



Living with Lowe Syndrome: A Guide for Families, Friends & Professionals.

2010 Lowe Syndrome Association, Inc.

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Living with Lowe Syndrome: A Guide for  
Families and Professionals, 4<sup>th</sup> Edition 2010

# **Living with Lowe Syndrome**

## **A Guide for Families, Friends & Professionals**

Lowe Syndrome Association, Inc.  
West Lafayette, Indiana

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## FOREWORD

It has been twenty-two years since the first edition of Living with Lowe Syndrome was published. The Lowe Syndrome Association is proud to present the fourth edition of the Living with Lowe Syndrome booklet. The many families who have relied on this booklet as an 'operating manual' for their individual(s), will notice that this booklet has almost tripled in size and vastly expanded in information since the original was published.

When Kaye McSpadden first started the Lowe Syndrome Association, she probably did not fully encompass how much that one act on her part would mean to all the families living with Lowe Syndrome. This book could not have been possible without all the work Kaye and the original six families did to gather information for the first edition. ***The Report on the Lowe's Syndrome Comprehensive Survey, 1990*** and all other surveys afterward have been the foundation for previous revisions of this booklet. In early 2008 the Board of Directors of the LSA made a decision to undertake an extensive survey now known as ***The 2008 Comprehensive Study on Lowe Syndrome***.

It is because of the 2008 survey and the 137 families who participated in the survey that this booklet can be revised. We would also like to extend our sincerest gratitude to the Medical and Scientific Advisory Board and the other professionals and volunteers from the LSA who assisted in editing and revising each section to ensure accuracy of the medical, behavioral and educational content of this book. Any errors in content, however, rest fully with me since final editorial decisions were mine.

New research and information gathered from the survey has enabled us to expand and add to all areas of the book. We have expanded and updated all the previous sections, as well as adding new information regarding Seizures, Abnormal Labs, Bones and Joints, Puberty and a new Parent Resource section. This new version of the Living with Lowe Syndrome book also includes an extensive section on Behavior along with suggestions on positive reinforcement techniques and a Developmental Milestones section that outlines the age at which individuals with Lowe syndrome achieved language, cognitive and motor skills. Even though this book contains information gathered from the survey, it is only a glimpse of the overall data that was gathered and published in the ***Report on the Comprehensive Survey on Lowe Syndrome, 2008***.

As you will read many times in this book, individuals with Lowe syndrome vary in ability, behavior, and medical need. It is important to remember that not every piece of information in this book will fit your individual and, as a parent or guardian, you should take and use only the pieces of information that relate to your individual with Lowe syndrome. Our hope is that by giving parents and guardians the knowledge, they will then use it in combination with the care they receive from their physicians to provide the best possible care and treatment for their child. We hope that all families living with Lowe syndrome use this book as a valued resource for their individual(s) with Lowe syndrome.

-Christine Knight, Director, Medical and Scientific Advisory Board  
May 1, 2010

## I. FREQUENTLY ASKED QUESTIONS

### **What is Lowe syndrome?**

Lowe syndrome (LS) is a rare genetic condition affecting males that causes physical and mental handicaps and medical problems. Also called the oculo-cerebro-renal syndrome of Lowe (OCRL), it was first described in 1952 by Dr. Charles Lowe and colleagues.

### **What causes Lowe syndrome?**

Lowe syndrome is caused by a defective gene that results in the deficiency of an enzyme called phosphatidylinositol 4,5-bisphosphate 5 phosphatase. This enzyme is essential to normal metabolic processes that take place in a small part of the cell called the Golgi apparatus. Because of the enzyme deficiency, cell functions that are regulated by the Golgi are abnormal, leading to various developmental defects including cataracts and problems in the brain and kidneys. For a detailed explanation of what causes Lowe syndrome refer to Section IV Genetics and Section V Research.

### **Why can't the missing enzyme just be replaced?**

Scientists must first better understand the subtle imbalance caused by the biochemical defect. It is possible that overcorrection could be just as harmful as the original lack of the enzyme. In addition, there is currently no method available to target therapies to the Golgi apparatus, the small sub-compartment of the cell where the Lowe syndrome enzyme is located.

### **How is Lowe syndrome inherited?**

The Lowe syndrome gene is located on the X-chromosome and inherited by passage of the X-chromosome from mother to child. Females who have the Lowe syndrome gene are carriers. In some cases, Lowe syndrome is the result of an original mutation and the mother is not a carrier. (See section on Carriers) Because Lowe syndrome is an X-linked syndrome, the majority of affected individuals are males. There have been a few cases of females diagnosed with Lowe syndrome. In the case of a female patient with Lowe syndrome, the female typically has one inactive X-chromosome and the active X-chromosome carries the mutation for Lowe syndrome. (See section on X-linked Inheritance)

### **Can Lowe syndrome be prevented?**

In families in which a case of Lowe syndrome has occurred, a slit-lamp eye examination can help determine carrier status of at-risk females. Prenatal testing is available at some laboratories that also offer testing for OCRL. Research currently underway may lead to a more definitive genetic test for carrier status. Various family planning options are available, including prenatal testing. Families should consult with a geneticist to learn more about their options.

### **Where are diagnostic tests done?**

To diagnose Lowe syndrome, a small skin sample called a fibroblast is taken and sent to a Biochemical Genetics Laboratory for testing. Some individuals may choose to have blood drawn and sent for testing to determine the DNA mutation of the gene. Prenatal diagnosis is also available at some labs. Physicians or Genetic Counselors may make arrangements for these tests by calling one of the laboratories at the numbers listed below.

| Laboratories offering clinical testing:                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>United States</b>                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Baylor College of Medicine</b><br><b>Medical Genetics Laboratories</b><br><b>Houston, TX</b><br><b>Contact:</b> Medical Genetics Laboratories<br><b>email:</b> geneticstest@bcm.tmc.edu <b>phone:</b> 1-800-411-GENE (4363) <b>fax:</b> 713-798-2787                                                                                                                                                                  |
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### What are the common features of Lowe syndrome?

- v Cataracts in both eyes, found at birth or shortly after
- v Glaucoma (in about half the cases)
- v Poor muscle tone and delayed motor development
- v Mental retardation, ranging from borderline to severe (in a few cases intelligence may be

normal)

- ✓ Seizures (in slightly fewer than half the cases)
- ✓ Significant behavior problems (in many, but not all, cases)
- ✓ Kidney involvement (“leaky” kidneys, or renal tubular acidosis)
- ✓ Short stature
- ✓ Tendency to develop rickets, bone fractures, scoliosis, and joint problems
- ✓ Maximum life span of about 35-40 years due to progressive kidney failure, although deaths have occurred at earlier ages due both to renal failure and to other causes. Life expectancy may increase as knowledge increases and new treatments are developed.

### **How is Lowe syndrome treated?**

There is no cure, but many of the symptoms of Lowe syndrome can be treated effectively through medication, surgery, physical and occupational therapies, vision therapy and orientation and mobility services, and special education. Nutritionists can also play a beneficial role in helping to outline and suggest appropriate diets.

### **What about research?**

In 1992 the gene that causes Lowe syndrome was found. In 1995 researchers discovered that the gene defect causes an enzyme deficiency. Researchers continue to investigate the function of the gene and the complicated biochemistry and cellular mechanisms of Lowe syndrome. Other areas of research in recent years include behavior problems, dental issues and clinical care. The Lowe Syndrome Association awarded the first research grant in 1988 to Richard A. Lewis, M.D., Baylor College of Medicine for **Refined gene mapping, carrier detection, and prenatal diagnosis of the Oculo-Cerebro-Renal Syndrome of Lowe.** To this day the LSA continues to fund research grants to study Lowe syndrome (OCRL). For a list of grants please go to the LSA website at [www.lowesyndrome.org](http://www.lowesyndrome.org).

### **What are individuals with Lowe syndrome like?**

Individuals with Lowe syndrome are generally affectionate and sociable. They love music and have a great sense of humor, and at times are obsessive about their likes and dislikes. Based on the 2008 Comprehensive Survey on Lowe Syndrome, individuals affected by Lowe syndrome have a variety of activities they enjoy. In each section of this book you will find information on Medical, Genetics/Research, Behavior and Educational needs of individuals with Lowe syndrome. Keeping in mind that individuals with Lowe syndrome vary in the complexity and need.



## II. BACKGROUND

### A. HISTORICAL REVIEW

Lowe syndrome was first recognized as a distinctive disease in 1952 by Drs. Lowe, Terrey, and MacLachlan at the Massachusetts General Hospital in Boston. They described three male children who had a similar set of problems that had not been previously associated with each other. Although they could not determine the cause of the disorder, they recognized a pattern to the symptoms and features and therefore described it as a "syndrome" - a set of symptoms which occur together.

The condition became known as "Lowe's syndrome" named after Dr. Charles Lowe, the senior member of the group that described it. Lowe syndrome is also known as the "oculo-cerebro-renal" syndrome of Lowe (*OCRL*), reflecting the three major organ systems involved in the disorder (eyes, brain, and kidney).

In subsequent years, doctors learned that Lowe syndrome is a hereditary condition that affects mostly males. It is caused by a single defective gene on the X-chromosome, one of the two sex-determining chromosomes (see Genetics, Section IV). Normally, this gene produces a specific enzyme that is essential to inositol metabolism. Because the gene is defective in Lowe syndrome, the enzyme cannot be produced. Therefore, the underlying cause of Lowe syndrome and its numerous features is the deficiency of this enzyme. (See Research, Section V).

### B. INCIDENCE AND PREVALENCE

Lowe syndrome is a rare disease. It has been identified in most cultures around the world and seems to have the same frequency in all populations. No one knows exactly how many individuals have Lowe syndrome. Estimates in the United States are between one and ten individuals per million people, or about 250-2500 actual cases. Based upon the Rare Disease Act of 2002 in the United States of American, a *rare disease* is defined strictly according to prevalence, as "any disease or condition that affects less than 200,000 persons in the United States,"<sup>[1]</sup> or about 1 in 1,500 people. There is currently no detailed documentation on the number of living individuals or deaths related to Lowe syndrome. Often families will notify the LSA when an individual has died due to complications of Lowe syndrome. Ages of known deaths have occurred ranging from 19 months to 56 years old.

<sup>[1]</sup> Based on data from the Rare Disease Act of 2002

### III. MEDICAL FEATURES

#### A. DIAGNOSIS

Through research we have learned that Lowe syndrome is the result of a mutation in a gene called OCRL1. A diagnosis of Lowe syndrome can be made by testing for the presence or absence of a specific enzyme in skin cells or by DNA analysis. Lowe syndrome is caused by low activity of the enzyme inositol polyphosphate 5-phosphatase. In this procedure, a small skin sample is taken from the patient, usually by a local physician. The sample must be sent to a specialized biochemical laboratory for culture and analysis. The Biochemical Genetics Laboratory in the Department of Molecular and Human Genetics at Baylor College of Medicine in Houston, Texas was the first laboratory that offered the test as a clinical service and continues to offer testing along with a handful of other biochemical labs. (For a list of labs see, Frequently Asked Questions, Section I) Results of the analysis are usually available in 4-8 weeks (because of the time required to grow the skin cells in culture). Physicians may arrange for the test by calling one of the biochemical labs.

A physician considers a diagnosis of Lowe syndrome when there are cataracts at birth, kidney dysfunction, and nervous system manifestations (such as hypotonia) in a male infant, especially if there is a family history indicating X-linked inheritance. The diagnosis of Lowe syndrome is usually made by a geneticist (a physician trained in genetics), but many other types of physicians have also made the diagnosis.

Before the development of the skin enzyme test in 1996 (see Research, Section V), diagnosing Lowe syndrome early in infancy was not always simple and straightforward. Although the cataracts and low muscle tone (hypotonia) are detectable at birth or shortly thereafter, other eye and nervous system manifestations may only develop later. Laboratory tests needed to detect kidney involvement may also not be abnormal immediately after birth (see Kidneys, Section III). Furthermore, the degree to which the kidneys, nervous system, and other organs are affected differs from person to person, even in the same family, and may change with age.

A deficiency of the Lowe syndrome enzyme in skin can determine if an individual is deficient in the enzyme that causes Lowe syndrome. A more definitive test called DNA Sequencing of the OCRL Gene, can determine without a doubt whether or not the individual carries the mutation for Lowe syndrome. Affected children are now typically diagnosed within the first few months of life due to increasing knowledge about Lowe syndrome and availability of the enzyme test and DNA sequencing.

#### B. EYES

The ocular features of Lowe syndrome include congenital cataracts (in all affected males), glaucoma (in about half of affected males), corneal degeneration, strabismus (crossed eyes), and nystagmus. The effectiveness of treatments for each of these several features varies, and any of these conditions may cause substantial visual disability.

In some rare cases in which the eye has become blind and severely painful, surgical removal of the eye, called enucleation, may be an option.



**1. Cataracts.** In all affected individuals, cataracts are present at birth, although they may not be noted or diagnosed until the child is several weeks old (and infrequently even older). A cataract is an opacity or a clouding of the lens of the eye. Normally, the lens in the eye, like the lens in a camera, is clear or transparent. The lens focuses light onto the retina, a thin sheet of nerve tissue that lines the back two-thirds of the eye. The retina functions like the film in a camera to “take the picture” and transmit it through the optic nerve to the brain, where one “sees”.

A cloudy or milky lens prevents the passage of light into the eye and thus limits the focusing of clear images onto the retina. It is important to remove the cataracts as early as possible, preferably within the first few days or weeks of life, to provide the clear and sharp images to the retina (and thus to the brain) and thus to promote the proper visual stimulation necessary for the infant brain and the visual system to develop as much useful vision as possible. The major factor determining the time to operate on a congenital (“present at birth”) cataract is the health of the infant; in some places, pediatric anesthesia is not available to put newborns to sleep safely for the duration of the cataract operation.

The opaque, gray-white lens is removed surgically with microscopic instruments after the infant is placed under general anesthesia. A small opening is made into the eye, typically at the edge of the area where the clear cornea joins the white of the eye (that junction zone is called the “limbus”). Microscopic instruments are inserted into this opening to cut up and fragment the cataract and to remove the small pieces.

This operation usually provides a clear pathway for images from the outside world to enter the eye. However, since the lens has been removed, the eye has lost much of its focusing ability. Eyeglasses or contact lens must compensate for this loss. For most children, removal of the cataracts and the use of glasses or contact lenses yield substantial improvement in vision. Surgical implantation of artificial [plastic] lenses is usually not recommended for several reasons. These include: the small size of the eyes of infants and the inability to predict reliably the “adult size” of the eyes later in life; the possible complications from glaucoma, which has a high rate of frequency in Lowe syndrome; the risk of other complications of surgery; the uncertainty of long-term stability of artificial lenses in infants in general; and the possibility of problems with the cornea in Lowe syndrome. Although ophthalmologists are investigating the implantation of some newer styles of artificial lenses in infants, these real and substantial complications in Lowe syndrome make such implantation highly investigational at this time.

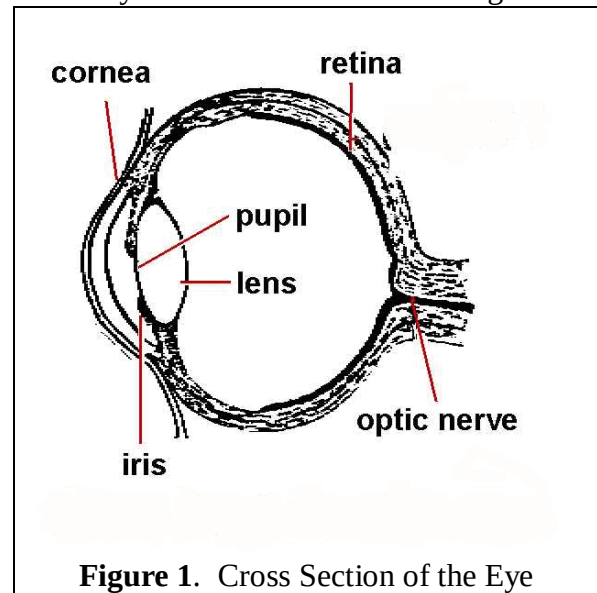


**Figure 1.** Cross Section of the Eye

**2. Lens Implants (Artificial Lens).** A few individuals have had lens implants. An Artificial Lens is a lens implanted into the eye, replacing the original human lens because the cataract has made it opaque. The implanted lens usually consists of a small plastic disc with plastic side struts to hold the lens in place within the eye. An artificial lens that is implanted years after the original cataract removal (called a “secondary lens implant”) must be sutured in place to remain stable. With any

procedure that involves surgically opening the eye, implantation carries risks, such as infection, loosening of the lens, lens rotation, inflammation, increased risk of glaucoma, and an increased possibility of retinal detachment.

