
# Helping your family understand and face CLN2 disease

The information included in this brochure is based on expert recommendations about caring for children with CLN2 disease. It contains resources, information, and useful tips to help you make a meaningful difference for a child with CLN2 disease.

This brochure is meant to support you and serve as a guide as you learn more about CLN2 disease. It is important to work closely with your child's doctor to find the right healthcare team and treatment plans for your child.

CLN2 disease–specific language, which may require further explanation, is used in this brochure. For educational purposes, these terms are highlighted in purple throughout the brochure, and definitions can be found on page 11.

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# What is CLN2 disease?

## CLN2 disease is a rare genetic disorder that affects children[1,2]

CLN2 disease is:

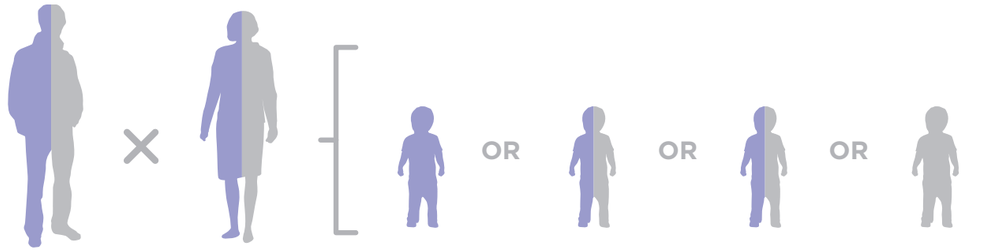
- Caused by a mutation in the *TPP1* gene, also referred to as the *CLN2* gene[2]
- One of the most common forms of neuronal ceroid lipofuscinoses (NCL)—NCLs are a group of disorders that are also known as Batten disease[3]
- Previously known as late-infantile NCL (LINCL), meaning that for most children, symptoms begin between the ages of 2 and 4[2]

CLN2 disease is an inherited disease that is passed down through families. Children with CLN2 disease are born with this condition, even though it may take months or years before they start showing signs. Diagnosis can be confirmed either through genetic or enzymatic testing.[2,4]

CLN2 disease is referred to as an autosomal recessive disorder[2]:

- Everyone has two copies of the *TPP1* gene. In people with CLN2 disease, both inherited genes (one from each parent) have mutations
- Parents of a child with CLN2 disease have a mutation in one of their *TPP1* genes
- Parents are carriers of the genetic mutation, which means they are healthy but can pass on the mutation to their children

**WHEN BOTH PARENTS CARRY THE MUTATED FORM OF THE GENE, EACH OF THEIR CHILDREN HAS A 25% CHANCE OF BEING AFFECTED BY CLN2 DISEASE[2,5]**




HEALTHY FATHER (CARRIER) | HEALTHY MOTHER (CARRIER) | HEALTHY CHILD (NONCARRIER) | HEALTHY CHILD (CARRIER) | HEALTHY CHILD (CARRIER) | CHILD WITH CLN2 DISEASE

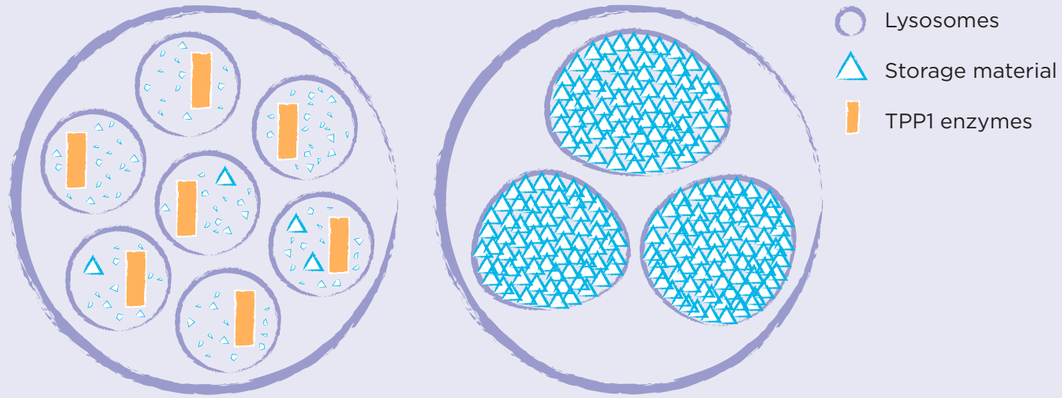


## CLN2 disease affects cells in the brain[6]

CLN2 disease is a type of lysosomal storage disorder. Lysosomes are inside every cell and contain enzymes that break down material in the cell. One of these enzymes is called tripeptidyl peptidase 1, or TPP1.[6]

