



# PERSEVERE

*Persist. Quest. Cure.*

**PERSEVERE** – To persist in an undertaking in spite of counter-influences, oppositions or discouragements.

*“We, the families of the children and adults affected by Niemann-Pick Disease,*

**Thank You**

*for joining us as we persevere in our quest to find a cure.”*

**National Niemann-Pick Disease Foundation**  
P.O. Box 310  
Fort Atkinson, WI 53538-0310

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[www.nnpdf.org](http://www.nnpdf.org)



## The National Niemann-Pick Disease Foundation

The National Niemann-Pick Disease Foundation (NNPDF) was established in 1992. It has grown to become an international, voluntary, non-profit organization comprised of parents, relatives and friends committed to finding a cure for all types of Niemann-Pick Disease.

*Our primary goals:*

- Promote research into the causes of Niemann-Pick Disease (NPD)
- Provide information to assist in the correct medical diagnoses and referrals of children with NPD
- Facilitate genetic counseling for parents who are known NPD carriers
- Encourage the exchange of research findings among scientists
- Support legislation that positively impacts patients and families affected by NPD

While there is little that can ease the emotional burden of NPD, interaction with other parents and families reduces feelings of isolation and despair.

*That's why the National Niemann-Pick Disease Foundation strives to:*

- Give and facilitate emotional support
- Provide assistance during a crisis
- Share resources and ideas including, but not limited to, doctors, clinics, insurance companies and additional health and human services
- Provide practical suggestions about the day-to-day care of those with NPD
- Establish enduring relationships with other families affected by NPD

*The vision of the members of the NNPDF is that individuals affected by Niemann-Pick Disease will have the same chance as their siblings and peers to run and play, to hope and achieve, and to live out their dreams.*

Please fill out the attached donation form and mail with your tax-deductible contribution to:



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## Research Is Our Only Hope

Researchers are working to improve methods of diagnosing and treating Niemann-Pick Disease due to Acid Sphingomyelinase Deficiency (ASMD)(NPD Types A, A/B and B). Researchers now know many of the disease-causing changes in the ASM gene and have begun to understand the connections between these mutations and severity of disease. Animals without functional ASM and with limited function of ASM have been developed in the lab and are being used to study disease progression and the effectiveness of various treatment strategies. Studies continue on enzyme replacement therapy (ERT) and other therapies for those who may not benefit from ERT. Other treatments may be on the horizon as more is learned about the disease process, but much work remains to be done!

*Research is the key to finding effective treatments, and one day, a cure for NPD.*

*We will PERSEVERE until the battle against NPD is won!*

*We need your help to achieve this goal.*



*experience a  
They have only their childhood to  
experience a lifetime.  
lifetime.*



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## The horror of Niemann-Pick Disease/ASMD is too great for most of us to imagine.

This rare, life-limiting and in severe cases, deadly, disease robs those diagnosed of their most precious gift – life. Niemann-Pick Disease (NPD) due to Acid Sphingomyelinase Deficiency (ASMD), is also known as NPD Types A, A/B, and B. When a family receives the soul-crushing diagnosis of NPD/ASMD for their child or loved one, they begin an incomprehensible journey ranging from activity restrictions, lifelong treatments, and medical complications, to a gradual decline, suffering and, in the most severe cases, death.

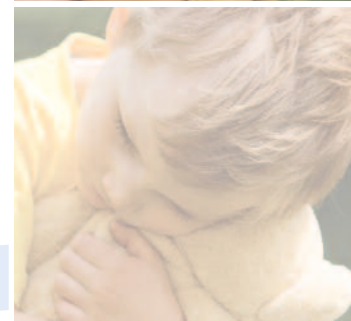
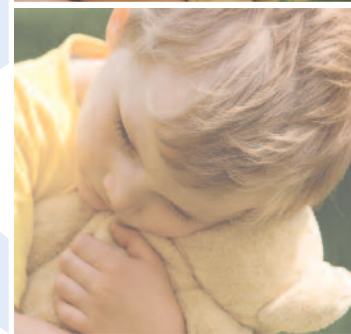
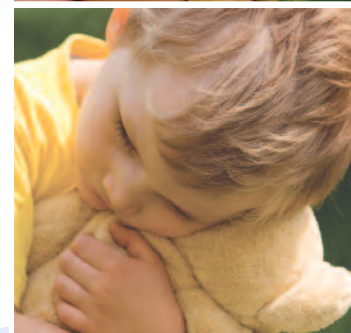
Researchers are working diligently to learn as much as they can about ASMD, but this is an uphill battle. ASMD is highly unpredictable, and the symptoms are similar to dozens of other conditions. Significant progress has been made, but diagnosis is still difficult and a cure has yet to be found.

You can help children and families facing Niemann-Pick Disease/ASMD. Please take a few moments to read and learn about the disease. Further, we ask you to reach out and offer support to families affected by ASMD. They are struggling to face the challenges of this devastating disease and the possible loss of a child or loved one, and they desperately need the support of family, friends, and their communities.