**3. Glaucoma.** Glaucoma develops in about half of individuals affected with Lowe syndrome. Glaucoma is a disease in which the pressure within the eye becomes so high that, if sustained, the optic nerve is damaged, and sight is permanently lost. Sustained, elevated pressure can cause the infant eye to enlarge abnormally, because unlike an adult eye, the outer coats of the eye (the white part, called the sclera), is relatively thin and stretchable under the increased pressure. Historically, this condition is called *buphthalmos* (literally, “ox eye” because of the great size).

Treatment of infantile glaucoma is difficult. Medicinal eye drops may be tried first to lower the pressure, but they are rarely effective by themselves. If eye drops do not work, various surgical procedures will attempt to create a new channel to allow the fluid inside the eye to leave more easily and thereby to lower the pressure inside. Sometimes an artificial valve is sutured onto the front of the eye to control release of fluid and thus decrease the pressure. Unfortunately, in some cases glaucoma is so severe that it cannot be controlled, ultimately causing the eye to become completely blind.

The risk of glaucoma is the major reason for frequent examinations under anesthesia during infancy and childhood. (Pressure measurements in a crying infant are notoriously unreliable.) If the child is able to cooperate when he is older, examinations in the ophthalmologist's office may be possible. Although the risk of glaucoma lessens considerably after the first year of life, it may develop even after many years of normal pressures. Some families have reported glaucoma diagnosed (or at least identified) between the ages of birth and 20 years. As a result, individuals with Lowe syndrome should have regular checks of the eye pressure at all ages.

**4. Corneal Degeneration.** The cornea is the clear “watch crystal” of the front surface of the eye. By their teenage years, about half of individuals with Lowe syndrome develop what appears to be scar tissue, often called a keloid, over the cornea. (Some physicians believe that this growth is not a true keloid but probably represents a fibroma or benign growth of fibrous tissue which resembles a growing scar.) The reason for this growth is unknown. Keloids may affect one or both eyes, can cause visual impairment when they cover the center of the cornea, and thus prevent light from entering the eye.

**5. Cornea Transplants.** Cornea transplants have been done in a small fraction of individuals with Lowe syndrome. The cornea is the clear part of the eye that covers the iris and the pupil. A cornea transplant can be from a donor cornea or a synthetic cornea. When choosing to undergo a corneal transplant, persons must determine the purpose and risks of doing the transplant. If the purpose is to improve visual acuity, then the outcome is dependent on the health of the eye and what the visual acuity was prior to corneal degeneration. As with all surgeries there are risks associated with the transplant. The risks for corneal transplant can include infection and possible rejection of a donor cornea. In general, the greatest concern is that the corneal transplants in infants and children are much less successful than those in adults; transplants should be the last option in management for corneal diseases in Lowe syndrome.

**6. Keloids.** Some individuals develop keloid formation on either one or both eyes. In some cases the keloids have resulted in vision loss. Keloids may be removed surgically but tend to recur. In addition, surgical removal may leave a scar that cannot be managed without creating more scarring. Medical treatment has been unsuccessful, and corneal transplantation is not recommended because of the difficulty with postoperative management, including drops to suppress rejection of the transplant, numerous examinations, and management of the associated problems. Post-operative evaluation and care is difficult in children in general and even more so in individuals with Lowe syndrome. In many cases, keloid formation results in progressive and severe visual impairment despite all treatments.

**7. Strabismus.** Many individuals with Lowe syndrome develop strabismus (crossed eyes), a condition in which the eyes are not straight and parallel and may not move well together. In infants, this usually means that one eye turns in. Crossed eyes in infancy may affect the development of the pathways for vision to the brain adversely and as a result, eyesight can be substantially impaired. Treatment begins with a complete evaluation of the movements of the eyes and of their muscles, followed by a careful refraction to check and to verify (and periodically change) the prescription for glasses or contact lenses. A good prescription can help the eyes focus and stay straight.

After the best possible refraction has been obtained, treatment continues by patching one eye (usually the preferred or straight eye, the one with better vision, to force improvement in the "lazy" eye with the poorer sight). As soon as the child can watch a target (an object) equally well with each eye, surgery is performed on the muscles of the eyes to align the eyes so they are straight. If the vision is good and equal, there is a reasonable chance that the eyes will remain straight after surgery. Even after surgery for strabismus, however, the child should be followed carefully for reoccurrence of eye crossing and for changes in refraction to maintain the best possible vision in each eye.

**8. Nystagmus.** Nystagmus occurs in many children with Lowe syndrome. The term 'nystagmus,' refers to an uncontrollable rhythmic movement of the eyes. While nystagmus by itself does not cause loss of vision, it is often associated with the many conditions related to poor vision. Occasionally, nystagmus may be aggravated by changes in brain function. The genetic defect that causes Lowe syndrome may also affect the development of the retina in the eye (which is, in reality, part of the brain). Nystagmus may be associated with abnormal function of the retina and the resultant poor vision. Unfortunately, there is no effective permanent treatment for nystagmus except to attempt to develop and to retain good vision as early in life as possible.

**9. Enucleation.** Under rare circumstances, especially when an eye is blind and profoundly painful, it may be necessary to remove the eye surgically in a procedure called 'enucleation'. After the eye is removed, the ophthalmologist will implant a ball to maintain the volume inside the orbit and to stimulate normal growth of the facial bones and eyelids.

After several weeks of healing, a "glass eye" shell is fitted over the healed surface. Recently developed surgical techniques use newer materials that provide better movement of the artificial shell. Because the shell is primarily cosmetic, its use is optional. Some parents may decide against the use of an artificial shell for their child, particularly if the child's level of cooperation is less than optimal.

**10. Optical Devices.** A variety of optical devices have been used by individuals with Lowe syndrome. Most individuals reported the use of glasses. Contact lenses are used by about half of all individuals. In addition to glasses and contact lenses some individuals have used magnifiers, monacles, strix machines, telescopes and Zoom Text software.

| <i>Optical Devices</i>          |                          | <b>Number of individuals reporting use of optical devices</b> | <b>Percentage of individuals reporting use of optical devices</b> |
|---------------------------------|--------------------------|---------------------------------------------------------------|-------------------------------------------------------------------|
|                                 | (Based on 137 Responses) | <b>125</b>                                                    | <b>91%</b>                                                        |
| <b><i>Type of Device(s)</i></b> | Glasses                  | 116                                                           | 85%                                                               |
|                                 | Contact Lenses           | 59                                                            | 43%                                                               |
|                                 | Magnifier                | 12                                                            | 9%                                                                |
|                                 | Monocle                  | 3                                                             | 2%                                                                |
|                                 | Strix Machine            | 1                                                             | 1%                                                                |
|                                 | Telescope                | 1                                                             | 1%                                                                |
|                                 | Zoom Text Software       | 1                                                             | 1%                                                                |

**11. Eye Exams.** Since the risk of retinal detachment increases after cataract surgery, and since most individuals with Lowe syndrome will not complain about loss of vision from retinal detachment, all individuals with Lowe syndrome should have their eyes dilated and carefully examined by an ophthalmologist every six to twelve months. Yearly eye exams were reported in almost all individuals. Anesthesia for eye exams was required for more than half of the individuals with Lowe syndrome.



### **C. BRAIN AND CENTRAL NERVOUS SYSTEM**

The nervous system includes the brain, spinal cord, and nerves, and it controls muscle tone. Lowe syndrome causes problems in most of these areas, including intellectual impairment, seizure disorders, behavior problems, physical changes in the brain, and hypotonia or poor muscle tone.

**1. Cognitive Disability.** The extent of intellectual disability in individuals with Lowe syndrome varies widely. Roughly a quarter of the individuals function intellectually in the low-normal or borderline ranges, and another quarter function in the mild to moderate range of cognitive disability. Others function in the severe range. Although it is not possible to predict intellectual outcome at birth, advancements in professional services for young children with cognitive disabilities may minimize the potential for developmental delay. Therefore, it is important as a parent, caregiver, and / or a professional to seek services for an individual with Lowe syndrome as early as possible.

**2. Seizure Disorders.** Seizures occur in about half of all persons with Lowe syndrome. Younger children may have febrile convulsions (seizures caused by fever). These do not usually require medication unless they recur. In older individuals, seizures are usually of a major-motor

or generalized type. In many cases, these seizure disorders respond well to medication (anticonvulsants or antiepileptic drugs, also known as AEDS). Some individuals develop refractory epilepsy or seizures that are difficult to control. The use of the vagus nerve stimulation device, or “pacemaker for the brain,” is under evaluation for individuals with Lowe syndrome. This device consists of an implanted generator and a nerve stimulation electrode which transmits antiepileptic electric signals to the brain through the vagus nerve in the neck.

Individuals with seizure disorders may undergo an EEG (electroencephalography) test, which will usually indicate abnormal brain wave patterns and occasionally help to locate the place in the brain where the seizure(s) begin, and may assist in the diagnosis and treatment of the seizures.

**3. Types of Seizures.** All seizures are the result of abnormal electrical disturbances in the brain. A seizure is defined as the physical findings or changes in behavior that occur after an episode of abnormal electrical activity in the brain. Seizures are classified into two categories: partial seizures and generalized seizures.

**Generalized Seizures.** Generalized convulsive seizures can be classified as atonic, tonic, clonic, tonic-clonic, myoclonic, or absence based on the clinical symptoms and EEG abnormalities.

**Tonic or Clonic Seizures.** In tonic seizures, the muscles contract, including respiratory muscles, usually for a brief time. Clonic seizures involve rhythmic shaking or spasms without rigidity of the muscles and are longer than tonic seizures.

**Grand Mal.** When combined, a generalized tonic-clonic seizure is also called a grand mal seizure. A generalized tonic-clonic seizure is a seizure that involves the entire body. Such seizures usually involve rigidity of a person’s muscles, violent contractions of the muscles and loss of consciousness.

**Atonic Seizures.** An individual who experiences an atonic seizure loses muscle tone. At times, it may affect only one part of the body or it can affect the whole body causing loss of muscle tone. When the whole body is affected, the person can suddenly fall, also known as a drop attack.

**Myoclonic.** Myoclonic seizures are seizures that involve brief jerky contractions of certain muscle groups, generally the face and the trunk portion of the body.

**Absence Seizures.** In an absence seizure, the individual may appear to be staring off into space with or without twitching movements of the eye muscles. This type of seizure usually lasts just a few seconds, but can be a few minutes in length.

**Partial Seizures.** (Simple, Partial, Secondary Generalized and Partial Complex). Partial seizures occur when seizure activity occurs in a limited area of the brain. Partial seizures can be further defined as Simple, which does not affect awareness or memory and Complex, which affect awareness or memory of the events before, during and immediately after the seizure and affect the individual’s behavior.

**Simple Partial Seizures.** During a Simple Partial Seizure the individual does not lose consciousness, but may experience jerking movements, tingling, or odd mental and emotional events, including déjà-vu, mild hallucinations, or extreme responses to smell and taste. After the seizure, the person may experience weakness in certain muscles.

**Complex Partial Seizures.** Complex Seizures that occur in the temporal lobe can cause loss of judgment, involuntary or uncontrolled behavior, or even unconsciousness. Patients may lose consciousness briefly and appear to be staring into space. Emotions can be exaggerated; some individuals may appear to be in a drunken state. Repetitive movements may appear with this type of seizure, such as chewing or smacking of lips. Seizures usually last no more than 2 minutes and can occur infrequently or as frequently as every day. Sometimes a throbbing headache may follow a complex partial seizure.

**Secondary, Generalized Seizures.** Simple or Complex seizures may sometimes change into Generalized Seizures, if the seizure spreads out from its origin. A Generalized Seizure affects the whole brain.

**Generalized, Soft Tremors.** Tremors involve involuntary rhythmic movements of muscles. The most common body parts affected are the hands, head, facial muscles, vocal cords, trunk of the body and legs.

| <b>Seizures</b>                  | Type of Seizure<br>(Based on 137 individuals between<br>the ages of 10 months to 56 years) | <b>Number of<br/>individuals<br/>reporting<br/>seizure<br/>activity</b> | <b>Percent of<br/>individuals<br/>reporting<br/>seizure<br/>activity</b> |
|----------------------------------|--------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------|
| <i>Age First Diagnosed</i>       | 6 months to 23 years                                                                       | <b>61</b>                                                               | <b>45%</b>                                                               |
| <b>Diagnosis by Age Groups</b>   | Birth to 1 year                                                                            | <b>7</b>                                                                | <b>11%</b>                                                               |
|                                  | 1+ year to 5 years                                                                         | <b>19</b>                                                               | <b>31%</b>                                                               |
|                                  | 5+ years to 9 years                                                                        | <b>14</b>                                                               | <b>23%</b>                                                               |
|                                  | 9+ years to 13 years                                                                       | <b>7</b>                                                                | <b>11%</b>                                                               |
|                                  | 13+ years to 18 years                                                                      | <b>11</b>                                                               | <b>18%</b>                                                               |
|                                  | 18+ years to 25 years                                                                      | <b>2</b>                                                                | <b>3%</b>                                                                |
| <b>Type Of Seizures Reported</b> | Generalized, Primary Generalized Tonic-Clonic                                              | <b>38</b>                                                               | <b>62%</b>                                                               |
|                                  | Generalized, Absence                                                                       | <b>18</b>                                                               | <b>29%</b>                                                               |
|                                  | Partial, Simple                                                                            | <b>17</b>                                                               | <b>28%</b>                                                               |
|                                  | Partial, Complex                                                                           | <b>15</b>                                                               | <b>25%</b>                                                               |
|                                  | Partial, Secondary, generalized                                                            | <b>9</b>                                                                | <b>15%</b>                                                               |
|                                  | Generalized, Clonic                                                                        | <b>8</b>                                                                | <b>13%</b>                                                               |
|                                  | Generalized, Atonic                                                                        | <b>6</b>                                                                | <b>10%</b>                                                               |
|                                  | Generalized, Myoclonic                                                                     | <b>4</b>                                                                | <b>7%</b>                                                                |
|                                  | Generalized, Tonic                                                                         | <b>3</b>                                                                | <b>5%</b>                                                                |
|                                  | Febrile                                                                                    | <b>2</b>                                                                | <b>3%</b>                                                                |
|                                  | Generalized, Soft Tremors                                                                  | <b>1</b>                                                                | <b>2%</b>                                                                |

|                                                           |                              |    |     |
|-----------------------------------------------------------|------------------------------|----|-----|
|                                                           | Grand Mal                    | 1  | 2%  |
|                                                           | Gelastic (laughing seizures) | 1  | 2%  |
|                                                           | Infantile spasms             | 1  | 2%  |
|                                                           | Self-induced                 | 1  | 2%  |
| Number of individuals still experiencing seizure activity | Yes                          | 37 | 61% |
|                                                           | No                           | 25 | 41% |
|                                                           | Don't Know                   | 12 | 20% |

## 4. Epilepsy

### What is epilepsy?

Epilepsy is a chronic medical condition defined by recurrent seizures. An epileptic seizure is an excessive electrical discharge from neurons. Epilepsy is common in many types of brain disorders, such as Lowe syndrome.

### How is epilepsy treated?

The majority of epileptic seizures are controlled with drugs called anticonvulsant medications. The first decision a family faces after a diagnosis of epilepsy is whether the patient should take an anticonvulsant medicine. All medicines may have side effects. The family and treating neurologist have to determine that the expected beneficial effects of the medication will outweigh the expected adverse effects. The decision depends on what harm the seizure might do and which particular anticonvulsant is recommended. Make sure you understand what adverse effects might occur, and how likely they are.

Side effects are more likely with higher doses so you should watch for them especially after dosage increases. Anti-epileptic drugs are usually started at low doses and increased gradually to try to find the lowest dose that controls the seizures. The most common side effects are what you would experience after taking medications such as diphenhydramine (Benadryl): sleepiness, lack of coordination, slowing of thought, nausea and the like. The body usually adapts in a few days after medication is increased. Serious side effects are specific to each medication, but fortunately, serious problems are extremely rare.

### Common seizure medication questions

What is the right medication?