The TPP1 enzyme is missing or not working properly in children with CLN2 disease. When this enzyme isn't working correctly, storage materials build up in the lysosome, particularly cells in the brain and the eyes.[3,7]

**CLN2 DISEASE IS ASSOCIATED WITH A BUILD-UP OF MATERIALS INSIDE BRAIN CELLS[3]**




**HEALTHY CELL**

In healthy brain cells, lysosomes use TPP1 to break down materials.[6]

**CLN2 CELL**

In CLN2 disease, the lysosome can't use TPP1 to break down materials. Instead, the lysosome stores materials. This buildup of materials is associated with damaging brain cells.[3,6]

**Over time, cells stop functioning normally. As this happens, the symptoms of CLN2 disease (for example, language delay, seizures, loss of movement, and visual impairment) appear.[3]**

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# How can I provide the best care for my child?

## Children with CLN2 disease should have a dedicated healthcare team[8]

Caring for a child with CLN2 disease is complex and impacts the family in many ways. Managing complex medical needs, such as a large number of appointments and medications can be challenging, even when the family has a routine that works.

Due to the range of symptoms and complications that children with CLN2 disease experience, experts agree that children should be under the care of a team of specialists. Talk to your child's doctor about which specialists they think should be included in your healthcare team.

### WHO MAY BE INVOLVED IN THE CARE OF MY CHILD?

These specialists may be a part of your healthcare team. Use the spaces below to fill in each specialist's name and contact information.

**Pediatric neurologist**
Leads team, primary management of CLN2 disease.

**Ophthalmologist**
Monitors and manages vision loss.

**Epilepsy specialist**
A neurologist who specializes in the treatment of seizures.

**Gastroenterologist**
Helps with feeding and digestive issues, like constipation and reflux.

**Geneticist**
May help confirm diagnosis through genetic testing and discuss family planning with parents.

**Orthopedist**
Helps with muscle and skeletal issues.

**Palliative care team**
Guides multidisciplinary team, assesses pain, and coordinates care at each stage of the disease.

**Physical therapist**
Helps support movement and independence.

**Speech therapist**
Helps with speech and language issues.

**Feeding therapist**
Helps with feeding issues as disease progresses.

**Dietitian**
Monitors and ensures proper nutrition.

**Social worker**
Links families with community resources during each stage of disease.



# Partner with your healthcare team every step of the way

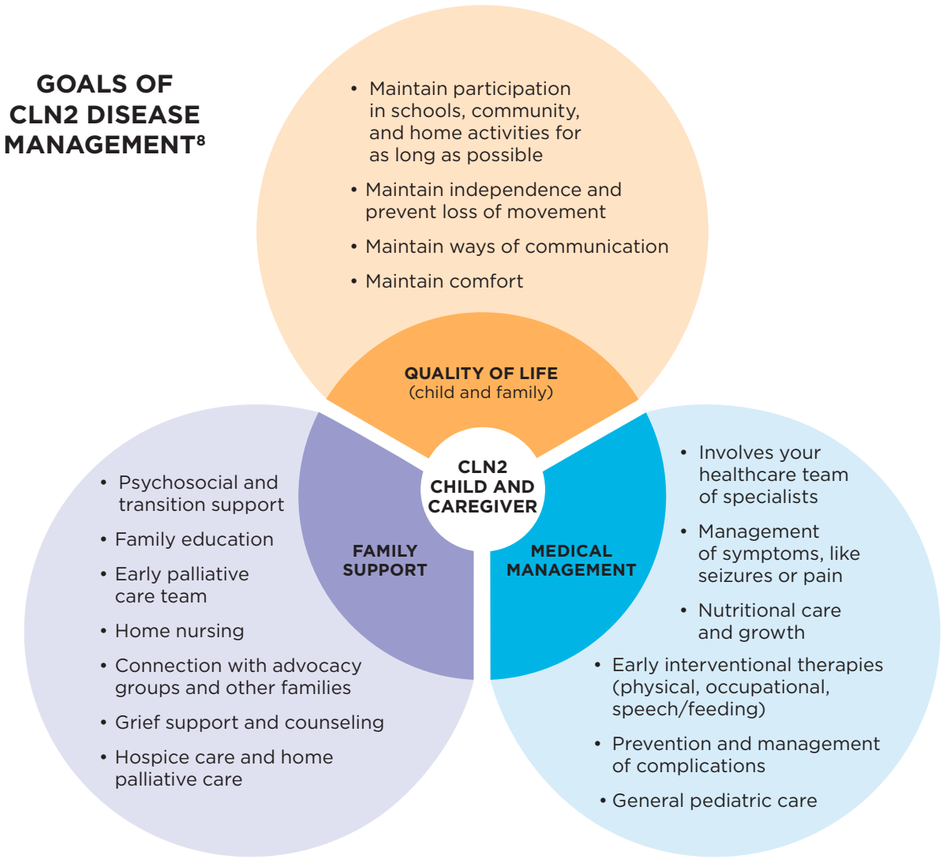
## Care goals and plans for your child may evolve over time

