**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
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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 (ASM) (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.
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 cholesteryl 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, a 1 in 2 chance that the child 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 ~1/100 to 1/100).

Niemann-Pick disease due to NPD 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 NPD between these two extremes do occur, and the diagnosis is sometimes called Intermediate NPB 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 NPD A/B due to ASMD 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:

- 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 (NPC)
- Later age at onset of symptoms
- Enlarged liver and spleen in childhood
- Gradually worsening function with susceptibility to respiratory infections
- Altered blood lipid profile
- Progressive evidence of cardiovascular and liver disease
- Decreased platelet count
- Delayed motor skills

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 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 NPB 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 gastrostomy tube and tube feeding may be considered
- Management of sleep disturbance

Current treatment strategies for NPC 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 NPC. 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 chelation therapy.