The 'right' medication for seizures is determined by educated trial and error, as unscientific as that sounds. Choosing the appropriate medication begins with making a diagnosis of the type of seizures the patient has. The EEG helps with this. Then a discussion of the several available drugs for this type of seizure, including potential side effects, cost, and ease of administration follows. If the first drug chosen does not control the seizures, then others are tried until one is found that works best. Sometimes two or even three drugs at the same time are used. Sometimes no drug or drug combination can be found that controls the seizures.

What is the right dose? Will a blood level tell me?

The right dose is the lowest dose that controls seizures and avoids side effects. This is not

the same for everyone, and has to be determined for each patient. Blood levels are available for most antiepileptic medications, and they help to determine the correct dose, but a blood level is just one factor that plays into this decision.

Is a generic version of an antiepileptic drug as good as the 'brand name' version?

Although generic and brand-name medications are the same chemical compound, there is some difference in how two drugs made by different manufacturers are metabolized. Each drug company's medication is metabolized slightly differently from that same drug made by another company. This is something to discuss with your doctor.

What are the risks of suddenly stopping a medication?

Seizure medications should always be tapered off gradually. The risk of suddenly stopping an anticonvulsant medicine is an immediate and sometimes dramatic increase in seizures. Although seizure medications are not addictive, the brain does adjust to them, and it takes time to readjust off the medication.

### **Other questions**

Are seizures dangerous?

Seizures almost always stop on their own, without any medical attention. Perhaps the biggest problem with a seizure in public is that they cause bystanders, who are well-intentioned, to panic. An ambulance is rarely needed, and only if the seizure is not stopping on its own. Ask your doctor for a 'time limit' for when to call an ambulance; this varies for seizure type and other factors. Usually just protecting the patient from hurting himself during the seizure is all that is needed.

My son was just diagnosed with epilepsy, and I am afraid to leave him, even at night, or to go anywhere. How does life get back to normal?

All parents have this fear, and the good news is that over time (usually a few weeks) you relax and life *does* get back to normal. The biggest family problem with seizures is the uncertainty, of not knowing when the next seizure will occur, or even if it will occur. Eventually most families decide to refuse to let this uncertainty run their life.

Do seizures damage the brain?

This is highly controversial, and the short answer is that for most seizure types we don't know. The current majority opinion among neurologists is that repeated seizures do cause slight neuronal injury over time. However, this depends on so many other factors that in a given patient there is not usually any noticeable adverse effect, even in patients with uncontrolled seizures over many years. Clearly though, it is best to try to control seizures if possible.

**5. Behavior Problems.** Although individuals with Lowe syndrome are often happy, loving, and sociable, many also have a characteristic pattern of behaviors that may interfere with everyday functioning. These include temper tantrums, stubbornness, unusual repetitive movements (especially of the hands), inability to concentrate or focus, and unusual obsessions or preoccupations. Some individuals may become violent and self-abusive. These behavioral patterns are thought to be a specific feature of Lowe syndrome. Some studies indicate that for many individuals, the most difficult period for behavior problems is between the ages of 8-13

years. In some cases, however, severe behavior problems continue into adulthood. Behavior modification techniques may be helpful for some. In some cases medication therapy may be effective. Some individuals have experienced improvement with the help of antidepressant and/or antipsychotic medications.

**6. Physical Changes in the Brain.** Brain images generated by MRI (magnetic resonance imaging) may demonstrate abnormalities in the brain's white matter. These abnormalities are caused by tiny fluid filled cysts which develop during the first year of life. The exact cause of this condition and its potential effect on brain function is unknown. Brain atrophy, or shrinkage, has also been reported.

**7. Hypotonia.** Hypotonia, or poor muscle tone, is present at or soon after birth. Hypotonia results in a 'floppy' appearance and poor muscle strength. During infancy, hypotonia causes problems with head control and feeding (due to poor sucking). As the individuals grow up, motor development is generally delayed in most areas. For instance, learning to walk is usually significantly delayed. Prior to age 2 years old, some children with Lowe syndrome develop the ability to walk alone. By the age of 4 years old, more than half have learned to walk alone. By the ages of 11 years, a majority of individuals with Lowe syndrome have developed the ability to



walk.

Although the hypotonia improves slowly with age, most individuals do not reach normal muscle tone or strength, and related problems can occur as they grow older. Loose or hypermobile joints are also common due to the poor muscle and tendon strength. About a quarter of all affected individuals will develop scoliosis, or curvature of the spine, due to weakness in the back muscles. The greatest risk for developing scoliosis occurs during the early teenage

through adult years. There is also an increased risk of developing hernias throughout life due to weak muscles in the abdomen. Eating problems may also result from poor muscle tone (See Eating Difficulties under Special Health Concerns, Section III) Eating Problems can also be found under Development and Education, Section VI).

Hypotonia in Lowe syndrome is due primarily to nervous system dysfunction. Individuals have a slight blood elevation of a muscle enzyme called creatinine kinase (CK). Special muscle tests, such as EMGs (electromyography) or muscle biopsies, typically have normal or minimally abnormal results and are **not** needed to establish a diagnosis of Lowe syndrome. Deep tendon reflexes (such as knee jerk) are usually absent by the first birthday. This may be due to nerve damage, which has occasionally been detected, but may also be due to nervous system dysfunction in the spinal cord. The absence of these reflexes causes no interference with normal function.

The most effective treatment for hypotonia is physical therapy, begun early in infancy if possible.

**8. Umbilical Hernia.** Due to the low muscle tone (Hypotonia) at birth, some children experience an umbilical hernia. An umbilical hernia is often the result of a bulge of the abdominal wall around the navel. Usually present at birth, it may not be noticeable until the umbilical cord has fallen off. Typically the umbilical gap closes prior to birth. If it does not close, tissue may bulge through the weak area in the abdominal wall around the navel. Diagnosis of an umbilical hernia can be done by a physician through examination of the abdomen and by evaluating the size, shape and appearance of the umbilical hernia.

Most umbilical hernias may close on their own without treatment (By age 5 years in the general population.). Surgery may be needed to repair an umbilical hernia that has not closed on its own. The likelihood that an umbilical hernia will heal on its own depends in part on how the muscle tone improves and how large the hernia is.



## D. KIDNEYS

**1. Kidney ‘Wasting’ and Replacement Therapy.** The primary kidney problem in Lowe syndrome is the abnormal ‘wasting,’ or loss, of certain substances into the urine, including bicarbonate, sodium, potassium, calcium, phosphate, amino acids, organic acids, albumin and other small proteins, and L-carnitine, and the obligatory loss of a large volume of urine fluid associated with the loss of these substances. In a normal kidney, these substances are filtered and then either excreted in the urine or reabsorbed as needed back into the body. Filtering is done by tiny filters, each one called a glomerulus (plural: glomeruli), which are attached to tiny tubes, called tubules, that empty into larger collecting tubes and form the urine that is excreted every day. Reabsorption of filtered substances needed back by the body occurs in the kidney tubules. The part of the tubule closest to the glomerulus is called the proximal tubule and is the most active site, accounting for about 85% of the reabsorption done by the kidney tubules every day. In kidneys affected by Lowe syndrome, the proximal tubules are abnormal. As a result, the filtered substances named above are not reabsorbed normally and end up being excreted, or ‘wasted,’ in large amounts in the urine. This reabsorption problem is generally known as the Fanconi-type renal tubular dysfunction, named after the Swiss pediatrician Dr. Guido Fanconi, who first described the condition in another disease. Fanconi syndrome is known to occur in several other genetic diseases and syndromes besides Lowe syndrome and often includes urine wasting of glucose, which is very rare in Lowe syndrome. In Lowe syndrome, the renal tubular dysfunction may be mild and involve only a few substances or may be severe and involve large losses of many substances and fluid.

The clinical signs of kidney abnormalities in Lowe syndrome are not present at birth, but usually become apparent by one year of age. Physicians who are not aware of this delay may be

reluctant to diagnose Lowe syndrome during the first year, if the usual blood and urine tests of kidney function are normal. Many physicians may not be aware that the first sign of kidney tubular dysfunction in Lowe syndrome patients is urine wasting of small 'tubular' proteins, such as retinol binding protein or N-acetyl glucosaminidase. Wasting of these tubular proteins can be diagnosed in the first few months of life, even before generalized amino aciduria or any other tubular dysfunction occurs. In an infant suspected to have Lowe syndrome, blood and urine screening tests for kidney abnormalities should be done about every three months in the first year of life, every six months in the second year, and then at least yearly thereafter until the full extent of the Fanconi syndrome becomes apparent.

Some of the substances lost in the urine, such as organic acids, amino acids and small tubular proteins, cause no clinical problem and do not need to be monitored or replaced. They are markers of tubular dysfunction and most helpful in diagnosing Lowe syndrome. Loss of albumin in the urine may be large in some patients, but just reflects poor tubular reabsorption of normally filtered albumin, so does not lower the blood albumin level or lead to body swelling typical of the clinical nephrotic syndrome.



On the other hand, some of the substances lost in the urine, like bicarbonate, sodium, potassium, phosphate and carnitine, are essential to normal body chemistry and need to be replaced. Excessive loss of these substances may result in serious metabolic problems, such as proximal renal tubular acidosis, hypokalemia, hypophosphatemia and carnitine deficiency (see Kidney Function Blood Tests and Kidney Function Urine Tests below). In addition, some patients may not make enough of the active form 1,25-dihydroxy vitamin D

(calcitriol), which is made in the kidney in normal proximal tubules. Medications can be used to replace the lost substances and normalize the blood levels in most patients. These medications may include sodium bicarbonate or citrate, potassium citrate, potassium chloride, sodium phosphate, levocarnitine or calcitriol. The type of medication and dosage must be individualized for each patient by his physician. Blood and urine testing is done at intervals to monitor the benefits of therapy and to determine the appropriate doses of replacement medication. In addition, because the kidneys are often not able to conserve water and concentrate urine normally, a larger than normal intake of and free access to fluids is needed to prevent dehydration.

## ***Kidney Function Blood Tests***

### **•Serum Chemistries**

- Sodium (Na)
- Potassium (K)
- Chloride (Cl)
- Total CO<sub>2</sub> or bicarbonate (HCO<sub>3</sub>) [test for acidosis]
- Calcium (Ca)
- Phosphorus (P)
- Magnesium (Mg)
- Uric acid
- Albumin, total protein
- Creatinine, blood urea nitrogen (BUN)

### **•Anemia tests for progressive kidney disease with anemia**

- CBC: hemoglobin, hematocrit
- Serum iron, ferritin, transferrin, T-saturation

### **•Special blood tests**

- Amino acids (at diagnosis only)
- Total and free plasma carnitine

### **•Bone-related serum tests**

- Calcium, phosphorus, alkaline phosphatase
- Parathyroid hormone (intact)
- Vitamin D-25-hydroxy, vitamin D-1,25-dihydroxy

## ***Kidney Function Urine Tests***

### **•Urinalysis**

- Protein (albumin)
- Glucose
- Blood
- Leukocyte esterase, nitrite
- pH (acidosis)
- Specific gravity (concentration)

### **•Random urine sample**

- Amino acids (at diagnosis only)
- Tubular proteins: retinol binding protein, N-acetylglucosaminidase or lysozyme (at diagnosis only)
- Protein (or total protein)
- Calcium (Ca)
- Creatinine (Cr)
- Ratios: protein/Cr, Ca/Cr

| <b>•24 hour urine collection (not possible if bed wetter or not toilet trained)</b> |
|-------------------------------------------------------------------------------------|
| –Total protein (protein electrophoresis not necessary)                              |
| –Creatinine and creatinine clearance                                                |
| For general stone evaluation—not Lowe syndrome specific:                            |
| –Calcium                                                                            |
| –Citrate                                                                            |
| –Oxalate (not needed; specific for another disease=primary hyperoxaluria)           |
| –Uric acid (not needed, if kidney stone does not contain uric acid)                 |

**2. Incidence of Renal Abnormalities.** This section contains data from the *Report on the Lowe Syndrome Comprehensive Survey - 2008*. The table below is a reflection of information reported in the survey. The survey examined 13 renal abnormal functions associated with Lowe syndrome to determine what percentage of individuals experienced abnormal renal functions.

| Type of Renal Abnormality                                                      | Age First Diagnosed  | Number of individuals reporting abnormality (Based on 137 total responses) | Percent of individuals reporting abnormality |
|--------------------------------------------------------------------------------|----------------------|----------------------------------------------------------------------------|----------------------------------------------|
| <b>Acidosis</b><br>(proximal renal tubular acidosis)                           | Birth to 16 years    | 99                                                                         | 72%                                          |
| <b>Proteinuria</b> (urine albumin wasting)                                     | Birth to 24 years    | 85                                                                         | 62%                                          |
| <b>Anemia</b> (low hemoglobin/hematocrit)                                      | Birth to 45 years    | 61                                                                         | 45%                                          |
| <b>Low Serum Phosphorous</b><br>(hypophosphatemia/rickets)                     | Birth to 45 years    | 60                                                                         | 44%                                          |
| <b>Low Serum Potassium</b> (hypokalemia)                                       | Birth to 45 years    | 60                                                                         | 44%                                          |
| <b>Low Serum Vitamin D-1,25</b><br>(calcitriol deficiency/rickets)             | Birth to 26 years    | 58                                                                         | 42%                                          |
| <b>Hypercalciuria</b><br>(urine calcium wasting)                               | Birth to 17 years    | 53                                                                         | 39%                                          |
| <b>High Serum Creatinine</b><br>(kidney failure/CKD)                           | Birth to 45 years    | 39                                                                         | 28%                                          |
| <b>Carnitine Deficiency</b> (low serum carnitine from urine carnitine wasting) | Birth to 20 years    | 34                                                                         | 25%                                          |
| <b>High Blood Pressure</b>                                                     | 2 months to 35 years | 7                                                                          | 5%                                           |
| <b>Low Serum Magnesium</b><br>(hypomagnesemia)                                 | Birth to 20 years    | 6                                                                          | 4%                                           |
| <b>High Serum Vitamin D-1,25</b> (may cause high serum Ca)                     | 3 years to 19 years  | 4                                                                          | 3%                                           |

**3. Kidney Calcification and Kidney Stones.** Kidney calcification, called **nephrocalcinosis**, occurs in more than half of individuals with Lowe syndrome and has been diagnosed between birth and 32 years old. Kidney calcification results from small particles of calcium being deposited

in the kidney tissue. Kidney stones, called **nephrolithiasis**, have been reported in some individuals with Lowe syndrome. A kidney stone is made up of minerals and salts in the urine that form into a small pebble-like solid. In Lowe syndrome, kidney stones are usually composed of either calcium oxalate or calcium phosphate. The exact cause of kidney calcifications and kidney stones in Lowe syndrome is not understood, but is likely related to the abnormal renal tubular function. Changes in the normal balance of water, salts, minerals and other substances in the urine (stone inhibitors and inducers) in any individual allows the potential for kidney calcifications and stones to form. Patients with Lowe syndrome appear more likely to develop these conditions than other children with diseases associated with renal Fanconi syndrome. Excess calcium in the urine may contribute to nephrocalcinosis or nephrolithiasis, especially when acidosis also occurs and is untreated for prolonged periods. However, extra citrate in the urine from tubular wasting, which also may occur in Lowe syndrome, may inhibit kidney calcification and stone formation by combining with calcium to keep the calcium in solution in the urine. Vitamin D metabolite therapy for treatment of rickets (see Rickets and Soft Bones under Orthopedic, Section III) may contribute to kidney calcifications or stones, if the serum calcium becomes too high (hypercalcemia) and leads to excretion of more calcium in the urine. Vitamin D metabolite therapy should be carefully monitored in patients with Lowe syndrome to try to prevent hypercalcemia. Calcium supplements should probably also be avoided, unless the blood calcium is low.

Kidney calcifications or kidney stones may cause microscopic amounts of blood to appear in the urine. Kidney stones may also cause visible blood to appear in the urine as well as severe pain, especially when the stone tries to pass through the urinary tract to be excreted. Kidney calcifications are best diagnosed by renal ultrasound. If a patient is suspected of having a kidney stone, a contrast X-ray study of the kidneys, like a computed tomography (CT) scan or intravenous pyelogram, may be needed to identify the exact position of the stone. If a stone does not pass on its own, extracorporeal shock wave lithotripsy (ESWL) may be used in many patients to break the stone into small pieces for passage out in the urine. Surgery for stone removal is rarely needed. A random (spot) urine calcium to creatinine ratio or a 24-hour urine calcium measurement may be helpful to assess the extent of calcium wasting and its subsequent response to any therapy. Thiazide diuretics are useful for kidney stone prevention in some individuals with calcium wasting. Whether thiazide diuretics are useful in Lowe syndrome patients, who have calcium wasting due to abnormal kidney tubules, is not really known, but may be used on a trial basis to see if urine calcium excretion can be decreased. Since diuretics also increase the amount of fluid excreted by the kidneys, if thiazide diuretic therapy is tried in a patient with Lowe syndrome, the patient should be carefully monitored by a physician to prevent dehydration.