Please consider making a tax-deductible donation to the NNPDF's programs of research and family support services. We are working toward a day when ASMD can be quickly and accurately

diagnosed and treated with 100 percent success. We are looking forward to the day when we can unite in celebration and shout, "We have prevailed in our Quest for a Cure!" Until then, we will PERSEVERE in the battle against this devastating disease. Together, we can make it happen. Together, we can make a difference!

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## The complexities of Niemann-Pick Disease/ASMD

The term "Niemann-Pick Disease" (NPD) refers to two categories of disease: 1) NPD due to Acid Sphingomyelinase Deficiency (ASMD), also known as NPD Types A, A/B, and B, and 2) NPD Type C (NPC), characterized by abnormal cholesterol and lipid processing in the cell, and caused by mutations in either of two genes, *NPC1* or *NPC2*.

(For more information about NPD Type C, please see the NNPDF's companion brochure.)

Niemann-Pick Disease due to ASMD is inherited as an autosomal recessive condition. This means that affected individuals have two altered copies of the gene called *SMPD1*, having inherited one copy from each parent. Each unaffected parent (called a carrier) of an affected individual has one altered copy of the disease-causing gene and one normally-functioning copy of that gene. For a couple who are both carriers, there is a 1 in 4 chance with each pregnancy that a child will be affected by ASMD, a 2 in 4 chance that the child, like the parents, will be a carrier of ASMD, and a 1 in 4 chance that the child will be neither a carrier nor affected.

ASMD NPD occurs in all ethnic groups, but as with all genetic disorders may be more common in certain groups than others. For example, the severe, neurological form (Type A, see below) appears to be more frequent among Ashkenazi Jewish individuals (carrier frequency of ~1:90 to 1:100).

Niemann-Pick Disease due to ASMD is usually classified into two groups: 1) Type A, in which affected individuals have severe neurological problems and usually do not survive past age 3, and 2) Type B, in which affected individuals do not have neurological problems and may survive into adulthood.

However, forms of ASMD NPD between these two extremes do occur, and the diagnosis is sometimes called Intermediate NPD A/B. There can be considerable overlap along the entire disease spectrum with symptoms ranging in onset, complexity and severity, and every patient's case is unique.

The symptoms of ASMD NPD are shared by a number of related lysosomal disorders. Further, the rate of disease progression varies from patient to patient, even within families where more than one child is affected. This variability contributes to the challenges in diagnosis, and often leads to delay in confirmation of the diagnosis.

### The following is a listing of recognized symptoms of these conditions:

#### Niemann-Pick Disease Type A (NPA)

- Onset of symptoms very early, usually within the first few months of life
- Enlarged liver and spleen
- Feeding difficulties
- Failure to Thrive (FTT)
- Irritability
- Progressive loss of motor skills, especially after one year of age
- Cherry red spot on retina
- Frequent respiratory infections

#### Niemann-Pick Disease Type B (NPB)

- Later age at onset of symptoms
- Enlarged liver and spleen in childhood
- Gradually worsening lung function with susceptibility to respiratory infections
- Altered blood lipid profile
- Progressive evidence of cardiovascular and liver disease
- Decreased platelet count
- Delayed growth, short stature

As noted above, not all patients diagnosed with ASMD fall distinctly into the categories of Type A or Type B. These patients may be termed Type A/B, and often, only time will tell whether their disease progression leans more toward Type A or toward Type B. The appearance of neurological symptoms may

indicate a tendency toward Type A disease, but again, the distinction between Types A and B may be blurred. This uncertainty can take an emotional toll on the individual and their family members, as well.

Current treatment strategies for NPA target management of symptoms to improve quality of life for affected individuals and their families. These include, but are not limited to:

- Physical and occupational therapy to maintain function
- Nutrition consultation; placement of naso-gastric or gastrostomy tube may be considered
- Management of sleep disturbance

Current treatment strategies for NPB include:

- Management of bleeding episodes, using transfusions if necessary
- Supplemental oxygen if needed
- Medication to control blood lipid levels
- Nutrition consultation

#### Developing Therapies

Infusion of manufactured enzyme has been utilized for a number of related lysosomal storage diseases. Called enzyme replacement therapy or ERT, this is currently being evaluated through a formal clinical trial for NPB. Other possible therapies that may be investigated in the future include gene therapy to replace the faulty *SMPD1* gene with a functional gene through modified cell transplantation, small molecule therapies such as substrate reduction therapy, and chaperone therapy.



National Niemann-Pick  
Disease Foundation

DONATION FORM

Please help us in our fight against Niemann-Pick Disease.

Your tax-deductible contribution helps to support our programs of research for Niemann-Pick Disease, support our NPD families and educate the public.

*Thank You  
for joining us as we persevere  
in our quest for a cure.*

Name: \_\_\_\_\_

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**Please fill out the donation form and  
mail with your tax-deductible contribution to:**

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*The National Niemann-Pick Disease Foundation has been designated  
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