Lipid storage diseases

What are lipid storage diseases?
Lipid storage diseases, or the lipidoses, are a group of inherited metabolic disorders in which harmful amounts of fatty materials (lipids) accumulate in various cells and tissues in the body. People with these disorders either do not produce enough of one of the enzymes needed to break down (metabolize) lipids or they produce enzymes that do not work properly. Over time, this excessive storage of fats can cause permanent cellular and tissue damage, particularly in the brain, peripheral nervous system (the nerves from the spinal cord to the rest of the body), liver, spleen, and bone marrow.

What are lipids?
Lipids are fat-like substances that are important parts of the membranes found within and between cells and in the myelin sheath that coats and protects the nerves. Lipids include oils, fatty acids, waxes, steroids (such as cholesterol and estrogen), and other related compounds.

These fatty materials are stored naturally in the body’s cells, organs, and tissues. Tiny bodies within cells called lysosomes regularly convert, or metabolize, the lipids and proteins into smaller components to provide energy for the body. Disorders in which intracellular material that cannot be metabolized is stored in the lysosomes are called lysosomal storage diseases. In addition to lipid storage diseases, other lysosomal storage diseases include the mucolipidoses, in which excessive amounts of lipids with attached sugar molecules are stored in the cells and tissues, and the mucopolysaccharidoses, in which excessive amounts of large, complicated sugar molecules are stored.

How are lipid storage diseases inherited?
Lipid storage diseases are inherited from one or both parents who carry a defective gene that regulates a particular lipid-metabolizing enzyme in a class of the body’s cells. They can be inherited two ways:

Autosomal recessive inheritance occurs when both parents carry and pass on a copy of the faulty gene, but neither parent is affected by the disorder. Each child born to these parents has a 25 percent chance of inheriting both copies of the defective gene, a 50 percent chance of being a carrier like the parents, and a 25 percent chance of not inheriting either copy of the defective gene. Children of either gender can be affected by an autosomal recessive pattern of inheritance.

X-linked (or sex-linked) recessive inheritance occurs when the mother carries the affected gene on the X chromosome. The X and Y chromosomes are involved in gender determination. Females have two X chromosomes and males have one X chromosome and one Y chromosome. Sons of female carriers have a 50 percent chance of inheriting and being affected with the disorder, as the sons receive one X chromosome from the mother and a Y chromosome from the father. Daughters have a 50 percent chance of inheriting the affected X chromosome from the mother and are carriers or mildly affected. Affected men do not pass the disorder to their sons but their daughters will be carriers for the disorder.

What are the types of lipid storage disease?
Gaucher disease is caused by a deficiency of the enzyme glucocerebrosidase. Fatty material can collect in the brain, spleen, liver, kidneys, lungs, and bone marrow. Symptoms may include brain damage, enlarged spleen and liver, liver malfunction, skeletal disorders and bone lesions that may cause pain and fractures, swelling of lymph nodes and (occasionally) adjacent joints, distended abdomen, a brownish tint to the skin, anemia, low blood platelets, and yellow spots in the eyes. Individuals affected most seriously may also be more susceptible to infection. The disease affects males and females equally.
Gaucher disease has three common clinical subtypes:

- **Type 1** (or nonneuronopathic type) is the most common form of the disease in the U.S. and Europe. The brain is not affected, but there may be lung and, rarely, kidney impairment. Symptoms may begin early in life or in adulthood and include enlarged liver and grossly enlarged spleen, which can rupture and cause additional complications. Skeletal weakness and bone disease may be extensive. People in this group usually bruise easily due to low blood platelet count. They may also experience fatigue due to anemia. Depending on disease onset and severity, individuals with type 1 may live well into adulthood. Many affected individuals have a mild form of the disease or may not show any symptoms. Although Gaucher type 1 occurs often among persons of Ashkenazi Jewish heritage, it can affect individuals of any ethnic background.