**4. Kidney Cysts.** A few individuals with Lowe syndrome have reported kidney cysts. Cysts are fluid filled sacs arising anywhere within the kidney. Simple cysts, which are small, round, and homogenous, cause no harm. They occur frequently in normal individuals, even in young children. In older patients, complicated cysts (multiloculated, echogenic or calcified) may be cancerous, so need full evaluation with CT scans or possibly MRI. Simple cysts are usually just monitored with renal ultrasound.

**5. Kidney failure.** Later in life, usually starting after the age of 10 years, the tiny filters of the kidney (the glomeruli) may start to fail. In Lowe syndrome, kidney failure usually progresses slowly and is not complete until age 30 or 40 years. The exact cause of the filtration failure in

Lowe syndrome is unknown, but is likely related to progressive injury to renal tubules leading to poor health and function of the attached glomerulus. Kidney failure is diagnosed by accumulation of waste products, like creatinine and urea nitrogen, in the blood. Creatinine and urea nitrogen are made every day by normal body metabolism and are good markers for kidney filtration function. Creatinine is made by the muscles, so blood levels of creatinine may be lower than expected for a given degree of kidney failure, if the muscle mass is decreased in Lowe syndrome. In that case, a 24-hour urine creatinine clearance gives a more accurate estimate of the kidney function than the blood creatinine alone. The degree of kidney failure, now referred to as chronic kidney disease or CKD, is classified into stages to help physicians better manage CKD. The stages of CKD are shown in the table below. Symptoms of fatigue, decreased appetite, nausea and vomiting associated with kidney failure usually do not occur until CKD stage 5, when kidney function is less than 15% of normal, and serum creatinine is 6-10 mg/dL or about 10 times normal. When patients reach CKD stage 4 and kidney function is between 15 and 30% of normal, physicians and families need to start thinking and planning for whether dialysis or transplant should be done when the patient reaches complete kidney failure, called end stage kidney disease (ESRD), which occurs in CKD stage 5. The quality of life on dialysis, whether the patient might be able to physically tolerate dialysis treatments, and whether comfort care might be the best option at ESRD should be carefully considered. Dialysis experience in Lowe syndrome is limited, but a few Lowe syndrome patients have been treated with chronic hemodialysis for several years, and at least one patient has done home peritoneal dialysis. Little is known about the success or long-term survival of kidney transplants in patients with Lowe syndrome. Based on the 2008 Comprehensive Survey, two individuals reported having had a kidney transplant, but other details were not available. Whether the kidney problems of Lowe syndrome will recur in kidney transplants is not known, but seems unlikely if the kidney problems are just due to genetic defects of Lowe syndrome within the kidney itself as currently suspected.

## 6. Stages of Chronic Kidney Disease (KDOQI)

(from the National Kidney Foundation Kidney Disease Outcomes Quality Initiative, 2002)

| <b>CKD Stage</b> | <b>Description</b>                          | <b>Glomerular Filtration Rate (GFR**) ml/min/1.73m<sup>2</sup></b> | <b>Action</b>                                  |
|------------------|---------------------------------------------|--------------------------------------------------------------------|------------------------------------------------|
| <b>1</b>         | Kidney damage* with normal or increased GFR | ≥90                                                                | Diagnosis & treatment, slow progression        |
| <b>2</b>         | Kidney damage with mild decrease in GFR     | 60-90                                                              | Estimate progression                           |
| <b>3</b>         | Moderate decrease in GFR                    | 30-59                                                              | Evaluate and treat complications               |
| <b>4</b>         | Severe decrease in GFR                      | 15-29                                                              | Prepare (plan) for dialysis, kidney transplant |
| <b>5</b>         | Kidney failure                              | <15                                                                | Dialysis, transplant, comfort care of symptoms |

\*Kidney damage for 3 months or more as defined by abnormal blood or urine tests, radiographic studies or pathology of the kidney

\*\*GFR may be estimated from serum creatinine or measured by 24 hour creatinine clearance or other clearance methodology (iothalamate, iothexol, inulin)

### **E. Other Abnormal Lab Findings.**

Patients with Lowe syndrome may have a variety of other abnormal laboratory findings, including high serum glutamic oxaloacetic transaminase (SGOT; also known as aspartate aminotransferase or AST), lactate dehydrogenase (LDH) and serum cholesterol levels, particularly high-density-lipoprotein cholesterol. AST and LDH are found in both liver and muscle. In most cases of Lowe syndrome, elevated serum AST (SGOT) and LDH result from impaired muscle integrity and are not related to liver problems. The reasons for elevation of serum cholesterol are not known, but might be related to factors other than Lowe syndrome.

**F. Prognosis.** Although it is not possible to predict the future for any particular individual, some general observations can be made. With appropriate medical care, many of the problems associated with the syndrome can be treated effectively, allowing life expectancy to extend well into adulthood, with some young individuals living into their 40's and 50's. Progressive kidney failure (see Kidney Failure under Kidneys, Section III) appears to present a significant limitation on life span. However, deaths from complications of Lowe syndrome have occurred at all ages due to infection, dehydration and pneumonia could lead to organ failure and subsequently death. These conclusions rely on current medical practice and may change significantly with more research and the advancement of new treatments.

### **G. ORTHOPEDIC (BONES AND JOINTS)**

**1. Rickets and Soft Bones.** Some children with Lowe syndrome have a history of rickets (growing children) or osteomalacia (adults). These conditions result from a combination of problems. As bones grow and form they need to 'ossify' or become solid. Phosphate, along with calcium, vitamin D, and other nutrients and hormones, as well as proper acid-base balance, are needed for proper ossification and bone remodeling with growth. Vitamin D is normally converted to its active metabolite, 1,25-dihydroxy vitamin D or calcitriol, in the kidney tubules. Since the kidney tubules are abnormal in Lowe syndrome, some patients may not make enough calcitriol to keep the bones strong and to enhance intestinal absorption of calcium, or kidney re-absorption of phosphate. Low blood phosphate, acidosis, hypotonia, vitamin D deficiency, and other kidney problems in Lowe syndrome all place the individuals at risk of developing rickets (in the growing child) or osteomalacia (in the adult). These conditions can lead to bowing of long bones and scoliosis.

Rickets or osteomalacia can be improved by giving oral preparations of neutral phosphate, in addition to the potassium and bicarbonate preparations mentioned above. A side effect of oral phosphate is loose stools, so the dosage must be started low and carefully monitored. Occasionally, vitamin D metabolite preparations, such as calcitriol or dihydrotachysterol, are needed. Therapy with these medications should be carefully monitored to prevent the complications of kidney stones or calcium deposits in the kidney tissue (see Kidneys, Section III). Since patients with Lowe syndrome may be predisposed to developing kidney calcifications even without vitamin D metabolite therapy, the kidneys should be checked for this condition by ultrasound or x-ray before starting, and at intervals during, any therapy with vitamin D metabolites. Plain vitamin D (parent compound) may not be effective as therapy because it may not be converted by the kidneys to the active metabolite.

All medications and dosages must be individualized for each child by his physician. Blood

and urine tests and X-rays are usually ordered periodically to help target and monitor treatment. Blood tests may be done to measure calcium, phosphorus, bicarbonate, alkaline phosphatase, vitamin D metabolites, and parathyroid hormone. Alkaline phosphatase is an enzyme made in bone. When the bone is actively breaking down as in rickets, or when the bone is actively growing and forming new bone, as during healing of rickets, the blood level of alkaline phosphatase will be elevated. The metabolites of vitamin D that are measured are 25-hydroxy vitamin D, which is made in the liver, and 1,25-dihydroxy vitamin D or calcitriol, which is made in the kidney. The 25-hydroxy vitamin D level indicates whether the body stores of vitamin D are adequate, while the calcitriol level indicates whether the kidney is activating adequate amounts of vitamin D. Parathyroid hormone is a hormone made in a gland in the neck near the thyroid. Parathyroid hormone regulates calcium levels in the body and may be elevated when a patient has rickets or is receiving too much phosphorus supplementation.

Urine tests may be done to measure phosphorus, calcium, albumin, creatinine, and pH and will indicate the severity of the urinary losses of calcium, phosphorus, albumin, and bicarbonate.

Changes for all medications should be made only by the physician since medical problems may develop if the medication doses are too high or too low.

**2. Fractures.** About half of the individuals experience bone fractures, which often involve the upper leg when they are learning to walk. Of the individuals who reported a bone fracture, half had more than one fracture, usually involving the arms and/or legs and/or finger, hands or wrists. Increased fracturing is often due to low bone density (osteopenia/osteoporosis), resulting from many of the same abnormalities in mineral and vitamin D metabolism that are involved in rickets but affecting all parts of the bone. In addition, muscle tension on the bones due to exercise and movement is necessary to keep the bones strong. When the muscles are weak (hypotonia), they do not perform this function well. Some fractures can probably be prevented if careful attention is paid to early diagnosis and treatment of hypophosphatemia, acidosis, vitamin D deficiency, and low bone density (osteopenia/osteoporosis). Promotion of routine weight bearing activity and exercise may also be beneficial.

| <b><i>Bone Fractures</i></b>   | <b>(Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals reporting bone fractures</b> | <b>Percent of individuals reporting bone fractures</b> |
|--------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------|
| <i>Age First Diagnosed</i>     | 4 months to 32 years                                                        | 63                                                    | 46%                                                    |
| Upper arm(s)                   |                                                                             | 10                                                    | 16%                                                    |
| Lower arm(s)                   |                                                                             | 10                                                    | 16%                                                    |
| Upper leg(s)                   |                                                                             | 20                                                    | 32%                                                    |
| Lower leg(s)                   |                                                                             | 24                                                    | 38%                                                    |
| Knee(s)                        |                                                                             | 7                                                     | 11%                                                    |
| Ankle(s)                       |                                                                             | 9                                                     | 14%                                                    |
| Feet or toe(s)                 |                                                                             | 6                                                     | 10%                                                    |
| Wrist(s), hand(s) or finger(s) |                                                                             | 17                                                    | 27%                                                    |
| Skull or facial                |                                                                             | 0                                                     | 0%                                                     |
| Collar bone                    |                                                                             | 5                                                     | 8%                                                     |
| Teeth                          |                                                                             | 1                                                     | 2%                                                     |

|                  |  |   |     |
|------------------|--|---|-----|
| Spinal bone(s)   |  | 1 | 2%  |
| Hip(s) or pelvis |  | 7 | 11% |

**3. Scoliosis.** Some individuals develop scoliosis, or curvature of the spine, by adolescence or adulthood. The severity of this condition varies from mild to severe. In severe cases, scoliosis can adversely affect mobility and cause back pain and diminished lung capacity. In some cases, this condition is treated effectively through the use of a brace or cast or surgery.

**4. Plantar Fasciitis.** Plantar fasciitis is a painful inflammation of the foot and generally occurs on the underside of the heel. In a few individuals, it has also been reported in the legs/calves and palms of hands. The pain is often most intense in the morning when pressure is first placed on the heel. Although no one treatment has been effective for everyone, there have been treatments noted by Lowe syndrome patients. Treatments have included, but may not be limited to the use of physical therapy, massage therapy, wearing orthotics and sometimes surgery.

**5. Palmar Fibromatosis.** A few individuals have experienced palmar fibromatosis. The term fibromatosis refers to a group of benign soft tissue tumors. These are generally found in one or both of the hands, soles or arch of the feet, fingers, legs or calves. Palmar fibromas tend to stay in one area, where as desmoid tumors tend to be more aggressive.

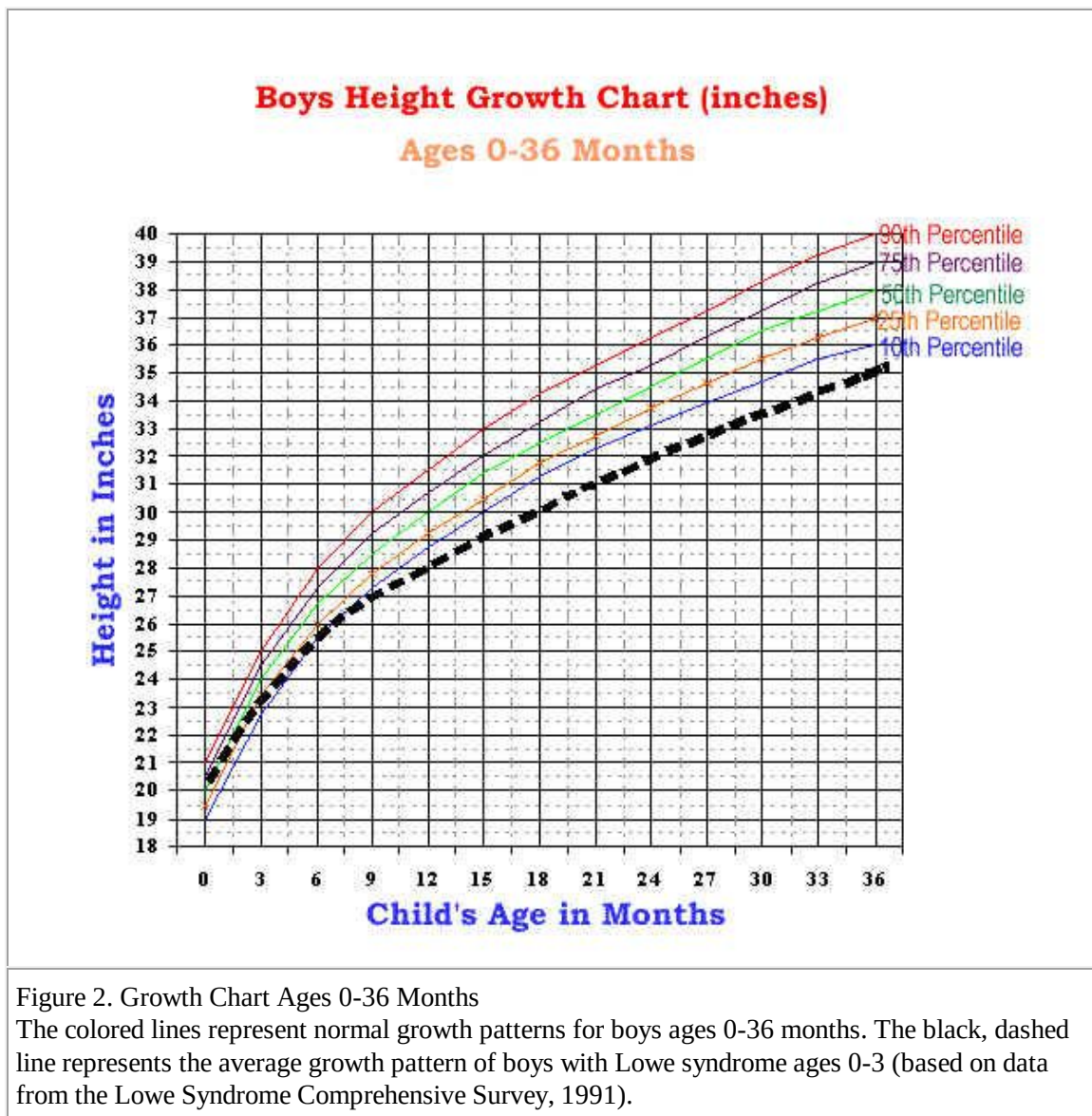
**6. Desmoid Tumors.** A few individuals have experienced desmoid tumors. These tumors have a tendency to develop in the connective tissue of the body that forms tendons and ligaments, usually in the feet/toes, buttocks, face, fingers, hands, knees, neck, ankles or lower legs. A desmoid tumor can be invasive to surrounding tissues and difficult to control. These tumors can develop in almost any site on the body and are usually difficult to remove because the tumor intertwines with surrounding tissues. A desmoid tumor looks like dense scar tissue. One treatment option for desmoid tumors would be to surgically remove the tumor, however most tumors tend to recur after surgery.

**7. Kyphosis.** Incidence of kyphosis has also been reported in individuals with Lowe syndrome. Kyphosis, also called “hunchback,” causes curvature of the upper spine. This can either be the result of a degenerative disease, such as arthritis, developmental problems, osteoporosis with compression fractures of the vertebrae or can result from trauma to the spine. Treatment for kyphosis may include body braces, such as the Milwaukee brace, physical therapy and sometimes surgery.