Typically, CLN2 disease can be broken down into 3 stages—early stage, rapidly progressive stage, and late stage. Children begin to develop symptoms during the early stage of the disease. When the disease progresses, the child enters a stage where symptoms start increasing rapidly. During the late stage, symptoms become even more severe and the child experiences loss of function. Your healthcare team will be in frequent communications with you to help determine care goals and plans, and then to check in with you and adjust plans based on the best interests for your child.

There are a number of ways to provide the best care for your child, including managing key symptoms of CLN2 disease in the following areas:

- Seizure management
- Movement disorders management
- Pain and nutritional management
- Sleep, respiratory, and vision management
- Physical, occupational, and speech therapy
- Educational, social, and family support

### GOALS OF CLN2 DISEASE MANAGEMENT[8]

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# Managing key symptoms

## Seizure management[8]

Your child's doctor may use medications to manage seizures, one of the most common symptoms of CLN2 disease. There are many anti-epileptic drugs (AEDs) available to help manage seizures. However, some AEDs may be more effective than others in the treatment of seizures that are related to CLN2 disease. It is important to work closely with your healthcare team to find the right AEDs for your child.

The goal of CLN2 disease seizure management should be to help control seizures enough to support your child's ability to function. A complete elimination of seizures is unlikely—instead, you and your healthcare team will focus on minimizing the effect of seizures on your child, particularly the most disabling and life-threatening ones. Your healthcare team will work to find the medication(s) and dosage that best control seizure activity with minimal side effects.

Medication(s) should be reevaluated periodically. It is possible that medication(s) that worked well in the past may no longer work as well for your child. Keep your healthcare team updated on any changes to your child's medications or if your child experiences any side effects from medication.

## Movement disorder management[8]

Three of the most common movement disorders associated with CLN2 disease are:

1. **Myoclonus**—a sudden, uncontrolled twitching of muscles[9]
2. **Dystonia**—uncontrolled muscle contractions[10]
3. **Spasticity**—increased muscle tone or muscle stiffness that interferes with movement or speech[11]

Experts agree that treatment should focus on reducing how often your child experiences these symptoms, lessening the severity of these symptoms, and preventing or relieving any pain children may experience.[8]

Certain medications and physical therapy may be used to help manage movement disorders and help maintain your child's range of motion, posture, and function. Your healthcare team may even recommend support equipment (an ankle brace) or items designed to adjust body posture (special pillows, a neck support, or a vest). Talk to your healthcare team about any movement disorder symptoms your child may be experiencing. You can work together to find a treatment that will best address your child's movement disorder symptoms.[8]

## Pain management[8]

CLN2 disease includes a range of symptoms, some of which may cause pain. Pain can come from multiple sources, including uncontrollable muscle contractions (also known as dystonia) or gastrointestinal symptoms such as reflux or constipation, among others.

As parents or caregivers, you play an important role in pain assessment. Your ability to understand your child's nonverbal reactions and/or signals—such as grimacing, restlessness, and distressed grunts or sounds—can help your healthcare team find the cause of pain. You are also the best source to help distinguish between when your child is in pain and when they're uncomfortable—for example, if they're feeling fearful, anxious, lonely, or bored. Once the cause of the pain is determined, your healthcare team can make recommendations to help your child. Playing relaxing music, reducing noise levels, or dimming lights can help create a calming environment for your child.