- **Type 2** (or acute infantile neuropathic Gaucher disease) typically begins within 3 months of birth. Symptoms include extensive and progressive brain damage, spasticity, seizures, limb rigidity, enlarged liver and spleen, abnormal eye movement, and a poor ability to suck and swallow. Affected children usually die before age 2.

- **Type 3** (the chronic neuronopathic form) can begin at any time in childhood or even in adulthood. It is characterized by slowly progressive but milder neurologic symptoms compared to the acute or type 2 Gaucher disease. Major symptoms include eye movement disorders, cognitive deficit, poor coordination, seizures, an enlarged spleen and/or liver, skeletal irregularities, blood disorders including anemia, and respiratory problems. Nearly everyone with type 3 Gaucher disease who receives enzyme replacement therapy will reach adulthood.

For type 1 and most type 3 individuals, enzyme replacement treatment given intravenously every two weeks can dramatically decrease liver and spleen size, reduce skeletal abnormalities, and reverse other manifestations. Successful bone marrow transplantation cures the non-neurological manifestations of the disease. However, this procedure carries significant risk and is rarely performed in individuals with Gaucher disease. Surgery to remove all or part of the spleen may be required on rare occasions (if the person has very low platelet counts or when the enlarged organ severely affects the person’s comfort). Blood transfusion may benefit some anemic individuals. Others may require joint replacement surgery to improve mobility and quality of life. There is currently no effective treatment for the brain damage that may occur in people with types 2 and 3 Gaucher disease.

**Niemann-Pick disease** is a group of autosomal recessive disorders caused by an accumulation of fat and cholesterol in cells of the liver, spleen, bone marrow, lungs, and, in some instances, brain. Neurological complications may include ataxia (lack of muscle coordination that can affect walking steadily, writing, and eating, among other functions), eye paralysis, brain degeneration, learning problems, spasticity, feeding and swallowing difficulties, slurred speech, loss of muscle tone, hypersensitivity to touch, and some clouding of the cornea due to excess buildup of materials. A characteristic cherry-red halo that can be seen by a physician using a special tool develops around the center of the retina in 50 percent of affected individuals.

Niemann-Pick disease is subdivided into three categories:

- **Type A**, the most severe form, begins in early infancy. Infants appear normal at birth but develop profound brain damage by 6 months of age, an enlarged liver and spleen, swollen lymph nodes, and nodes under the skin (xanthomas). The spleen may enlarge to as great as 10 times its normal size and can rupture, causing bleeding. These children become progressively weaker, lose motor function, may become anemic, and are susceptible to recurring infection. They rarely live beyond 18 months. This form of the disease occurs most often in Jewish families.

- **Type B** (or juvenile onset) does not generally affect the brain but most children develop ataxia, damage to nerves exiting from the spinal cord (peripheral neuropathy), and pulmonary difficulties that progress with age. Enlargement of the liver and spleen characteristically occurs in the pre-teen years. Individuals with type B may live a comparatively long time but many require supplemental oxygen because of lung involvement. Niemann-Pick types A and B result from accumulation of the fatty substance called sphingomyelin, due to deficiency of an enzyme called sphingomyelinase.

- **Type C** may appear early in life or develop in the teen or even adult years. Niemann-Pick disease type C is not caused by a deficiency of sphingomyelinase but by a lack of the NPC1 or NPC2 proteins. As a result, various lipids and particularly cholesterol accumulate inside nerve cells and cause them to malfunction. Brain involvement may be extensive, leading to inability to look up and down, difficulty in walking and swallowing, progressive loss of hearing, and progressive dementia. People with type C have only moderate enlargement of their spleens and livers. Those individuals with Niemann-Pick type C who share a common ancestral background in Nova Scotia were previously referred to as type D. The life expectancies of people with type C vary considerably. Some individuals die in childhood while others who appear to be less severely affected can live into adulthood.

There is currently no cure for Niemann-Pick disease. Treatment is supportive. Children usually die from infection or progressive neurological loss. Bone marrow transplantation has been attempted in a few individuals with type B with
mixed results.