**8. Short Stature.** Individuals with Lowe syndrome are generally of normal length at birth but by one year of age, most have fallen well below the normal range of height (see Figures 2 and 3). Growth



continues, but at a slower rate than normal. The average adult height is about 5 feet, 1 inch or 155 cm. The underlying cause of the short stature is unknown. Studies are being done to determine the effectiveness and safety of human growth hormone therapy. Reportedly, several children with Lowe syndrome have been successfully treated with human growth hormone. However, the effectiveness and the benefits of the supplementation must be balanced against the significant expense of the therapy and the potential social and psychological factors.



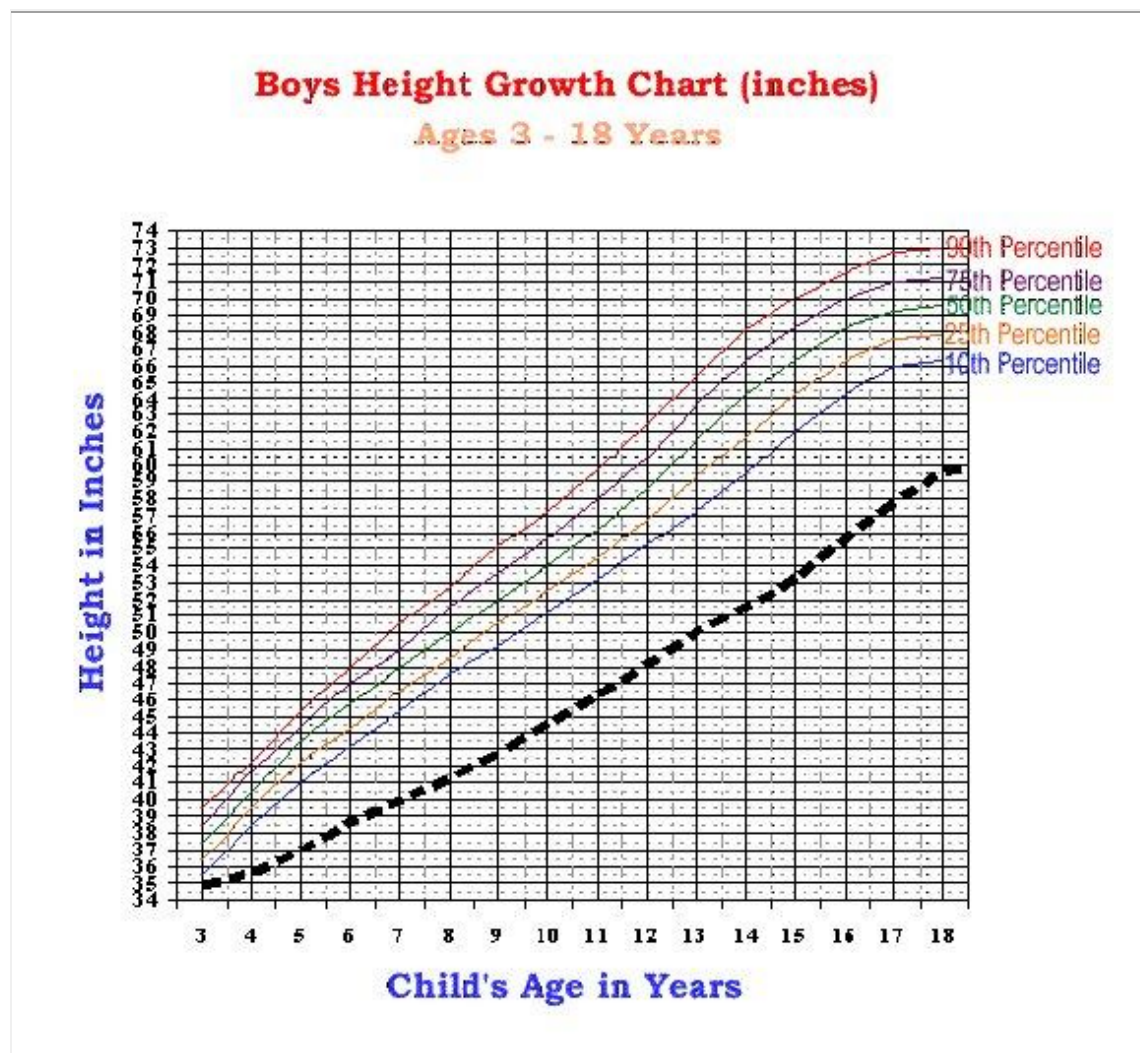


Figure 3. Growth Chart Ages 3-18 years

The colored lines represent normal growth patterns for boys ages 3-18 years old. The black, dashed line represents the average growth pattern of boys with Lowe syndrome ages 3-18 (based on data from the Lowe Syndrome Comprehensive Survey, 1991).

**9. Growth Hormone.** Growth Hormone has been used in some individuals to treat growth deficiency and decreased bone density. Growth hormone in some individuals can stimulate growth and cell reproduction and regeneration. As with every treatment option, the potential benefits need to be weighed against the potential side effects, costs and limitations.

|                                       |     | Number of individuals reporting use | Percent of individuals reporting use |
|---------------------------------------|-----|-------------------------------------|--------------------------------------|
| <b>Growth Hormone</b>                 |     | 23                                  | 17%                                  |
| Used to Treat Growth Deficiency       | Yes | 20                                  | 87%                                  |
|                                       | No  | 3                                   | 13%                                  |
| Used to Treat Bone Density/Deficiency | Yes | 11                                  | 48%                                  |
|                                       | No  | 12                                  | 52%                                  |

**10. Joint Swelling and Arthritis.** Other orthopedic problems associated with Lowe syndrome include joint swelling and arthritis of individuals. These problems are particularly prevalent in the teenage and adult years. In some cases these problems can be quite severe and debilitating, impairing the ability to walk or impairing fine motor abilities depending on which areas of the body are affected. The affected locations include the knees, fingers, feet/toes, ankles, hips, shoulders, wrists, elbows, and neck. The underlying cause is unknown and there is no effective therapy except treatment for pain. Some individuals have had success with physical therapy, physical exercise and massage therapy to treat painful joints.



**11. Wheelchair and Walking Devices.** Wheelchair or walking devices have been necessary for some individuals ranging in age between birth to 40 years. Some individuals reported the need for a wheelchair or walking device as “always,” whereas some reported needing assistance “occasionally.”

## H. DENTAL

**1. Teeth.** Many individuals with Lowe syndrome require extensive dental care. A high palate, small mouth, rickets, and other bone and metabolic factors often result in crowding, poor alignment, the susceptibility to decay, and delayed shedding of primary teeth. Many children experience ‘yellowing of the teeth’ from metabolic imbalance due to renal problems, tartar formation on the teeth or dentin filling in the root canal space. Misalignment of the teeth can often be caused by high, narrow palates, poor tongue postures, low oral muscle tone and a double row of teeth. Some individuals experience a double row of teeth. Regular dental care should be started when the first baby teeth have erupted. Behavior and behavior management often play a significant role in dental treatment for individuals with Lowe syndrome.



roots of the teeth in place are destroyed by plaque bacteria. Plaque bacteria forms when gingivitis goes uncontrolled. The result is loss of bone causing the teeth to become loose when the roots are unable to remain anchored to the gums.

**3. Extractions.** Extractions have been reported in many individuals with Lowe syndrome. Of the teeth needing to be extracted, primary or baby teeth are most often extracted. Extraction of permanent teeth was reported less often, although some individuals require extractions of permanent teeth.

Reasons for having teeth removed may include infection and decay, overcrowding, obstruction of other teeth, and loose teeth.

**4. Dental Cysts.** Dental cysts are sacs filled with fluid or soft material that has built up under the tissue around the teeth. Some individuals experienced dental cysts, also known as blood cysts, during tooth eruption. Some dental cysts will resolve independently, however other dental cysts may need to be treated by a dentist.

**5. General Anesthesia for Dental Procedures.** Many individuals need general anesthesia for dental procedures. Often children with Lowe syndrome are resistant to dental procedures and need to have simple procedures such as cleanings, exams, and x-rays done under the use of anesthesia. As children aged and matured, some reported no longer needing anesthesia for dental procedures.

**6. Dental Surgery.** Dental surgery is needed in many individuals. Families have reported the need for dental surgery to treat a variety of dental problems, including filling cavities, enamel coating application, removal of teeth, dental implants, crowns, periodontal work, removal of gums, surgery for a double row of teeth and removal of wisdom teeth.



## **7. Braces and Orthodontic Devices**

In a very small percentage of individuals braces and other orthotic devices have been successful in treatment of high palate, overcrowding of the teeth and the misalignment of the teeth. Success with braces is often determined by the temperament and ability to tolerate the necessary procedures involved in placing and wearing orthotic appliances.

## **I. SPECIAL HEALTH CONCERNS**

Lowe syndrome often gives rise to other, more generalized health concerns in addition to those previously discussed.

**1. Conditions Causing Metabolic Imbalance.** Any circumstance which interferes with the ability of children with Lowe syndrome to take in their usual amount of daily fluids and medicines may increase their risk for developing metabolic imbalance. This is more likely to occur with illnesses such as colds, flu, vomiting, or diarrhea. It may also occur when uncontrolled seizures interfere with normal fluid intake. At these times parents should seek prompt medical attention because intravenous fluids and medications may be needed.

Also, some children may need intravenous fluid and medication therapy to prevent metabolic imbalance when having surgery, anesthesia, or other procedures which require a period without eating or drinking.

**2. Respiratory Illness.** Children with Lowe syndrome may be more susceptible to developing

pneumonia because of hypotonia (see Hypotonia under Brain and Central Nervous System, Section III) which may cause an inability to cough strongly and effectively. They should be monitored carefully during episodes of respiratory illness. Parents may learn to administer postural drainage therapy, which may help to loosen mucous plugs in the lungs.

**3. Eating Difficulties.** Hypotonia can affect the ability to suck and swallow, causing several potential problems including inadequate nutritional and fluid intake and inability to take



medications. Also, poorly coordinated swallowing abilities can increase the risk for aspiration pneumonia (which can result when food or liquid goes down the trachea and into the lungs instead of down the esophagus and into the stomach). Specialists in occupational, speech and language therapy may be able to provide 'feeding training' to help improve the ability to suck and swallow.

If a child is not able to take in his daily nutritional requirements, alternate methods of feeding may need to be considered. One method is the use of a nasogastric (NG) feeding tube which is placed through the mouth or nose into the stomach. The NG tube is not permanent. Another method is the gastrostomy tube (G-tube or button) which is surgically placed directly into the stomach through the abdominal wall.

A nutritionist may be able to give advice on how to meet dietary needs.

**4. Gastroesophageal Reflux.** Another common problem in Lowe syndrome is gastroesophageal reflux (GER), a condition often associated with hypotonia. In GER, the sphincter muscle at the top of the stomach does not stay shut, allowing food or liquids to come back up the esophagus. This often causes heartburn, vomiting, and esophageal irritation from stomach acid. It also causes an increased risk for aspiration pneumonia. To diagnose this condition physicians may order an upper GI series and a scintiscan (X-rays with isotope) for reflux. Treatments may include adaptations such as eating upright and elevating the head of the bed, medications, and/or surgery.



**5. Constipation.** More than half of the individuals with Lowe syndrome have constipation. Poor muscle tone may contribute significantly to this problem. Some doctors believe, however, that constipation is a specific feature in Lowe syndrome and represents a direct effect of the gene upon the intestinal muscles, causing an inability to move the stool effectively.

Treatment includes adequate amounts of fiber in the diet and plenty of water. If dietary control is ineffective, medication may need to be considered. This should be done only under a physician's care. Enemas are not recommended because they can lead to serious metabolic imbalances that could be life threatening.

**6. Cysts.** Cysts, a common problem in Lowe syndrome, can occur in many places, including the mouth, kidneys, brain, and skin. Dental cysts appear to be quite common with teething but usually resolve after permanent teeth are in. In older individuals with Lowe syndrome, cysts in kidney and skin appear to be more frequent. Cysts in the brain have also been reported.

In adults with Lowe syndrome, skin cysts around the lower back and buttocks can become quite painful and occasionally become infected. The cause of the cysts is not known, but it probably is a specific effect of Lowe syndrome. Treatment for cysts varies depending on type and / or location of the cyst.

**7. Undescended Testes.** Undescended testes, or cryptorchidism, occurs at birth in almost half of the boys. The testes descended naturally with time in some of those affected, between the ages of 1 month to 18 years, as reported in the ***Report on the Lowe Syndrome Comprehensive Survey - 2008***. If the testes do not descend naturally, boys should be evaluated prior to 1 year of age to determine if surgical correction or other medical therapy is needed.

**8. Puberty.** In general, puberty is slightly delayed in individuals with Lowe syndrome, but otherwise follows a typical progression. In individuals with Lowe syndrome puberty has been reported to begin between the ages of 9 years and 26 years, with the average being 15 years old. This is about 2 years later than typical individuals. Based on the ***Report on the Lowe Syndrome Comprehensive Survey - 2008***, 53 individuals were observed as going through puberty, 51 reported having

pubic hair, developing between the ages of 9 years and 22 years, with the average age of pubic hair development being 15 years. Normal deepening of the voice as a result of puberty was reported in 37 young men, with ages ranging between 10 years and 22 years, the average being 15 years. Masturbation was reported in 23 individuals and 10 individuals were reported to have experienced an ejaculation.

As with typically developing individuals, individuals with Lowe syndrome should learn about the male and female body, reproductive system, sexual development and contraception. For some individuals, too much detail may not be appropriate. It will be up to the parents to determine what information their child is able to absorb and comprehend. All children need to learn about appropriate place for private acts, such as dressing and being naked. Children with a developmental disability may have more difficulty understanding verbal explanations and may need visual cues to comprehend what is expected of them. A picture of a child fully dressed symbolizes that wearing clothes is appropriate. Whereas, a picture of the bathroom door closed, shows a child that the bathroom is a private place. It's important to remember that no behavior is good or bad, only that certain behaviors are expected in all children. In some situations, young individuals will need special guidance



about appropriate times and places for masturbation. Social stories may be another effective tool for teaching children which behaviors should be done in private and which behaviors are acceptable in public. A child's ability to understand the difference between public and private is essential to understanding what body parts are okay for others to touch and which body parts need permission to be touched.

Because individuals with Lowe syndrome tend to be friendly, trusting, agreeable and willing to please, they may be at risk for abuse, especially sexual abuse. Attention may need to be given to teach adolescents about appropriate and inappropriate touch or "good touch and bad touch." Family counselors and programs, such as *Circles*, are available to support families in teaching about sexuality and personal boundaries.

At this time, no known individual with Lowe syndrome has ever reproduced an offspring and no data are available.



## IV. GENETICS

Lowe syndrome is a genetic disease, which means that the condition is always caused by an altered gene. In many families, Lowe syndrome is passed from a carrier mother (which means she carries the altered gene) to her affected son. In that situation, female relatives of the mother may also have the altered gene and may be at risk of having individuals with Lowe syndrome. In other situations, the mother of the affected boy is not a carrier of the altered gene. In that situation, the mother and her female relatives are not at risk of having more children with Lowe syndrome.

Families in which Lowe syndrome occurs should understand whether the condition is inherited in their family, the likelihood of reoccurrence of the disease in subsequent children of the same couple, who else in the family could be a carrier and how to determine this, and what resources are available to clarify those risks and to assist with decisions about personal family planning.

### A. UNDERSTANDING HOW LOWE SYNDROME IS INHERITED

**1. Genes.** Lowe syndrome is due to an “inborn error of metabolism”. Metabolism refers to the complex physical and chemical processes involved in the maintenance of life and the functions of every cell in our bodies. All these processes are controlled by genes, the basic units of life that we each inherit from our parents. When a mutation (an alteration or a change) occurs in a gene, an imbalance or “error” in metabolism may result, causing a disease or disability.

Most mutations of genes occur spontaneously, usually for unknown reasons. They are not caused by being exposed to drugs or alcohol or emotional events during pregnancy. Once a mutation occurs, however, it becomes “fixed” in a person's genetic material. If that individual survives and grows up, he or she then has the potential to pass or transmit the altered gene to subsequent generations. Thus the disorder becomes hereditary in that family.

