROGRESSIVE AND OFTEN LIFE THREATENING[1]

- ASMD is a genetic, autosomal recessive, lysosomal storage disorder caused by deficiency of the enzyme acid sphingomyelinase (ASM), resulting in the buildup of the substrate sphingomyelin
- Accumulation of sphingomyelin in major organs can lead to progressive, multisystemic damage and early death
- 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
- Both children and adults can be affected by multisystemic manifestations and an unpredictable disease course

ASMD is a spectrum of disease with variable onset and severity[1-3]

	TYPE A	TYPE A/B	TYPE B (MOST COMMON*)
Onset	Early infancy	Infancy to childhood	Infancy to adulthood
Phenotype	Rapid progression, severe multiorgan manifestations, and neurodegeneration	Slower progression, variable multiorgan manifestations, and neurodegeneration	Slower progression, multiorgan manifestations with little to no neurological involvement
Life expectancy	2 to 3 years of age	Childhood to mid-adulthood	Childhood to late adulthood

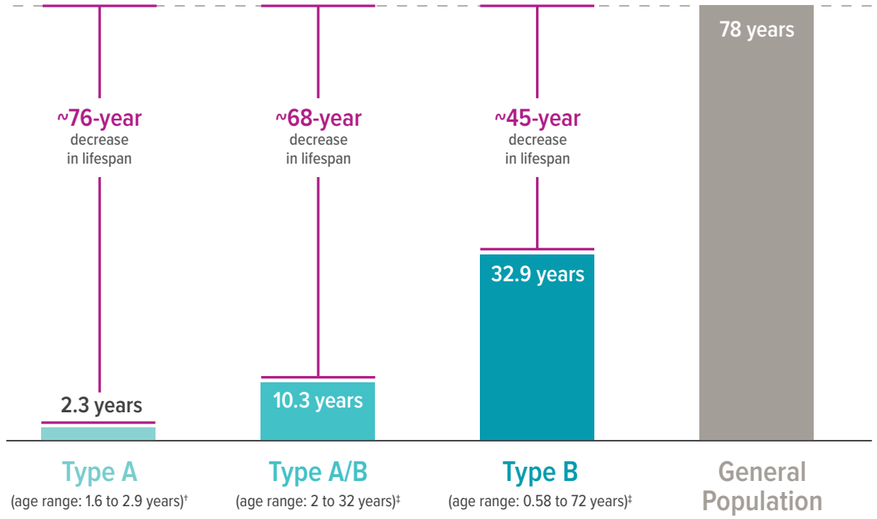
*Based on patient population from a multicenter, historical cohort study (N=100).[3]

PATIENTS WITH ASMD CAN EXPERIENCE SIGNIFICANT MORBIDITY AND EARLY MORTALITY[1]

Death is often premature in patients with ASMD type B[4]:

By the age of 35, ASMD type B patients have ~30% reduced survival probability compared to the US general population*

Reduction in life expectancy of patients with ASMD compared to general population[5-7]



Early diagnosis is imperative for initiating disease management and family screening.[2]