**Fabry disease**, also known as alpha-galactosidase-A deficiency, causes a buildup of fatty material in the autonomic nervous system (the part of the nervous system that controls involuntary functions such as breathing and heart beat), eyes, kidneys, and cardiovascular system. Fabry disease is the only X-linked lipid storage disease. Males are primarily affected, although a milder and more variable form is common in females. Occasionally, affected females have severe manifestations similar to those seen in males with the disorder. Onset of symptoms is usually during childhood or adolescence. Neurological signs include burning pain in the arms and legs, which worsens in hot weather or following exercise, and the buildup of excess material in the clear layers of the cornea (resulting in clouding but no change in vision). Fatty storage in blood vessel walls may impair circulation, putting the person at risk for stroke or heart attack. Other symptoms include heart enlargement, progressive kidney impairment leading to renal failure, gastrointestinal difficulties, decreased sweating, and fever. Angiokeratomas (small, non-cancerous, reddish-purple elevated spots on the skin) may develop on the lower part of the trunk of the body and become more numerous with age.

People with Fabry disease often die prematurely of complications from heart disease, renal failure, or stroke. Drugs such as phenytoin and carbamazepine are often prescribed to treat pain that accompanies Fabry disease but do not treat the disease. Metoclopramide or Lipisorb (a nutritional supplement) can ease gastrointestinal distress that often occurs in people with Fabry disease, and some individuals may require kidney transplant or dialysis. Enzyme replacement can reduce storage, ease pain, and preserve organ function in some people with Fabry disease.

**Farber disease**, also known as Farber’s lipogranulomatosis, describes a group of rare autosomal recessive disorders that cause an accumulation of fatty material in the joints, tissues, and central nervous system. It affects both males and females. Disease onset is typically in early infancy but may occur later in life. Children who have the classic form of Farber’s disease develop neurological symptoms within the first few weeks of life that may include increased lethargy and sleepiness, and problems with swallowing. The liver, heart, and kidneys may also be affected. Other symptoms may include joint contractures (chronic shortening of muscles or tendons around joints), vomiting, arthritis, swollen lymph nodes, swollen joints, hoarseness, and nodes under the skin which thicken around joints as the disease progresses. Affected individuals with breathing difficulty may require a breathing tube. Most children with the disease die by age 2, usually from lung disease. In one of the most severe forms of the disease, an enlarged liver and spleen can be diagnosed soon after birth. Children born with this form of the disease usually die within 6 months.

Farber disease is caused by a deficiency of the enzyme called ceramidase. Currently there is no specific treatment for Farber disease. Corticosteroids may be prescribed to relieve pain. Bone marrow transplants may improve granulomas (small masses of inflamed tissue) on people with little or no lung or nervous system complications. Older persons may have granulomas surgically reduced or removed.

**The gangliosidoses** are comprised of two distinct groups of genetic diseases. Both are autosomal recessive and affect males and females equally.

**GM1 gangliosidoses.** The GM1 gangliosidoses are caused by a deficiency of the enzyme beta-galactosidase, resulting in abnormal storage of acidic lipid materials particularly in the nerve cells in the central and peripheral nervous systems. GM1 gangliosidosis has three clinical presentations:

- GM1 (the most severe subtype, with onset shortly after birth) may include neurodegeneration, seizures, liver and spleen enlargement, coarsening of facial features, skeletal irregularities, joint stiffness, distended abdomen, muscle weakness, exaggerated startle response, and problems with gait. About half of affected individuals develop cherry-red spots in the eye. Children may be deaf and blind by age 1 and often die by age 3 from either cardiac complications or pneumonia.
- Late infantile GM1 gangliosidosis typically begins between ages 1 and 3 years. Neurological symptoms include ataxia, seizures, dementia, and difficulties with speech.
- GM1 gangliosidosis develops between ages 3 and 30. Symptoms include decreased muscle mass (muscle atrophy), neurological complications that are less severe and progress at a slower rate than in other forms of the disorder, corneal clouding in some people, and sustained muscle contractions that cause twisting and repetitive movements or abnormal postures (dystonia). Angiokeratomas may develop on the lower part of the trunk of the body. The size of the liver and spleen in most affected individuals is normal.