**2. Chromosomes.** Genes are grouped together in packages called chromosomes. Except for red blood cells and the reproductive cells, every human cell contains 23 pairs of chromosomes, or a total of 46 chromosomes. One member of each pair of these chromosomes comes from the father and the other member of each pair comes from the mother. The reproductive cells, the ovum (egg) and the sperm, each contain 23 chromosomes. At the moment of conception, the sperm and the ovum fuse, thus creating a cell with 23 pairs of chromosomes and all the genetic material for another human being.

Twenty-two pairs of chromosomes contain genes that determine general body characteristics, like eye color, stature, and growth. The twenty-third pair is different because it determines the sex of the offspring. This pair includes the “X” and “Y” chromosomes. Females (XX) have two X-chromosomes (one from each parent). Each of the female's ova or eggs will carry either one or the other X-chromosome (but not both). Males (XY) have one X-chromosome (from the mother) and one Y-chromosome (from the father). Therefore, each sperm in the male will carry either an X-chromosome or a Y-chromosome (but not both). If the father passes on a sperm that carries his X-chromosome, the resulting offspring will be female (XX); if he passes on a sperm that carries his Y-chromosome, the offspring will be male (XY).

**3. X-Linked Inheritance.** Since the early 1960's, physicians have known that the defective gene causing Lowe syndrome is located on the X-chromosome. Diseases caused by genes that are located on the X-chromosome are called "X-linked" and have a distinctive pattern of inheritance. X-linked diseases typically affect only males but are "carried" and passed on by females. Women who are Lowe syndrome carriers have one X-chromosome with one normal copy of the Lowe gene (X) and one X-chromosome with a defective Lowe gene (X\*). Females who have one defective copy of the Lowe syndrome gene (XX\*) are protected from developing the full Lowe syndrome by the normal copy of the gene (although some may develop cataracts in early to mid-adulthood). Males who have an X-chromosome with the mutated Lowe gene (X\*Y) will be **affected** with Lowe syndrome, since the only X chromosome that male has is the one that contains a defective Lowe syndrome gene and the Y-chromosome contains no equivalent information that could compensate for the defective gene.

**4. Carriers.** A female who has a defective Lowe syndrome gene on one of her X-chromosomes is called a genetic "carrier" because she bears or carries this information in the form of one copy of a mutated Lowe gene, on one of her two X-chromosomes. With each pregnancy, she has a 50% chance (one out of two) of passing on the X-chromosome with the defective Lowe gene to her child. (Since she has two X-chromosomes, she may pass either one or the other X-chromosome to her offspring, with equal probability.)

- v If the child is a male, there is a 50% chance that he will inherit the mother's X-chromosome with the mutated Lowe gene, and, because he is male and received a Y from his father, will have Lowe syndrome. If he inherits his mother's X-chromosome with the normal gene, he will be an unaffected (normal) male.
- v If the child is a female (because she inherits her father's X-chromosome), there is a 50% chance she will inherit the mother's X-chromosome with the mutated Lowe gene and thus be a carrier just like the mother; similarly, there is a 50% chance she will not be a carrier because she will inherit the normal X-chromosome.

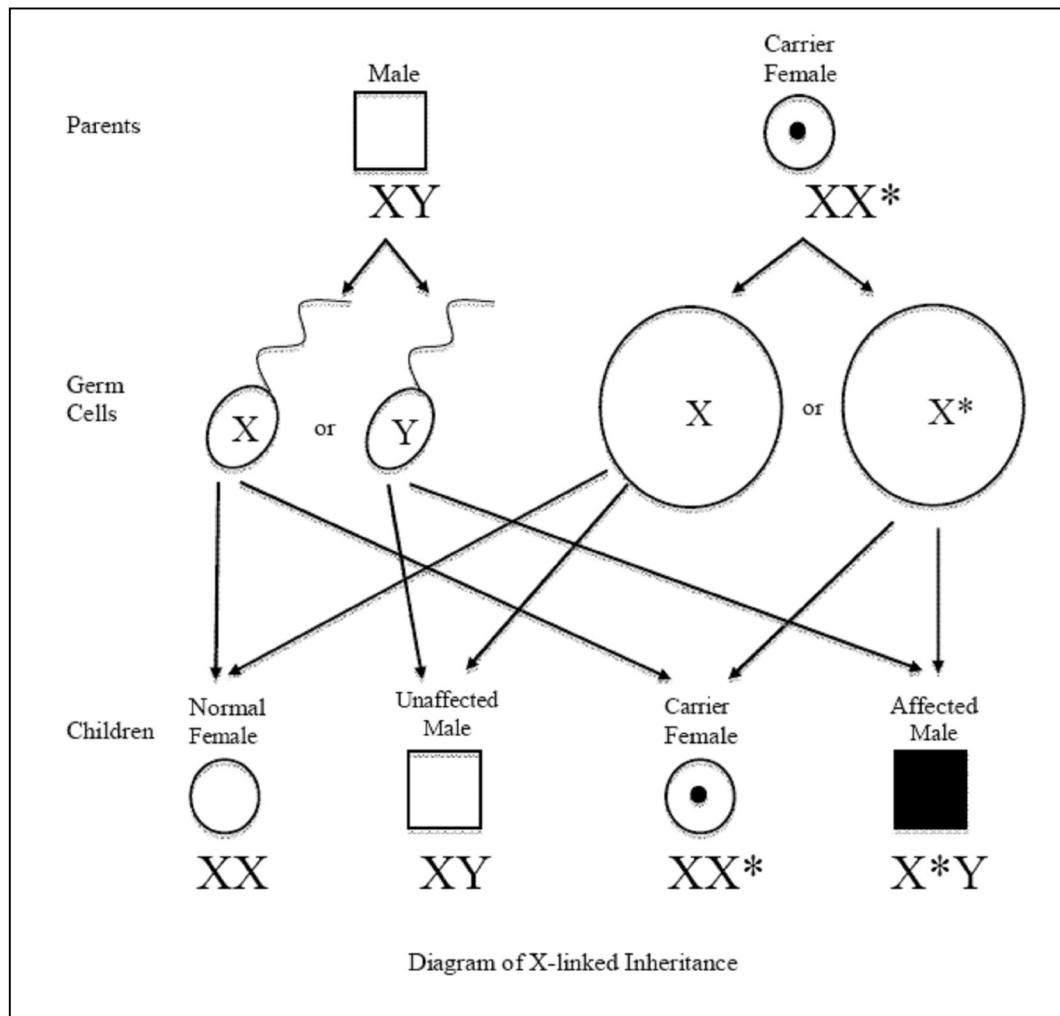
Thus, in any one pregnancy any carrier female has one chance in four of having an affected child, and that child will be a male. (See Diagram 1)

In summary, with each pregnancy a carrier female has one chance in four (a 25% risk) of having a boy with Lowe syndrome; one chance in four of having a normal boy; one chance in four of having a carrier daughter; and one chance in four of having a normal daughter. Obviously, these probabilities apply only to women who are genetic carriers. As discussed in the following section, however, in some families the affected male Lowe child is the first individual in the family with the condition. Determining whether the mother is a carrier or not, holds tremendous importance in predicting the outcomes of future pregnancies and of those of her female relatives.

**5. New Mutations.** A number of males with Lowe syndrome occur as the first and only affected individuals in their families by history. In such cases, it is still possible the mother is a carrier and it is simply a matter of luck that no one previously in the family had shown signs of the disease. On the other hand, it is possible that the mother is not a carrier; that is, her genetic makeup may not include the altered gene. Rather, the gene in the single ovum (egg) which developed into the

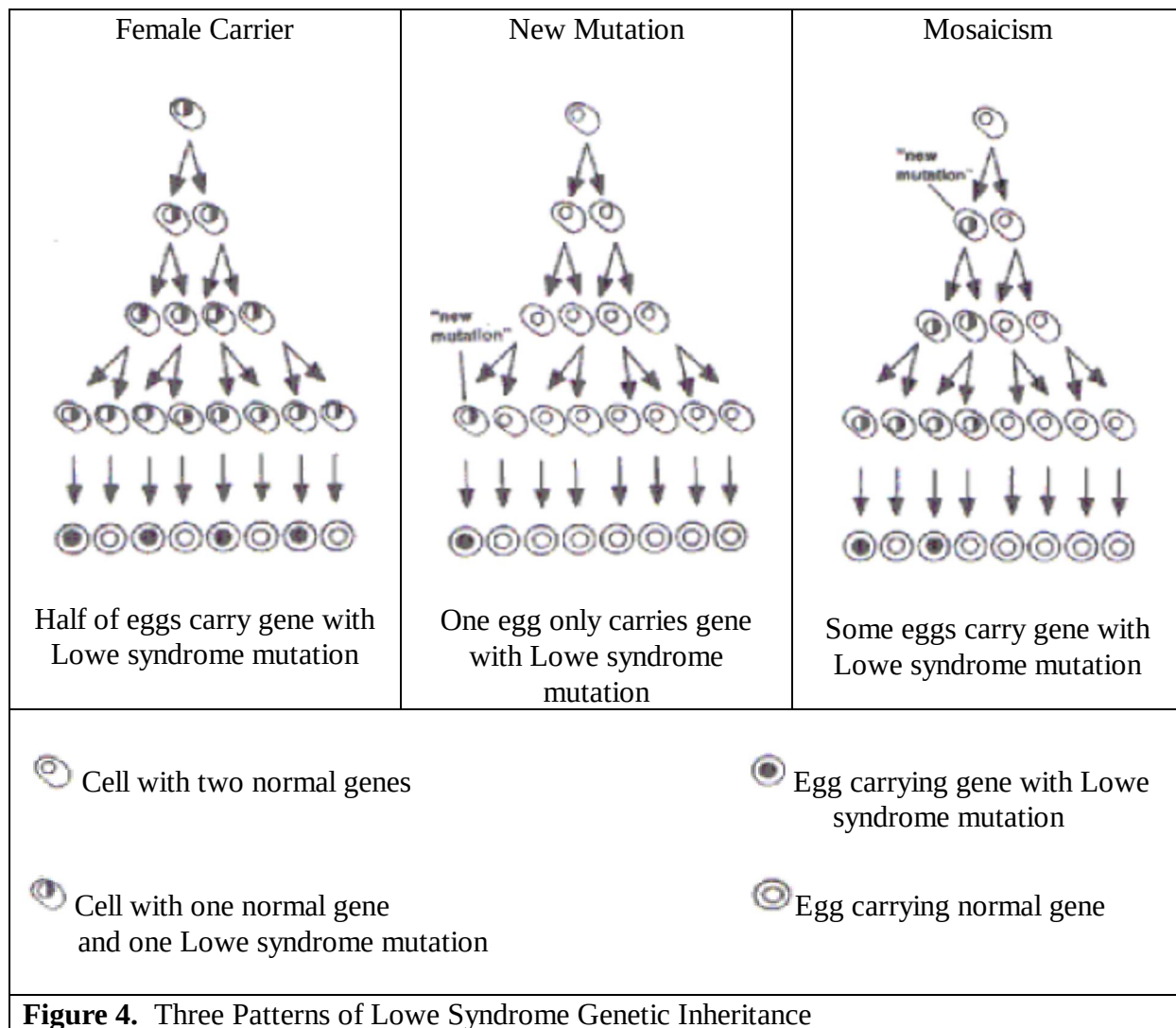
boy with Lowe syndrome may have become altered. An alteration in a previously normal gene is called a mutation. Since the boy is the first person with this altered gene, he is affected as the result of a new genetic event, referred to as a “new mutation.”

When Lowe syndrome is the result of a new mutation, the mother is not a carrier. Her risk of having another child with Lowe syndrome is no greater than that faced by non-carrier females in the general population. To determine if a boy with Lowe syndrome is the result of a new mutation, the mother must undergo carrier testing (see “Carrier detection” and “Non-carriers” in the following section).



**6. Mosaicism.** In a few rare families, a child affected with Lowe syndrome may be neither a new mutation nor an inherited mutation coming from a carrier mother. In these few exceedingly rare situations, the mother may have had a new mutation occur during her own prenatal development. In this case, the mutation may be present in a minority of her cells, including those from which some of her eggs are derived. The cells of her body, other than the cells in the ovary, may not carry the mutation and so she may not have any signs on her eye exam of being a carrier. Yet more than one egg will carry the mutation, so she will have some risk greater than zero of having another

son with Lowe syndrome or a daughter who is a carrier. This situation, in which a woman has some cells carrying a mutation and other cells that do not, is called ‘mosaicism’ (see Figure 4 below). More than one egg, but fewer than half, will carry a Lowe syndrome mutation. Mosaicism has been documented in Lowe syndrome.



## B. CLINICAL TESTING

Laboratory-based diagnosis and carrier testing have moved from the research arena into standard clinical genetics practice. The discovery of the enzyme deficiency led to the development of a simple and reliable biochemical test. A biochemical test is a direct assay of the enzyme phosphatidylinositol 4,5-biphosphate 5 phosphatase. The test was initially developed in 1996 and has become a standard test in the clinical laboratory at Baylor College and at the University Hospital in Grenoble, France. The enzyme assay is now commonly used to diagnose affected patients as well as to carry out prenatal diagnosis. For the enzyme test in an affected male, a small skin biopsy is necessary; a sample of blood cannot be used for the enzyme test. For prenatal diagnosis, cells obtained either by chorionic villus sampling or amniocentesis can be used for the

enzyme assay.

Diagnosis can also be performed by direct analysis of the Lowe syndrome gene to find the mutation responsible for the disease. A blood sample is obtained from the individual suspected of having Lowe syndrome and the entire gene is sequenced to find the particular alteration in the gene in that family. To date, over 100 different mutations have been found in different patients with Lowe syndrome worldwide. Thus, most families typically have a mutation unique to their family.

### C. GENETIC COUNSELING.

Couples who are at-risk for having an affected child with Lowe syndrome should explore their family planning options with the guidance of their physician and/or a genetic counselor. Geneticists and genetic counselors can help to determine the chances of having an affected child. Trying to determine whether or not a woman is a carrier is very important because it has substantial impact on the risks for having other affected sons (or grandsons). Her carrier status may also be relevant to the status of her female relatives (her sisters and her aunts and their daughters, among others).

**1. Carrier Detection.** Families at-risk for having a boy with Lowe syndrome may wish to investigate their chances of having an affected child. Women who are at-risk include the mothers and sisters of affected individuals, as well as the boy's maternal aunts and their daughters. Thus, determining whether or not a woman is a carrier may also be critically important to extended family members who may wish to plan their own families. Geneticists and genetic counselors can advise couples about their reproductive risks.

In some cases, a woman's carrier status can be determined from her family history. For instance, the mother of a son with Lowe syndrome is presumed to be a genetic carrier if there has been a previous case of Lowe syndrome in her family (such as her brother or her mother's brother). If there were no other known cases of Lowe syndrome in the family, however, the mother of an affected boy may or may not be a carrier, since her son's condition could be the result of a new gene mutation in that male or of mosaicism in her ovaries. However, even in the absence of any history of Lowe syndrome in a family, one cannot assume that the mother is not a carrier. The carrier status of the mother must be determined by examination and/or by testing. In most cases, especially in women after puberty, carrier status can be determined by an eye examination performed by an ophthalmologist (a physician specializing in diseases of the eye). The examination must be done with the pupils dilated (with eye drops). Approximately 95% of all carriers of the gene for Lowe syndrome have subtle changes in the lenses of their eyes, especially in the teenage and adult years. These changes, which appear as tiny dots and flecks in the lens in a characteristic distribution and pattern, typically cause no effect on vision and, if not looked for diligently, may be mistakenly dismissed as normal variations. Therefore, the geneticist should insist that the examination only be made by an ophthalmologist with substantial experience with the subtle variations of the lens opacities of Lowe syndrome carriers.

If a reliable examination detects these characteristic lens opacities in an at-risk female of any age, then she is a carrier. If the opacities are not present in an adult female, she is probably not a carrier. This conclusion cannot be made with absolute certainty, however, especially if she is younger than 15 years old. Although the tiny dots and flecks in the lens of female carriers usually do not cause visual problems, some carrier women have developed visually significant

cataracts in their twenties, thirties and forties which have required cataract surgery much earlier than the usual expected age in the general population.