## Nutritional management

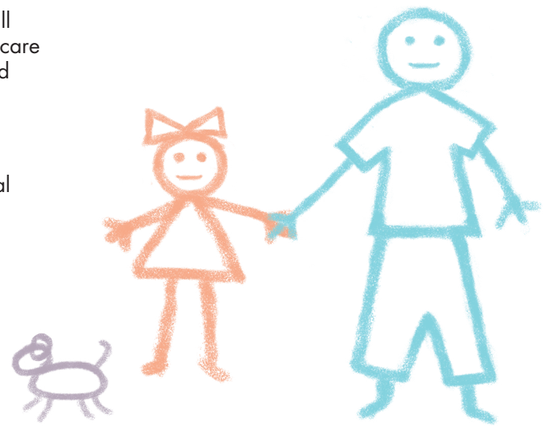
As CLN2 disease progresses, certain feeding and digestive issues may occur, including[2,7,8]:

- Swallowing difficulties
- Reflux (stomach acid flowing back into the food pipe, or esophagus)
- Constipation

When caring for a child with CLN2 disease, it is important to keep them in good nutritional status, prevent deficiencies, and make sure they maintain an appropriate growth rate. Achieving these goals may require supplementing their diet with formula, vitamins, and minerals. To prevent constipation, it is important to include an appropriate amount of water and fiber in your child's diet, and consider medications that may help relieve this symptom.[8]

As swallowing difficulties increase, managing your child's secretions will become very important. Your healthcare team will recommend treatments and help you develop the right plan for your child.

You and your healthcare team should discuss your child's nutritional status and any feeding abilities or restrictions you encounter. Together, you can identify potential issues and ways they can be addressed, such as special diets and other methods of feeding, such as a feeding tube.



# Managing key symptoms (continued)

## Sleep disturbances

As your child's disease progresses, you may notice that they experience sleep disturbances. Sleep disturbances are common in CLN2 disease, and include difficulties in falling asleep, staying asleep, waking due to uncontrolled muscle twitching (myoclonus), sleepiness during the daytime, and sleep-disordered breathing.

When children experience poor sleep, it can have an effect on seizure control, as well as behavioral and cognitive responses. Establishing a fixed bedtime routine for your child may help minimize your child's sleep disturbances. Other strategies you may consider include creating a comfortable environment for your child with music, massage, or weighted blankets, or using over-the-counter supplements or medications that your healthcare team recommends.

## Respiratory strategies

In later stages of CLN2 disease, respiratory (breathing) problems may occur more frequently and could have a harmful effect on your child. There are a few ways that you can help prevent or reduce them. Vaccinating your child, yourself, and other family members against preventable respiratory diseases, like the flu, is recommended by experts. Talk to your child's doctor about how to best provide care for your child's respiratory issues, including if your child may benefit from medications (like bronchodilators) or supplemental oxygen.

## Vision considerations

Vision loss is a major symptom of CLN2 disease and usually occurs around the age of 7 to 10 years old. Your healthcare team may use a tool called optical coherence tomography, or OCT, to monitor the progression of your child's vision loss. Although no treatment is available for vision loss, you may want to avoid giving your child any medication that may be harmful to the retina (back of the eye).



# Other ways to keep your child moving forward

## Physical, occupational, and speech therapy strategies

Experts agree that children with CLN2 disease can benefit from therapies that are adapted for the specific challenges they face. Since children with CLN2 disease lose skills rapidly, it may be helpful to start your child on physical, occupational, and speech therapy soon after diagnosis. You may also want to talk to your healthcare team about any adaptive devices that may be beneficial to your child.