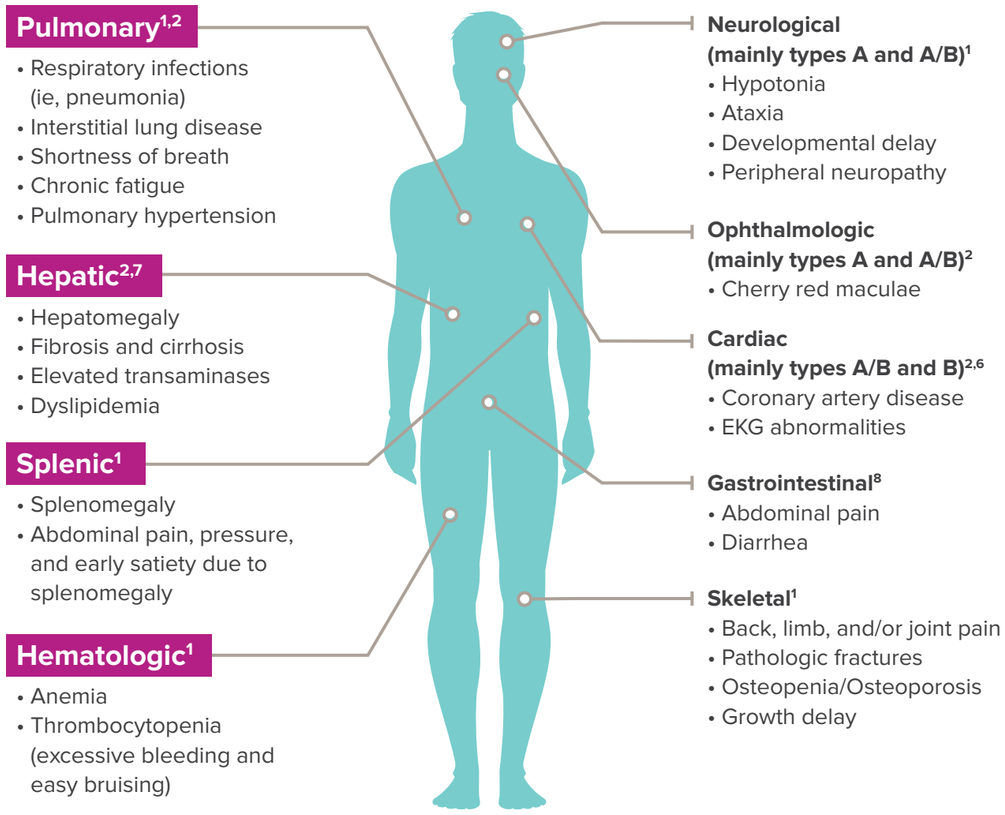
*Data extrapolated from a Kaplan-Meier curve generated in an 11-year natural history study that evaluated morbidity and mortality in 59 patients with ASMD type B. At entry, 30 patients were in the pediatric age group (<18 years of age) and 29 patients were adults (≥18 years of age). There were 9 deaths during the follow-up period. Reduction in survival probability is absolute, not relative. US general population as of 2017.[4]

†Based on data from a natural history study of 10 patients with ASMD type A, during which all 10 patients died.[7]

‡Based on a natural history study of 85 patients with ASMD, 27 patients were identified with ASMD type A/B and 58 patients were identified with ASMD type B. Of the 27 patients with ASMD type A/B, 26 patients died. Of the 58 patients with ASMD type B, 52 patients died.[6]

IDENTIFY ASMD SIGNS AND SYMPTOMS TO ENABLE EARLY DIAGNOSIS AND SYMPTOM MANAGEMENT[1,2]

ASMD can present with multiorgan and life-limiting symptoms[1]



Percentage of patients who experience hallmark signs and symptoms of ASMD[1,3]*:

*Symptom prevalence data for splenomegaly, interstitial lung disease, hepatomegaly, and thrombocytopenia are only for patients with ASMD type B. Gastrointestinal issues symptom prevalence is for all ASMD types.

EKG=electrocardiogram.

SYMPTOMS OF ASMD MAY OVERLAP WITH OTHER DISEASES, INCLUDING GAUCHER DISEASE[2]

Misdiagnosis is common—patients can experience diagnostic delays of ~5 years[2,8]*

- The signs and symptoms of ASMD often mimic those of other diseases, such as acute lymphoblastic leukemia, non-Hodgkin lymphoma, chronic hepatitis B, congestive heart failure, and cystic fibrosis[2,9,10]
- Gaucher disease – another rare lysosomal storage disorder – shares significant phenotypic overlap with ASMD. Similar to ASMD, Gaucher disease is characterized by multisystemic and progressive symptoms that vary in onset and clinical presentation.[2,11]

ASMD and Gaucher disease often present with symptoms similar to other, more commonly seen conditions[1,2,9-22]