There is no blood test or skin test that can reliably determine the carrier status for all at-risk females at this time. For carrier testing, the specific change (mutation) in the DNA sequence that causes the disease must be used to identify carriers; biochemical testing is not effective for carrier detection. Because most families typically have a mutation unique to their family, DNA sequencing in a search for the mutation responsible for Lowe syndrome is necessary in each family that decides to pursue carrier testing by DNA sequence analysis. Preferably, a sample from an affected male in the family is first obtained and the entire gene is sequenced to find the particular alteration in the gene in that family. Once the alteration is found, females at risk for being carriers in the family are tested specifically only for that same alteration. This type of genetic mutational analysis is not commonly available in standard clinical testing laboratories but can be obtained at specialized molecular Genetic laboratories in the United States and Europe ([http://www.ncbi.nlm.nih.gov/sites/GeneTests/lab/clinical\\_disease\\_id/2509?db=genetests](http://www.ncbi.nlm.nih.gov/sites/GeneTests/lab/clinical_disease_id/2509?db=genetests)).

When the specific mutation responsible for Lowe syndrome is not known, families with a strong family history of Lowe syndrome can be analyzed using DNA markers near the mutant gene to trace the inheritance of the abnormal gene in the family. This approach to carrier detection and prenatal diagnosis is called 'linkage' and may be pursued in specialized molecular genetic laboratories.

**2. Non-Carriers.** When a careful eye examination of the mother of a child with Lowe syndrome is normal (that is, the characteristic lens opacities are not present), there are three possible explanations for the Lowe syndrome in her child. First, and most commonly, the child is the result of a new genetic mutation in the egg that developed into him. In this case, the mother does not carry any other mutated Lowe syndrome genes in the rest of her eggs. She is not a carrier and she is no more likely to have another child with Lowe syndrome than any other non-carrier female in the general population. Second, and more rarely, is that she really is a carrier but falls into the group of 5% of all carriers who fail to show significant changes in their lenses. Her probability of having a child with Lowe syndrome is 25% with each pregnancy (50% for each male pregnancy). Third, and most rarely, the mother may be mosaic for the mutation in her ovaries. In this case, she may have additional eggs carrying the Lowe syndrome mutation without showing signs in the lenses of her eyes. Her risk of having another child with Lowe syndrome or a daughter who is a carrier would be much greater than that of the general population, but not the full risk that a true carrier female has (see Carriers, in previous paragraph).

Unfortunately, there is no reliable biochemical or molecular test to diagnose mosaicism. For that reason, even women with normal eye examinations will be offered prenatal testing because of the risk of unsuspected mosaicism. However, whether the mother of a child with Lowe syndrome is a non-carrier or represents a mosaic situation, her sisters or other female relatives (except for her daughters) are not at risk for being carriers because, in either case, the mutation occurred as a new genetic event in the mother herself. These risks are summarized in the accompanying table.

| <b>Risks for (1) Lowe syndrome in future male children and (2) being a female carrier depending on the carrier status of the mother</b> |                                                             |                                                             |                                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|--------------------------------------------------------------------------|
| <b>Mother's Status</b>                                                                                                                  | <b>Risk of Lowe syndrome in future sons</b>                 | <b>Risk a daughter could be a carrier</b>                   | <b>Risk mother's sisters or other female relatives could be carriers</b> |
| Carrier                                                                                                                                 | 50%                                                         | 50%                                                         | Significantly increased but exact risk varies                            |
| Non-carrier                                                                                                                             | Population risk (low)                                       | Population risk (low)                                       | Population risk (low)                                                    |
| Mosaic (rare)                                                                                                                           | Significantly increased but exact risk cannot be determined | Significantly increased but exact risk cannot be determined | Population risk (low)                                                    |

**3. Family Planning Options.** At-risk couples have a wide range of options available to them. Some may choose to "take their chances" with a pregnancy, while others may consider prenatal testing. Some couples may be interested in adoption or in techniques that would use a donor egg from a non-carrier female. Others may be interested in methods to increase their chances of conceiving a female since females, even if carriers, do not develop most features of the disease.

If prenatal testing is chosen, testing to determine if the fetus is male or female is a well established procedure and is widely available. If the fetus is determined to be a male, a prenatal enzyme analysis test, identical to the test used to diagnose Lowe syndrome, is available. Enzyme analysis can be used for prenatal diagnosis even if carrier status has not been established firmly. It can also be used whether or not gene analysis has succeeded in identifying the specific gene alteration in the family. Prenatal testing can be accomplished by CVS (chorionic villus sampling), which is done at 11-13 weeks, or amniocentesis, which is done at 15-18 weeks. At the present time the analysis for the OCRL enzyme test can only be carried out at a Biochemical Genetics Laboratory. (See Frequently Asked Questions, Section I)

Many factors will affect a couple's family planning decisions, including their personal, family, ethical, and religious views, as well as financial, educational, and geographical considerations. Ultimately, the right decision for any individual or family is the one with which they are comfortable now and will remain comfortable as they look back in the future.

## V. RESEARCH

### A. EARLY RESEARCH HISTORY

During the first three decades after Lowe syndrome was recognized, research efforts led to a better overall understanding of the syndrome. In 1954 the specific form of kidney involvement associated with the syndrome was recognized. X-linked inheritance was suggested in 1957, and the ability to identify female carriers by eye examination was confirmed in 1976. However, not until the past decade were researchers able to make any significant progress in identifying the underlying defect.

Several factors that have frustrated researchers' efforts over the years have changed. First, because Lowe syndrome is rare, there was a general lack of investigation. This situation changed somewhat in 1983 when the Lowe Syndrome Association (LSA) was founded. With the establishment of the LSA, researchers had access to a large pool of willing participants for the first time. Second, until the 1995 discovery that Lowe syndrome is caused by an enzyme deficiency, the biochemical manifestations in Lowe syndrome were found to be too nonspecific for easy investigation. There was no single abnormal metabolite which would point to a specific pathway to investigate. Third, there are no naturally occurring animal models for the disease.

Researchers have been restricted by the necessary limitations placed on investigations that can be done on the patients themselves. This situation is now changing as researchers use molecular methods to study what the Lowe syndrome gene and protein does in a cell and to develop laboratory animal models.

### B. DISCOVERY OF THE LOWE SYNDROME GENE AND ENZYME

The dramatic advances in the field of genetics during the past decade have opened new avenues of research and have led to significant advances in understanding Lowe syndrome. The first big step towards identifying the underlying defect took place in 1986 when Drs. Lewis and Nussbaum and their colleagues at Baylor College of Medicine succeeded in assigning the Lowe syndrome gene to a small region in the middle portion of the long arm of the X-chromosome. Subsequent work by many collaborating scientists ultimately culminated in identifying the gene in which mutations cause Lowe syndrome in 1992. The gene which, when defective, causes Lowe syndrome is known as *OCRL1*, named after the OculoCerebroRenal syndrome of Lowe. Three years later, Dr. Nussbaum and his colleagues, then at the National Institutes of Health, announced the discovery that the defective gene causes a deficiency of an enzyme. An enzyme is a protein that carries out a specific chemical reaction. The Lowe syndrome gene is the blueprint for a particular enzyme that splits a phosphate molecule off of a large molecule called phosphatidylinositol 4,5-biphosphate and, therefore the protein is called “*phosphatidylinositol 4,5-biphosphate 5 phosphatase*” or PIP<sub>2</sub>-5Pase for short. PIP<sub>2</sub>-5Pase helps regulate part of the machinery responsible for moving certain substances in and out of the cell, a process called “cellular trafficking”. The most recent evidence suggests that because this enzyme is deficient in Lowe syndrome, cellular trafficking is abnormal.

### C. CURRENT BIOMOLECULAR RESEARCH

What has become clear is that the Lowe syndrome protein does more than just function as an enzyme. It is a multifunctional protein; its activity as an enzyme is only one of the ways it is involved in cellular trafficking. The focus of research now is in determining exactly which

components of cellular trafficking are disturbed in Lowe syndrome and how a loss of the PIP<sub>2</sub>-5Pase activity leads to developmental defects such as cataracts, kidney dysfunction and problems with the nervous system. These questions are being investigated in cultured cells by a growing list of scientists located in the United States, England, France, Italy and Chile. A number of these projects have received funding from the LSA over the past 10 years.

One useful tool for understanding the relationship between a defect in PIP<sub>2</sub>-5Pase and Lowe syndrome would be an animal that has the condition so that tissues from its kidneys, brain and eyes could be directly studied in the laboratory. In 1998 researchers successfully mutated the Lowe syndrome gene in a laboratory mouse. However, the mouse did not exhibit the expected characteristics of Lowe syndrome. By engineering a mouse to mimic human metabolism of phosphatidylinositol 4,5-biphosphate more closely, researchers at the University of California in San Francisco have created a mouse that shows many of the same kidney defects seen in Lowe syndrome. A similar approach to modeling the disease for Lowe syndrome in fish is also underway.

#### **D. CLINICAL RESEARCH**

Areas other than genetics have also been investigated. Researchers at the National Institutes of Health studied clinical aspects of the syndrome in a large number of individuals over a span of several years during the 1980's and early 1990's. Their discoveries led to a better understanding of the natural course of the syndrome and better treatment techniques for many of the problems. Other important research projects included a study that helped to establish a causal link between the syndrome and behavioral problems. Unfortunately, the rarity of the condition and a lack of clinical investigators committed to studying the disease has left many questions unanswered and much more work remains to be done in the area of clinical research.

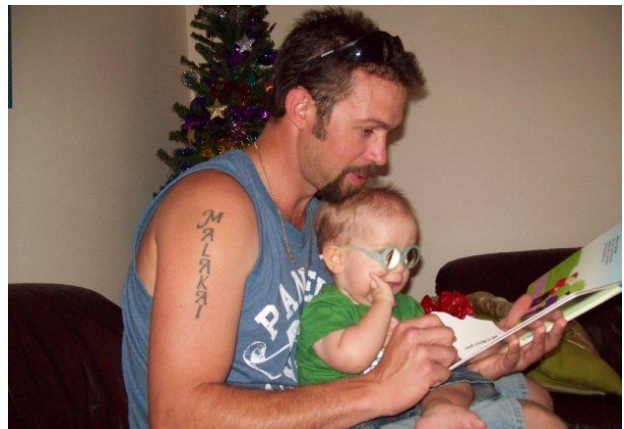
#### **E. THE LSA AND RESEARCH**

Good medical research is a partnership between scientists, physicians and affected families. Cooperation and sharing of ideas has led to rapid advances in understanding the cause of Lowe syndrome and may lead to more effective therapies. By providing funds for medical and scientific research, the LSA helps to encourage innovative thinking and interest in a rare condition that otherwise might go unnoticed.

Another way the LSA supports research is by encouraging its parent members to register with the Brain and Tissue Bank (BTB) for Developmental Disorders at the University of Maryland. The BTB collects relevant tissues after surgery or after death and stores them for future research purposes. Supported by the National Institute of Child Health and Human Development, the BTB is dedicated to the 'improved understanding, care and treatment of developmental disorders.' LSA families are encouraged to consider registering with the program. For more information contact the LSA, or contact the Brain and Tissue Bank listed below.

NICHD Brain & Tissue Bank for Developmental Disorders  
University of Maryland, Department of Pediatrics  
655 W. Baltimore St., BRB 13-013  
Baltimore, MD 21201-1559  
Phone: 1-800-847-1539 or 410-706-1755  
Website: [www.btbankfamily.org](http://www.btbankfamily.org)

One research project tends to lead to another as knowledge increases and new areas for investigation are developed. Although there have been dramatic advances in the understanding of Lowe syndrome since it was first recognized, there is much that remains a mystery. With advances in medical and scientific technology and with the strong support of the LSA, the future will undoubtedly see researchers finding more answers to the many profound and baffling questions that remain. For a complete list of research grants funded by the Lowe Syndrome Association since 1988, visit our website at [www.lowesyndrome.org](http://www.lowesyndrome.org).





## VI. DEVELOPMENT AND EDUCATION

Individuals with Lowe syndrome are unique and not all alike. The presence and severity of symptoms varies from child to child, even in the same family. As a result, the age of achieving major developmental milestones varies. However, some general statements can be made about the development and educational needs of individuals with Lowe syndrome based on the observations of families in the Lowe Syndrome Association (LSA) as well as on recent research findings.



Because of their physical and developmental disabilities, individuals with Lowe syndrome are usually significantly delayed in most areas of development. While development generally follows the normal sequence, the level of development in one area (language, for instance) may be more advanced than in another (gross motor skills, for instance). Various therapies and educational programs can help affected individuals develop to their maximum potential.

In general, children with Lowe syndrome, even those with behavior problems, are known to have ‘bubbling’ personalities. They are loving and sociable and have a wonderful sense of humor. Many have a special feel for music. When healthy and in a stimulating environment, they are often happy and alert. With help, they can grow and develop into functioning members of their families and communities and can be enjoyed and appreciated for their unique personalities and accomplishments.



**A. DEVELOPMENTAL/BEHAVIOR ACTIVITIES.** This section contains data from the *Report on the Lowe Syndrome Comprehensive Survey - 2008*. All the tables in this section are a reflection of information reported in the survey and are based on an individual’s development when the survey was taken. The table below lists Behavior Activities that individuals with Lowe syndrome engaged in at the time of the survey.

| Behavior Activities<br>(Based on responses from 137 survey participants) | Number of individuals Engaging in Activity | Percent of individuals Engaging in Activity | Number of individuals reporting this as their Favorite Activity | Percent of individuals reporting this as their Favorite Activity |
|--------------------------------------------------------------------------|--------------------------------------------|---------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|
|                                                                          | Engages in Activity                        |                                             | Favorite Activity                                               |                                                                  |
| Computer games and activities                                            | 63                                         | 46%                                         | 34                                                              | 25%                                                              |
| Conversation with another peer                                           | 51                                         | 37%                                         | 8                                                               | 6%                                                               |
| Conversation with an adult                                               | 73                                         | 53%                                         | 32                                                              | 23%                                                              |
| Conversation with a sibling                                              | 56                                         | 41%                                         | 17                                                              | 12%                                                              |

|                                                                                                         |     |            |    |            |
|---------------------------------------------------------------------------------------------------------|-----|------------|----|------------|
| <b>Taking pictures with a camera</b>                                                                    | 31  | <b>23%</b> | 14 | <b>10%</b> |
| <b>Writing in a journal</b>                                                                             | 20  | <b>15%</b> | 3  | <b>2%</b>  |
| <b>Going for walks</b>                                                                                  | 75  | <b>55%</b> | 42 | <b>31%</b> |
| <b>Enjoys going to the store to shop</b>                                                                | 78  | <b>57%</b> | 43 | <b>31%</b> |
| <b>Having books read to them</b>                                                                        | 66  | <b>49%</b> | 30 | <b>22%</b> |
| <b>Listening to tapes or records</b>                                                                    | 84  | <b>61%</b> | 61 | <b>45%</b> |
| <b>Looking at or reading books</b>                                                                      | 68  | <b>50%</b> | 31 | <b>23%</b> |
| <b>Playing arcade games</b>                                                                             | 16  | <b>12%</b> | 7  | <b>5%</b>  |
| <b>Playing musical instruments</b>                                                                      | 46  | <b>34%</b> | 20 | <b>15%</b> |
| <b>Playing sports activities alone<br/>(skateboarding, roller skating,<br/>jogging, billiards)</b>      | 13  | <b>9%</b>  | 4  | <b>3%</b>  |
| <b>Playing team sports (baseball,<br/>basketball, soccer)</b>                                           | 18  | <b>13%</b> | 5  | <b>4%</b>  |
| <b>Playing video games by self</b>                                                                      | 24  | <b>18%</b> | 16 | <b>12%</b> |
| <b>Playing video games with others</b>                                                                  | 24  | <b>18%</b> | 14 | <b>10%</b> |
| <b>Playing with action figures</b>                                                                      | 7   | <b>5%</b>  | 2  | <b>1%</b>  |
| <b>Playing with cars, planes, etc.</b>                                                                  | 40  | <b>29%</b> | 25 | <b>18%</b> |
| <b>Playing with dolls</b>                                                                               | 11  | <b>8%</b>  | 4  | <b>3%</b>  |
| <b>Playing with an imaginary friend</b>                                                                 | 5   | <b>4%</b>  | 1  | <b>1%</b>  |
| <b>Playing with stuffed animals</b>                                                                     | 32  | <b>23%</b> | 6  | <b>4%</b>  |
| <b>Playing with toys that have bright<br/>lights</b>                                                    | 73  | <b>53%</b> | 48 | <b>35%</b> |
| <b>Playing with toys that make<br/>sounds/noises, (i.e. Animal noises,<br/>automobile noises, etc.)</b> | 82  | <b>60%</b> | 47 | <b>34%</b> |
| <b>Playing with toys that talk</b>                                                                      | 64  | <b>47%</b> | 31 | <b>23%</b> |
| <b>Playing with toys that vibrate or<br/>stimulate</b>                                                  | 65  | <b>47%</b> | 22 | <b>16%</b> |
| <b>Plays board games by self, (i.e.<br/>Checkers, dominos, scrabble,<br/>chutes and ladder, etc.)</b>   | 5   | <b>4%</b>  | 1  | <b>1%</b>  |
| <b>Plays board games with others</b>                                                                    | 29  | <b>21%</b> | 10 | <b>7%</b>  |
| <b>Rides a bike, two wheels, three<br/>wheels</b>                                                       | 34  | <b>25%</b> | 13 | <b>9%</b>  |
| <b>Riding in a car</b>                                                                                  | 100 | <b>73%</b> | 54 | <b>39%</b> |
| <b>Singing</b>                                                                                          | 69  | <b>50%</b> | 42 | <b>31%</b> |
| <b>Watching DVDs</b>                                                                                    | 85  | <b>62%</b> | 65 | <b>47%</b> |
| <b>Watching television</b>                                                                              | 96  | <b>70%</b> | 66 | <b>48%</b> |
| <b>Water play/swimming</b>                                                                              | 88  | <b>64%</b> | 65 | <b>47%</b> |
| <b>Works on puzzles alone</b>                                                                           | 23  | <b>17%</b> | 4  | <b>3%</b>  |
| <b>Works on puzzles with others</b>                                                                     | 35  | <b>26%</b> | 3  | <b>2%</b>  |