## Types of therapy

- Physical—training that promotes comfort and extends independence through the use of therapy chairs (exercise their ability to sit upright) and standing devices (support muscle function and the ability to stand). Experts recommend children with CLN2 disease go to physical therapy 2 to 3 times a week if resources are available. Caregivers can learn exercises, postures, and positioning techniques that can be integrated into their child's daily routines
- Occupational—exercises to help children maintain skills and activities of daily living
- Speech—early development of alternative communication methods, like symbols and gestures, can help your child communicate after speech loss
- Complementary—alternative treatments like exercises within a pool (hydrotherapy), horseback riding to help with balance and coordination (hippotherapy), or music therapy can help decrease your child's anxiety, pain, and boredom, as well as provide them with opportunities for social interaction and enjoyment. Music may be especially comforting to children with CLN2 disease since hearing is preserved through later stages of the disease

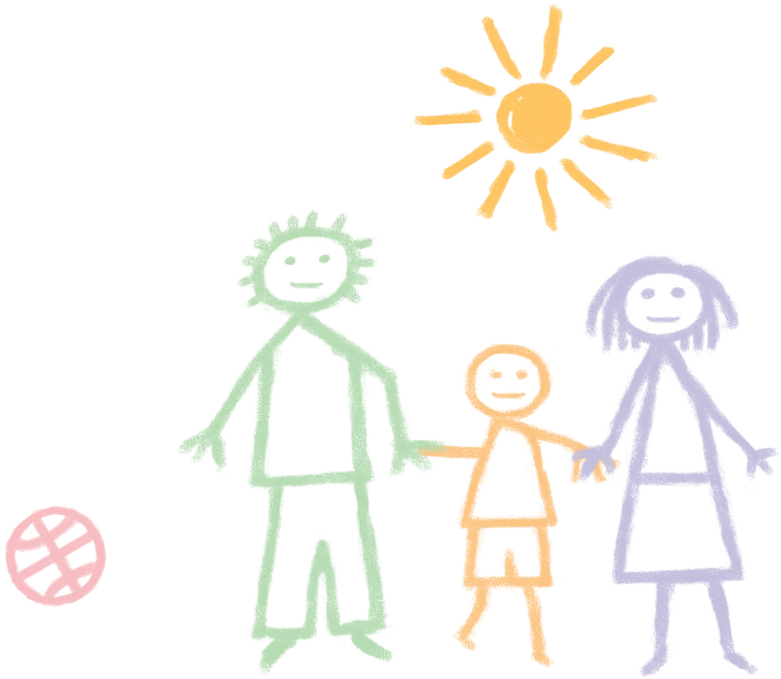
# Additional strategies to help your child

## Educational and social strategies can positively impact life for children with CLN2 disease[8]

Maintaining regular school attendance is extremely valuable for children with CLN2 disease and their families. It gives you and your child a sense of routine, social interaction, and involvement in your community. Consider working closely with your healthcare team and your child's school staff to ensure that your child's specific needs are being met in school.

It may become difficult to communicate with your child as language, motor skills, and vision decline. To help you continue communicating with your child, experts suggest early use of alternative communication methods like symbols and gestures, when possible.

Family support is key when caring for a child with CLN2 disease. Close interactions between your healthcare team and your family are beneficial to the ongoing care of your child. It also may be helpful to be aware of the impact that your child's disease may have on you as a caregiver, your spouse, or your child's siblings. If you need any support, talk to your healthcare team—they're your partners in this journey and can connect you with services and resources that may be valuable to you and your family.



# Glossary[2,5,7,9-12]

**Anti-epileptic drugs (AEDs)**
Drugs that can help manage seizures.

**Autosomal recessive disease**
A pattern of inheritance where 2 mutated genes (1 from each parent) are passed to their child, which then causes a certain disease.

**Batten disease**
An extremely rare autosomal, recessive, neurodegenerative disorder that begins in childhood. It is named for Dr Batten, who discovered the disease.

**Carrier**
Someone who only carries one mutated gene for an autosomal recessive disease, and therefore, does not have the disease.

**CLN2 disease**
A rare autosomal recessive disorder where lysosomes don't have enough of the TPP1 enzyme to break down materials in cells.

**Dystonia**
Involuntary muscle contractions that cause repetitive or twisting movements.

**Enzyme**
Proteins that cause reactions to occur in cells.

**Genetic mutation**
A permanent alteration to the genetic material in DNA.

**Late-infantile**
An age range that generally includes toddlers to very young children. This age range is used to describe when signs of a disease typically begin to appear.

**Lysosome**
Lysosomes are found within cells, and contain enzymes. One of their primary purposes is to recycle particles using enzymes.

**Lysosomal storage disorder (LSD)**
An inherited disease that is characterized by an abnormal build-up of various materials in lysosomes in the body's cells as a result of a reduced amount of a particular enzyme. Nearly 50 various types of LSD have been identified to date.