**GM2 gangliosidoses.** The GM2 gangliosidoses also cause the body to store excess acidic fatty materials in tissues and cells, most notably in nerve cells. These disorders result from a deficiency of the enzyme beta-hexosaminidase. The GM2 disorders include:
• **Tay-Sachs disease** (also known as GM2 gangliosidosis-variant B) and its variant forms are caused by a deficiency in the enzyme hexosaminidase A. The incidence has been particularly high among Eastern European and Ashkenazi Jewish populations, as well as certain French Canadians and Louisianan Cajuns. Affected children appear to develop normally for the first few months of life. Symptoms begin by 6 months of age and include progressive loss of mental ability, dementia, decreased eye contact, increased startle response to noise, progressive loss of hearing leading to deafness, difficulty in swallowing, blindness, cherry-red spots in the retina, and some paralysis. Seizures may begin in the child’s second year. Children may eventually need a feeding tube and they often die by age 4 from recurring infection. No specific treatment is available. Anticonvulsant medications may initially control seizures. Other supportive treatment includes proper nutrition and hydration and techniques to keep the airway open. A rare form of the disorder, called late-onset Tay-Sachs disease, occurs in people in their 20s and early 30s and is characterized by unsteadiness of gait and progressive neurological deterioration.

• **Sandhoff disease** (variant AB) is a severe form of Tay-Sachs disease. Onset usually occurs at the age of 6 months and is not limited to any ethnic group. Neurological signs may include progressive deterioration of the central nervous system, motor weakness, early blindness, marked startle response to sound, spasticity, shock-like or jerking of a muscle (myoclonus), seizures, abnormally enlarged head (macrocephaly), and cherry-red spots in the eye. Other symptoms may include frequent respiratory infections, heart murmurs, doll-like facial features, and an enlarged liver and spleen. There is no specific treatment for Sandhoff disease. As with Tay-Sachs disease, supportive treatment includes keeping the airway open and proper nutrition and hydration. Anti-seizure medications may initially control seizures. Children generally die by age 3 from respiratory infections.

**Krabbe disease** (also known as globoid cell leukodystrophy and galactosylceramide lipidosis) is an autosomal recessive disorder caused by deficiency of the enzyme galactocerebrosidase. The disease most often affects infants, with onset before age 6 months, but can occur in adolescence or adulthood. The buildup of undigested fats affects the growth of the nerve’s protective insulating sheath (myelin sheath) and causes severe deterioration of mental and motor skills. Other symptoms include muscle weakness, reduced ability of a muscle to stretch (hypertonia), muscle stiffening (spasticity), sudden shock-like or jerking of the limbs (myoclonic seizures), irritability, unexplained fever, deafness, blindness, paralysis, and difficulty when swallowing. Prolonged weight loss may also occur. The disease may be diagnosed by enzyme testing and by identification of its characteristic grouping of cells into globoid bodies in the white matter of the brain, demyelination of nerves and degeneration, and destruction of brain cells. In infants, the disease is generally fatal before age 2. Individuals with a later onset form of the disease have a milder course of the disease and live significantly longer. No specific treatment for Krabbe disease has been developed, although early bone marrow transplantation may help some people.

**Metachromatic leukodystrophy**, or MLD, is a group of disorders marked by storage buildup in the white matter of the central nervous system and in the peripheral nerves and to some extent in the kidneys. Similar to Krabbe disease, MLD affects the myelin that covers and protects the nerves. This autosomal recessive disorder is caused by a deficiency of the enzyme arylsulfatase A. Both males and females are affected by this disorder. MLD has three characteristic forms: late infantile, juvenile, and adult.

Late infantile MLD typically begins between 12 and 20 months following birth. Infants may appear normal at first but develop difficulty in walking and a tendency to fall, followed by intermittent pain in the arms and legs, progressive loss of vision leading to blindness, developmental delays and loss of previously acquired milestones, impaired swallowing, convulsions, and dementia before age 2. Children also develop gradual muscle wasting and weakness and eventually lose the ability to walk. Most children with this form of the disorder die by age 5.