	ASMD	Gaucher disease	Acute lymphoblastic leukemia	Non-Hodgkin lymphoma	Chronic hepatitis B	Congestive heart failure	Cystic fibrosis
Hepatomegaly/ Splenomegaly	•	•	•	•	•	•	•
Anemia	•	•	•	•	•		
Thrombocytopenia	•	•	•	•	•		•
Fatigue	•	•	•	•	•	•	•
Bone pain	•	•	•	•			
Abdominal pain	•	•	•	•	•	•	•
Growth delay	•	•					
Liver fibrosis†	•				•		•
Interstitial lung disease†	•						
Dyslipidemia†	•						
Elevated transaminases	•				•		•

The dots in the table above represent the most commonly presenting symptoms in each of the respective diseases.

> The multiorgan symptoms of ASMD and Gaucher disease can cause severe damage over time. **Early detection is the first step** to prompt diagnosis and symptom management[1]

*Based on a prospective, cross-sectional survey of 59 ASMD type B patients.

†This symptom is not seen as commonly in Gaucher disease type 1.

INCLUDE ASMD AND GAUCHER IN YOUR DIFFERENTIAL DIAGNOSIS AND PARALLEL TEST

A diagnostic approach for ASMD based on expert guidelines[2]:

Splenomegaly and hepatomegaly are often the first presenting signs of ASMD. Further evaluations may reveal other compounding symptoms that should prompt diagnostic testing[2]

Splenomegaly +/- hepatomegaly

↓

One or more features suggestive of ASMD:

Infants and children	After childhood
• Interstitial lung disease • Thrombocytopenia • Cherry red maculae • Developmental delay • Hypotonia • Low HDL-C	• Interstitial lung disease • Thrombocytopenia • Low HDL-C • Pathologic fractures

→ **NO**

Rule out other causes:
- Gaucher disease
- Infection
- Malignancy
- Liver disease
- Congestive heart failure
- Hematologic disease

↓

YES

↓

Test for ASMD

Guidelines recommend parallel testing for ASMD and Gaucher disease due to overlap of clinical manifestations[2,12*]

ASMD	Gaucher disease
ASM biochemical enzyme assay	ß-glucosidase enzyme assay

Adapted from McGovern MM et al. *Genet Med.* 2017;19(9):967-974.[2]
*Guidelines are based on a consensus of opinion from an international group of experts in ASMD.[2]

TAKE THE STEP TOWARD AN ACCURATE DIAGNOSIS

Diagnostic testing for ASMD is simple.[2]

Perform an ASM biochemical enzyme assay on isolated peripheral blood leukocytes, dried blood spots (DBS), or skin fibroblasts*

↓

Low residual ASM activity

↓

ASMD diagnosis confirmed

Additional diagnostic confirmation can be achieved using molecular genetic testing

*Limitations to DBS testing include the potential effects of anemia and recent transfusions on results. Skin fibroblasts or *SMPD1* gene sequencing can be used in equivocal cases.[2]

EVREN
Living with ASMD type B

An accurate diagnosis can help initiate an appropriate management plan[1,2]

- Monitoring of clinical signs is essential to help track the course of disease
- Multidisciplinary healthcare teams can provide supportive care to help manage some of the key symptoms of ASMD
- Genetic counseling is important to educate patients on the autosomal recessive nature of ASMD and the potential risk of inheritance in other family members

IS ASMD PRESENTING IN YOUR PRACTICE?

Pediatric case study[2]: Alice presented with abdominal distension and other gastrointestinal symptoms at age 2.

AGE 0

Birth
- **Normal growth and development**

AGE 2

Pediatrician visit
- **Abdominal distension, chronic diarrhea, and feeding difficulties**
  Clinical findings: Hepatosplenomegaly
- **Laboratory findings:** Dyslipidemia, elevated liver transaminases, thrombocytopenia, and leukopenia
- **Referral to pediatric gastroenterologist**

Pediatric gastroenterologist
- **Clinical findings:** Mild jaundice and frequent vomiting
- **Differential diagnosis:** Food allergies, leukemia/lymphoma, Gaucher disease, and ASMD

ASMD type A/B diagnosed through parallel testing for ASMD and Gaucher disease*
- **Laboratory findings:**
  Reduced ASM enzyme activity in leukocytes:
  1.735 nmol/mg/17 h (normal range: 8.8-30.62 nmol/mg/17 h)†

AGE 4

Follow-up visit
- **Clinical findings:** Ataxia, delayed motor milestones, and reduced fine motor skills
- **Referral to pediatric neurologist**

Alice has delayed physical and mental development, but remains interactive and responsive. Her symptoms are managed by a multidisciplinary team of specialists.