**Myoclonus**
Erratic, jerky contraction of groups of muscles.

**Neuronal ceroid lipofuscinoses (NCLs)**
A group of rare, genetic, neurodegenerative disorders.

**Neurodegenerative**
Having a decline or change in brain function.

**Progressive disease**
A disease that gradually increases in severity.

**Spasticity**
A condition in which certain muscles are continuously contracted. This contraction causes stiffness or tightness of the muscles.

**Tripeptidyl peptidase 1 (TPP1)**
A reduced amount of this enzyme is what causes CLN2 disease.

# How can I connect with others?

## Connect with a growing community of support and advocacy for CLN2 disease and Batten disease

You are not alone—there are many support resources for families and caregivers of children with CLN2 disease. Caring for a child who has CLN2 disease can be emotionally and physically demanding. That's why finding other parents and professionals to talk to can make the disease easier to manage. If you have a child with Batten disease, these organizations welcome you and want to answer your questions.

### Batten Disease Support and Research Association (BDSRA)

The BDSRA is committed to providing family support services and has experience coordinating travel logistics for CLN2 families. If you have a child with CLN2 disease, the BDSRA welcomes you and wants to answer your questions.

**Join the BDSRA community at bdsrafoundation.org or 1-800-448-4570**

### Noah's Hope

Created by a family with 2 children affected by CLN2 disease, this organization has raised funds for research all over the world.

**Learn more at NoahsHope.com**

### Hope4Bridget

Dedicated to raising awareness and funding for research, this site shares support and experience from a family raising a daughter with CLN2 disease.

**Learn more at Hope4Bridget.com**

## Visit CLN2family.com today for more information about CLN2 disease

This website is an additional resource in the CLN2 disease community that provides support for families and caregivers. Register online to stay informed of the latest news in CLN2 disease.

**References: 1.** Kohlschütter A, Schulz A. CLN2 disease (classic late infantile neuronal ceroid lipofuscinosis). *Pediatr Endocrinol Rev.* 2016;13(Suppl 1):682-688. **2.** Mole SE, Williams RE. Neuronal ceroid-lipofuscinoses. 2001 Oct 10 [Updated 2013 Aug 1]. In: Pagon RA, Adam MP, Ardinger HH, et al, eds. GeneReviews®. **3.** Haltia M. The neuronal ceroid-lipofuscinoses: from past to present. *Biochim Biophys Acta.* 2006;1762:850-856. **4.** Fietz M, AlSayed M, Burke D, et al. Diagnosis of neuronal ceroid lipofuscinosis type 2 (CLN2 disease): Expert recommendations for early detection and laboratory diagnosis. *Mol Genet Metab.* 2016;119:160-167. **5.** NIH, National Institute of Neurological Disorders and Stroke. Batten disease fact sheet. Available at: http://www.ninds.nih.gov/disorders/batten/detail_batten.htm#3063_1. Accessed September 19, 2016. **6.** Mole SE, Williams RE, Goebel HH. Correlations between genotype, ultrastructural morphology and clinical phenotype in the neuronal ceroid lipofuscinoses. *Neurogenetics.* 2005;6:107-126. **7.** Schulz A, Kohlschütter A, Mink J, Simonati A, Williams R. NCL diseases – clinical perspectives. *Biochim Biophys Acta.* 2013;1832:1801-1806. **8.** Williams RE, Adams HR, Blohm M, et al. Management strategies for CLN2 disease. *Pediatr Neurol.* 2017; doi: 10.1016/j.pediatrneurol.2017.01.034. **9.** NIH, National Institute of Neurological Disorders and Stroke. Myoclonus fact sheet. Available at: http://www.ninds.nih.gov/disorders/myoclonus/detail_myoclonus.htm. Accessed September 19, 2016. **10.** NIH, National Institute of Neurological Disorders and Stroke. Dystonias fact sheet. Available at: http://www.ninds.nih.gov/disorders/dystonias/detail_dystonias.htm. Accessed September 19, 2016. **11.** NIH, National Institute of Neurological Disorders and Stroke. NINDS spasticity information page. Available at: http://www.ninds.nih.gov/disorders/spasticity/spasticity.htm. Accessed September 19, 2016. **12.** National Organization for Rare Diseases. Lysosomal storage disorders. Available at: http://rarediseases.org/rare-diseases/lysosomal-storage-disorders. Accessed September 19, 2016.