Juvenile MLD typically begins between ages 3 and 10. Symptoms include impaired school performance, mental deterioration, ataxia, seizures, and dementia. Symptoms are progressive with death occurring 10 to 20 years following onset.

Adult symptoms begin after age 16 and may include ataxia, seizures, abnormal shaking of the limbs (tremor), impaired concentration, depression, psychiatric disturbances and dementia. Death generally occurs within 6 to 14 years after onset of symptoms.

There is no cure for MLD. Treatment is symptomatic and supportive. Bone marrow transplantation may delay progression of the disease in some cases. Considerable progress has been made with regard to gene therapies in animal models of MLD and in clinical trials.

**Wolman disease**, also known as acid lipase deficiency, is a severe lipid storage disorder that is usually fatal by age 1.
This autosomal recessive disorder is marked by accumulation of cholesteryl esters (normally a transport form of cholesterol) and triglycerides (a chemical form in which fats exist in the body) that can build up significantly and cause damage in the cells and tissues. Both males and females are affected by this disorder. Infants are normal and active at birth but quickly develop progressive mental deterioration, enlarged liver and grossly enlarged spleen, distended abdomen, gastrointestinal problems, jaundice, anemia, vomiting, and calcium deposits in the adrenal glands, causing them to harden.

Another type of acid lipase deficiency is cholesteryl ester storage disease. This extremely rare disorder results from storage of cholesteryl esters and triglycerides in cells in the blood and lymph and lymphoid tissue. Children develop an enlarged liver leading to cirrhosis and chronic liver failure before adulthood. Children may also have calcium deposits in the adrenal glands and may develop jaundice late in the disorder.

Enzyme replacement for both Wolman’s disease and cholesteryl ester storage disease is currently under active investigation.

How are these disorders diagnosed?

In some states, some of these disorders (most notably and controversially Krabbe disease) are screened for at birth.

In older children, diagnosis is made through clinical examination, enzyme assays (laboratory tests that measure enzyme activity), genetic testing, biopsy, and molecular analysis of cells or tissues. In some forms of the disorder, urine analysis can identify the presence of stored material. In others, the abnormality in enzyme activity can be detected in white blood cells without tissue biopsy. Some tests can also determine if a person carries the defective gene that can be passed on to her or his children. This process is known as genotyping.

Biopsy for lipid storage disease involves removing a small sample of the liver or other tissue and studying it under a microscope. In this procedure, a physician will administer a local anesthetic and then remove a small piece of tissue either surgically or by needle biopsy (a small piece of tissue is removed by inserting a thin, hollow needle through the skin).

Genetic testing can help individuals who have a family history of lipid storage disease determine if they are carrying a mutated gene that causes the disorder. Other genetic tests can determine if a fetus has the disorder or is a carrier of the defective gene. Prenatal testing is usually done by chorionic villus sampling, in which a very small sample of the placenta is removed and tested during early pregnancy. The sample, which contains the same DNA as the fetus, is removed by catheter inserted through the cervix or by a fine needle inserted through the abdomen. Results are usually available within 2-4 weeks.

How are these disorders treated?

Currently there is no specific treatment available for most of the lipid storage disorders but highly effective enzyme replacement therapy is available for type 1 and type 3 Gaucher disease. Enzyme replacement therapy is also available for Fabry disease, although it is not as effective as for Gaucher disease. However, anti-platelet medications can help prevent strokes and medications that lower blood pressure can slow the decline of kidney function in people with Fabry disease. The U.S. Food and Drug Administration has approved the drug migalastat (Galafold) as an oral medication for adults with Fabry disease who have a certain genetic mutation. Eliglustat tartrate, an oral drug approved for Gaucher treatment, works by administering small molecules that reduce the action of the enzyme that catalyzes glucose to ceramide. Medications such as gabapentin and carbamazepine may be prescribed to help treat pain (including bone pain). Restricting one’s diet does not prevent lipid buildup in cells and tissues.