Case adapted from McGovern MM et al. *Genet Med.* 2017;19(9):967-974.[2] This case is for representative purposes only and is not associated with patient in the photo on the adjacent page.

*Testing uses an ASM biochemical enzyme assay for ASMD and ß-glucosidase enzyme assay for Gaucher disease.[2,12]

†Normal lab values vary from institution to institution.

GARRETT
Living with
ASMD type A/B

Early diagnosis of ASMD is a priority for appropriate symptom management.[1,2]

IS ASMD PRESENTING IN YOUR PRACTICE?

Adult case study[2]: John was diagnosed with anemia as a child and presented with respiratory issues and an abnormal lipid profile in his 20s.

AGE 7

Pediatrician visit
- **Lethargy and limited physical activity**
  Clinical findings: Blood tests revealed anemia
- **Diagnosis:** Anemia

20

Internist visit
- **Shortness of breath after exercise, low HDL**
- **Referral to pulmonologist**

Pulmonologist
- **Clinical findings:** Interstitial lung disease found on chest X-ray and CT
- **Misdiagnosis:** Sarcoidosis

30

Internist visit
- **Clinical findings:** Abdominal pain, and thrombocytopenia
- **Referral to hematologist-oncologist**

Hematologist-oncologist
- **Clinical findings:** Small mass on abdominal MRI
- **Differential diagnosis:** Leukemia and lymphoma, as well as lysosomal storage disorders, including Gaucher disease and ASMD

ASMD type B diagnosed through parallel testing for ASMD and Gaucher disease*
- **Laboratory findings:**
  Reduced ASM enzyme activity in leukocytes:
  0.7553 nmol/mg/17 h (normal range: 8.8-30.62 nmol/mg/17 h)†

40

Follow-up visit
- **Clinical findings:** Increased hepatosplenomegaly and abdominal pain
- **Laboratory findings:** Increased aminotransferases and imaging revealed liver fibrosis

John is currently undertaking lifestyle changes to manage his liver fibrosis.
A liver transplant is also being considered if his symptoms progress to cirrhosis of the liver.

Case adapted from McGovern MM et al. *Genet Med.* 2017;19(9):967-974.[2] This case is for representative purposes only and is not associated with patient in the photo on the adjacent page.

HDL=high-density lipoprotein; CT=computed tomography.

*Testing uses an ASM biochemical enzyme assay for ASMD and ß-glucosidase enzyme assay for Gaucher disease.[2,12]

† Normal lab values vary from institution to institution.

JJ
Living with ASMD

You can play a critical role in early detection of ASMD and reduce diagnostic delays.

Show your patients the way to their ASMD diagnosis

- ASMD, historically known as Niemann-Pick types A, A/B, and B, is a multisystemic disease that can reduce lifespan by decades[1,4]
- The hallmark symptoms that affect children and adults are[1]:
  - Hepatomegaly
  - Splenomegaly
  - Thrombocytopenia
  - Pulmonary dysfunction
- Include ASMD and Gaucher disease in your differential to enable early diagnosis and symptom management[1,2]

SUSPECT ASMD? TEST TO KNOW

- Diagnostic testing is simple. Confirm a diagnosis of ASMD with an ASM biochemical enzyme assay[2]
- Guidelines recommend **parallel testing** for ASMD and Gaucher disease due to overlap of clinical manifestations[2]

For more information on ASMD and testing, visit **ASMDfacts.com/hcp**

(BUSINESS CARD)

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