What research is being done?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world. As part of its mission, the NINDS conducts and funds research on lipid storage diseases and other inherited metabolic disorders that affect the brain and nervous system.

In past research, investigators at the NINDS made significant contributions to research on lipid storage disorders and their treatment. These scientists identified the enzymes affected in people with Gaucher and Fabry diseases. NINDS
scientists also discovered a gene that is mutated in the majority of individuals with Niemann-Pick disease type C. NINDS researchers developed highly effective enzyme replacement therapy for Gaucher and Fabry diseases, as well as a mouse model of Fabry disease for use in research to understand the disease and develop treatments, which has enabled ongoing and promising research to develop gene therapy for this disease.

The NINDS, along with other NIH institutes, supports the Lysosomal Disease Network, a network of centers that addresses some of the major challenges in the diagnosis, management, and therapy of rare diseases, including the lipid storage diseases. The LDN is a member of the NIH Rare Diseases Clinical Research Network program, which supports collaborative consortia of rare disease researchers and disease community partners. Research on lipid storage disorders within the LDN includes longitudinal studies of the natural history and/or treatment of these disorders. Additional studies will emphasize the quantitative analysis of the central nervous system structure and function, and develop biomarkers (signs that can indicate the diagnosis or progression of a disease) for these disorders.

Research funded by NINDS focuses on better understanding how neurological deficits arise in lipid storage disorders and on the development of new treatments targeting disease mechanisms, including gene therapies, cell-based therapies, and pharmacological approaches.

Mutations in the gene that provides instructions for the protein glucocerebrosidase cause Gaucher disease as well as an increased risk for Parkinson’s disease and Lewy Body Dementia, all of which are marked by increased buildup of the protein alpha-synuclein. Using fly and mouse models of glucocerebrosidase deficiency, scientists hope to learn how this deficiency impairs the breakdown of lysosomal proteins, including the breakdown of alpha-synuclein. Other research is looking at anomalies in metabolic pathways that may contribute to neuronal dysfunction and degeneration in aging and sporadic Parkinson’s disease. A better understanding of the mechanisms involved in these diseases could lead to the development of new treatments.

Krabbé disease attacks the insulating sheath (myelin) around nerve fibers (axons) that is important for neuron function and survival. Hematopoietic stem cell transplant (HSCT)—using stem cells from umbilical cord blood or bone marrow—has been shown to benefit some individuals when given early in the course of the disease. For example, a small clinical study found that treating infants at high risk for developing early-onset Krabbé disease with HSCT before they were 7 weeks old led to improved quality of life and longer lifespans compared to untreated children or children who received HSCT after 6 weeks of age. Scientists plan to test hematopoietic stem cell transplantation plus gene therapy in an animal model of Krabbé disease to study disease mechanisms and any positive effects of combined therapy. Also in an animal model, NINDS-funded scientists are testing a combined treatment approach that uses a harmless virus to increase protein production, along with blood stem cell transplantation and small molecule-based drugs, to reduce neuroinflammation, cell death, and nerve cell degeneration seen in the disease.

Niemann-pick type C1 (NPC1) disease is characterized by the accumulation of cholesterol and other lipids in the brain and other organs. A barrier to the development of therapies for NPC1 disease is the lack of outcome measures for clinical trials. NINDS-funded researchers will test if a cholesterol oxidation byproduct ("oxysterol") is a biomarker that can be used to evaluate therapies as well as screen newborns for NPC1 disease.

NINDS-funded research on gangliosidosis is expanding the use of gene therapy delivered using an adeno-associated virus (AAV) to a larger area of the brain using an animal model of Tay-Sachs and Sandhoff diseases. A related project will study the effectiveness of whole-body AAV therapy in treating the disease.

NINDS-funded studies are underway to develop new and improved treatments for Farber, Tay-Sachs, Sandhoff, Fabry, and Gaucher diseases, as well as cholesterol metabolism disorders. Among NIH-funded projects, researchers hope to improve on imaging techniques to aid in newborn screening for lysosomal storage diseases, including Wolman’s disease and cholesteryl ester storage disease, and to correct cholesterol metabolism dysfunction and markedly increase the life of the animal models of cholesterol storage disease.

Many neurological disorders do not have effective treatment options. Clinical trials offer hope for many people and an opportunity to help researchers find better ways to safely detect, treat, or prevent disease. For more information about finding and participating in a clinical trial, visit NIH Clinical Trials and You.

In addition to NINDS, other NIH Institutes and Centers conduct and support research on lipid storage disorders,
including the National Institute on Aging, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the National Heart, Lung, and Blood Institute, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). More information on research on lipid storage diseases supported by NINDS and other NIH Institutes is available through the NIH RePORTER, a searchable database of current and previously funded research. Also, Genetics Home Reference provides consumer-friendly information about the effects of genetic variations on human health.

Where can I get more information?

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
(800) 352-9424
https://www.ninds.nih.gov

Information also is available from the following organizations:

Ara Parseghian Medical Research Foundation [For Niemann-Pick Type C Disease]
3530 East Campo Abierto
Suite 105
Tucson, AZ 85718-3327
victory@parseghian.org
Tel: 520-577-5106
Fax: 520-577-5212

Children's Gaucher Research Fund
P.O. Box 2123
Granite Bay, CA 95746-2123
research@childrensgaucher.org
Tel: 916-797-3700
Fax: 916-797-3707

Fabry Support & Information Group
108 NE 2nd Street, Ste. C
P.O. Box 510
Concordia, MO 64020-0510
info@fabry.org
Tel: 660-463-1355
Fax: 660-463-1356

Hide and Seek Foundation for Lysosomal Storage Disease Research
6475 East Pacific Coast Highway
Suite 466
Long Beach, CA 90803
info@hideandseek.org
Tel: 877-621-1122
Fax: 818-762-2502

Hunter's Hope Foundation (Krabbe Disease)
P.O. Box 643
6368 West Quaker Street
Orchard Park, NY 14127
Tel: 716-667-1200

ISMRD-International Advocate For Glycoprotein Storage Diseases
20880 Canyon View Drive  
Saratoga, CA 95070  
info@ismrd.org  
Tel: 734-449-1190  
Fax: 734-449-9038

**March of Dimes**  
1275 Mamaroneck Avenue  
White Plains, NY 10605  
askus@marchofdimes.com  
Tel: 914-997-4488; 888-MODIMES (663-4637)  
Fax: 914-428-8203

**MLD Foundation (Metachromatic Leukodystrophy)**  
21345 Miles Drive  
West Linn, OR 97038  
503-656-4808  
800-617-8387

**National Fabry Disease Foundation**  
4301 Connecticut Avenue, NW  
Suite 404  
Washington, DC 20008-2369  
info@fabrydisease.org  
Tel: 800-651-9131  
Fax: 800-651-9135

**National Gaucher Foundation, Inc.**  
5410 Edson Lane, Suite 220  
Rockville, MD 20852  
ggf@gaucherdisease.org  
Tel: 800-504-3189  
Fax: 770-934-2911

**National Niemann-Pick Disease Foundation, Inc.**  
P.O. Box 49  
401 Madison Avenue, Suite B  
Ft. Atkinson, WI 53538  
nnpdf@nnpdf.org  
Tel: 920-563-0930; 877-CURE-NPC (287-3672)  
Fax: 920-563-0931

**National Organization for Rare Disorders (NORD)**  
55 Kenosia Avenue  
Danbury, CT 06810  
orphan@rarediseases.org  
Tel: 203-744-0100; Voice Mail: 800-999-NORD (6673)  
Fax: 203-798-2291

**National Tay-Sachs and Allied Diseases Association**  
2001 Beacon Street  
Suite 204  
Boston, MA 02135  
info@ntsad.org  
Tel: 800-90-NTSAD (906-8723)  
Fax: 617-277-0134