## B. SCHOOL SETTINGS AND ACADEMICS



There are many different school settings for individuals with disabilities. School settings differ from town to town, state to state and country to country. It is the parent's role, along with the school district, to determine the most appropriate school environment for the child. In the United States children with disabilities have an Individualized Educational Plan (IEP) developed by school personnel and parents, to determine the most appropriate setting for the child. In the United States, an Education Plan for a child under the age of 3 years is frequently termed an Individualized Family Service Plan (IFSP). This type of plan enables families to receive services for their child who does not yet qualify for school age services and is often offered through Early Intervention. It is developed by parents and early intervention service providers. The table below reflects data from the ***Report on the Comprehensive Survey on Lowe Syndrome – 2008*** and shows the different types of preschool settings/programs children with Lowe syndrome have attended.

| Preschool Setting | TOTAL NUMBER IN PRESCHOOL SETTING (Based on 125 Responses) | Number of individuals reporting preschool setting 125 | Percent of individuals reporting preschool setting 91% |
|-------------------|------------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------|
|                   | Teacher who comes to the home                              | 26                                                    | 21%                                                    |
|                   | Therapist who comes to the home                            | 85                                                    | 68%                                                    |
|                   | Private pre-school for children with disabilities          | 22                                                    | 18%                                                    |
|                   | Private pre-school for children without disabilities       | 14                                                    | 11%                                                    |
|                   | Public pre-school for children with disabilities           | 67                                                    | 54%                                                    |
|                   | Public pre-school for children without disabilities        | 30                                                    | 22%                                                    |
|                   | Montessori pre-school                                      | 1                                                     | 1%                                                     |
|                   | Home schooled                                              | 5                                                     | 4%                                                     |
|                   | Day visits to a vision center                              | 1                                                     | 1%                                                     |
|                   | Daycare for all children                                   | 1                                                     | 1%                                                     |
|                   | Play group                                                 | 1                                                     | 1%                                                     |

For individuals with disabilities, an Individualized Education Plan can work in many ways to assist the individual in the home or school setting. An IEP can determine what type of services, such as physical therapy, occupational therapy, speech therapy and/or vision therapy may be needed to promote the skills necessary to grow and develop. It can also be beneficial in determining the level of academic support needed for accessing the school curriculum. For example, will your child need a large or small group setting for learning? Will your child need additional reading or math support in the classroom setting or in a setting that is separate from the

classroom? Access to specialized services varies from state to state and town to town in the United States and in countries outside the United States. It is important to work in partnership with your school staff, therapists and doctors to determine the most appropriate, learning environment for each child and the level of services needed to get the most appropriate education. Even though school placement varies from one child to another, an academic plan must be developed to encourage learning in all children with disabilities. As reported in the ***Report on the Lowe Syndrome Comprehensive Survey – 2008***, a majority of individuals with Lowe syndrome have been able to learn basic academic skills, such as learning how to count and learning number recognition, identifying colors, and learning to read and write. The following table further outlines the number of individuals performing the activities, at the time of the survey.

| <b>ACADEMIC</b>                  | <b>QESITON (Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was preformed</b> |
|----------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
|                                  | <b>Recognizes and identifies letters of alphabet</b>                                | <b>73</b>                                        | <b>53%</b>                                        | <b>6 years 3 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 15 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Counts five or more objects</b>                                                  | <b>74</b>                                        | <b>54%</b>                                        | <b>5 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 2 years 2 months to 20 years                                                        |                                                  |                                                   |                                        |
|                                  | <b>Reads a paragraph in a book</b>                                                  | <b>38</b>                                        | <b>28%</b>                                        | <b>8 years 7 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 16 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Identifies numbers up to 10</b>                                                  | <b>72</b>                                        | <b>53%</b>                                        | <b>6 years 6 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 15 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Writes numbers up to 10</b>                                                      | <b>41</b>                                        | <b>30%</b>                                        | <b>7 years 1 month</b>                 |
| <i>Age Skill First Performed</i> | 3 years to 14 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Identifies numbers up to 100</b>                                                 | <b>39</b>                                        | <b>28%</b>                                        | <b>7 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 4 years to 15 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Writes numbers up to 100</b>                                                     | <b>25</b>                                        | <b>18%</b>                                        | <b>8 years 1 months</b>                |
| <i>Age Skill First Performed</i> | 6 years to 16 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Performs simple addition and subtraction</b>                                     | <b>35</b>                                        | <b>26%</b>                                        | <b>9 years</b>                         |
| <i>Age Skill First Performed</i> | 4 years to 15 years                                                                 |                                                  |                                                   |                                        |

|                                  |                                                        |           |             |                           |
|----------------------------------|--------------------------------------------------------|-----------|-------------|---------------------------|
|                                  | <b>Performs multiplication</b>                         | <b>4</b>  | <b>3%</b>   | <b>8 years 9 months</b>   |
| <i>Age Skill First Performed</i> | 7 years to 11 years                                    |           |             |                           |
|                                  | <b>Performs division</b>                               | <b>7</b>  | <b>5%</b>   | <b>10 years</b>           |
| <i>Age Skill First Performed</i> | 8 years to 12 years                                    |           |             |                           |
|                                  | <b>Identifies currency</b>                             | <b>35</b> | <b>26%</b>  | <b>11 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 7 years to 34 years                                    |           |             |                           |
|                                  | <b>Correctly counts out the currency for an item</b>   | <b>8</b>  | <b>6%</b>   | <b>11 years 11 months</b> |
| <i>Age Skill First Performed</i> | 8 years to 20 years                                    |           |             |                           |
|                                  | <b>Identifies fractions</b>                            | <b>4</b>  | <b>3%</b>   | <b>9 years 9 months</b>   |
| <i>Age Skill First Performed</i> | 8 years to 13 years                                    |           |             |                           |
|                                  | <b>Tells time</b>                                      | <b>32</b> | <b>23%</b>  | <b>10 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 5 years to 16 years                                    |           |             |                           |
|                                  | <b>Tells time and understands the concept</b>          | <b>20</b> | <b>15%</b>  | <b>11 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 5 years to 18 years                                    |           |             |                           |
|                                  | <b>Writes full alphabet</b>                            | <b>36</b> | <b>26 %</b> | <b>7 years 10 months</b>  |
| <i>Age Skill First Performed</i> | 5 years to 16 years                                    |           |             |                           |
|                                  | <b>Identifies paper currency</b>                       | <b>20</b> | <b>15%</b>  | <b>10 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 6 years to 18 years                                    |           |             |                           |
|                                  | <b>Correctly counts out paper currency for an item</b> | <b>8</b>  | <b>6%</b>   | <b>11 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 9 years to 18 years                                    |           |             |                           |
|                                  | <b>Identifies double digit fraction numbers</b>        | <b>3</b>  | <b>2%</b>   | <b>10 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 9 years to 13 years                                    |           |             |                           |

## C. INFANCY AND THE EARLY YEARS

**1. Early Intervention.** Research has proven that early intervention with children with disabilities and their families is both crucial and effective. If support and services are provided as early as the need is apparent, a child's development will progress more quickly than if left unattended until they are of school age.

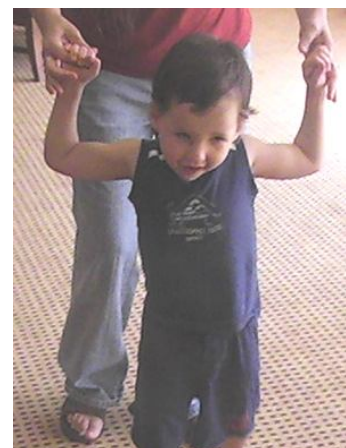


In recognition of the effectiveness and critical importance of early intervention, the United States Congress passed a law in 1986 which extends the rights previously given to school age children (age 5 or 6 years) with disabilities to children with disabilities from ages three through five. This law also assists states in developing early intervention programs for children from birth through age two who need special services.

Parents play an important role in their child's development and education and should learn all they can about programs that can help their child develop. Parents may contact their local school system or state department of education for information on programs and rules in their state.

**2. Physical Development.** Infants with Lowe syndrome benefit greatly from physical therapy. Some families contract for physical therapy service on a private basis. Others benefit from infant intervention programs provided by local communities. Professional therapists can often train parents to carry out a therapy program in the home. In the early years goals may include holding the head up in a prone position, rolling over, sitting alone, and scooting or crawling. As in most areas, progress is usually slow. However, most affected individuals will achieve these goals between a few months and five years of age.

**3. Walking.** Generally, physical therapy continues during these years, with an emphasis on walking and other gross motor skills. Learning to walk is usually mildly to significantly delayed. Prior to age 2 years old, some children with Lowe syndrome develop the ability to walk alone. By the age of 4 years old, more than half have learned to walk alone. By the age of 11 years, a majority of individuals with Lowe syndrome have developed the ability to walk. During the period from 11 months to 11 years of age, individuals with Lowe syndrome learn to walk alone, with most having developed the skill by the age of seven. Other significant achievements in motor skills have been reported in children with Lowe syndrome. The table below is based on data reported in the ***Report on the Comprehensive Lowe Syndrome Survey – 2008***. These milestones were achieved at various age ranges and are reported as *Age Skill First Performed*, underneath each skill. The data is based on 137 individuals who reported performing the activity at the time of the survey. A few of the other motor skills listed in the Motor Skills Table, include rolling over, crawling, sitting unsupported and riding a tricycle.



| <b>MOTOR SKILLS</b>              | <b>QESITON (Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was preformed</b> |
|----------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
|                                  | <b>Grasps objects</b>                                                               | <b>132</b>                                       | <b>96%</b>                                        | <b>1 year 4 months</b>                 |
| <i>Age Skill First Performed</i> | Birth to 7 years                                                                    |                                                  |                                                   |                                        |
|                                  | <b>Rolls over from stomach to back</b>                                              | <b>131</b>                                       | <b>96%</b>                                        | <b>1 year 1 month</b>                  |
| <i>Age Skill First Performed</i> | 1 month to 5 years                                                                  |                                                  |                                                   |                                        |
|                                  | <b>Sits alone, unsupported, for extended period (over 1 minute)</b>                 | <b>124</b>                                       | <b>91%</b>                                        | <b>1 year 7 months</b>                 |
| <i>Age Skill First Performed</i> | 5 months to 10 years                                                                |                                                  |                                                   |                                        |
|                                  | <b>Picks up objects with a pincer grasp</b>                                         | <b>112</b>                                       | <b>82%</b>                                        | <b>2 years</b>                         |
| <i>Age Skill First Performed</i> | 1 month to 10 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Transfers objects from one hand to the other</b>                                 | <b>122</b>                                       | <b>89%</b>                                        | <b>1 year 8 months</b>                 |
| <i>Age Skill First Performed</i> | 3 months to 8 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Crawls</b>                                                                       | <b>105</b>                                       | <b>77%</b>                                        | <b>1 year 10 months</b>                |
| <i>Age Skill First Performed</i> | 6 months to 6 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Builds a tower of 6 cubes</b>                                                    | <b>69</b>                                        | <b>50%</b>                                        | <b>3 years 5 months</b>                |
| <i>Age Skill First Performed</i> | 1 year 6 months to 15 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Walks alone</b>                                                                  | <b>100</b>                                       | <b>73%</b>                                        | <b>3 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 11 months to 11 years                                                               |                                                  |                                                   |                                        |
|                                  | <b>Skips on both feet and hops</b>                                                  | <b>39</b>                                        | <b>29%</b>                                        | <b>6 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 4 years to 12 years                                                                 |                                                  |                                                   |                                        |
|                                  | <b>Runs (although maybe stiffly)</b>                                                | <b>75</b>                                        | <b>55%</b>                                        | <b>1 year 2 month</b>                  |
| <i>Age Skill First Performed</i> | 1 year to 10 years                                                                  |                                                  |                                                   |                                        |
|                                  | <b>Walks up stairs without hand being held</b>                                      | <b>68</b>                                        | <b>50%</b>                                        | <b>6 years 2 months</b>                |

|                                  |                                                         |           |            |                         |
|----------------------------------|---------------------------------------------------------|-----------|------------|-------------------------|
| <i>Age Skill First Performed</i> | 1 year, 10 months to 16 years                           |           |            |                         |
|                                  | <b>Rides tricycle</b>                                   | <b>54</b> | <b>39%</b> | <b>5 years 6 months</b> |
| <i>Age Skill First Performed</i> | 1 year to 14 years                                      |           |            |                         |
|                                  | <b>Throws ball overhand</b>                             | <b>74</b> | <b>54%</b> | <b>5 years 7 months</b> |
| <i>Age Skill First Performed</i> | 1 year to 14 years                                      |           |            |                         |
|                                  | <b>Catches a medium sized bounced ball</b>              | <b>64</b> | <b>47%</b> | <b>6 years 3 months</b> |
| <i>Age Skill First Performed</i> | 2 years, 5 months to 16 years                           |           |            |                         |
|                                  | <b>Knows right from left and number of fingers</b>      | <b>58</b> | <b>42%</b> | <b>8 years 1 months</b> |
| <i>Age Skill First Performed</i> | 3 years to 25 years                                     |           |            |                         |
|                                  | <b>Writes letters and/or numbers, i.e. not scribble</b> | <b>46</b> | <b>34%</b> | <b>7 years 2 months</b> |
| <i>Age Skill First Performed</i> | 3 years to 14 years                                     |           |            |                         |

**4. Speech and Language Development.** Delayed speech and language development, with speech being the ability to produce sound and language as the understanding and expression of thoughts and feelings in oral form, is particularly frustrating for many parents during these years. Several factors contribute to delayed speech and language, including physical characteristics such as low muscle tone, vision impairment, high palate, and frequent illnesses; delays in intellectual development that affect the understanding of word meanings, ability to process and organize information, and ability to use the information to communicate meaningfully. Environmental factors such as limited play and learning opportunities, minimal social activities, and limited ability to move independently around the environment also play a role.



Despite significant language delays, most individuals with Lowe syndrome eventually learn to talk. By the age of two years, half of the affected children can imitate simple words. By age four, almost all can talk to some extent, and most can combine two words into a phrase. Many, in fact, eventually develop into very talkative individuals. The table below is based

on data reported in the ***Report on the Comprehensive Lowe Syndrome Survey – 2008***.

Language skills were achieved at various age ranges and are reported as *Age Skill First Performed*, underneath each skill. The data is based on 137 individuals who reported performing the activity at the time of the survey.

| <b>LANGUAGE</b>                  | <b>QUESITON (Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was first preformed</b> |
|----------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------------|
|                                  | <b>Turns head toward a sound source</b>                                              | <b>131</b>                                       | <b>96%</b>                                        | <b>7 months</b>                              |
| <i>Age Skill First Performed</i> | Birth to 7 years                                                                     |                                                  |                                                   |                                              |
|                                  | <b>Vocalizes pleasure and displeasure sounds</b>                                     | <b>132</b>                                       | <b>96%</b>                                        | <b>10 months</b>                             |
| <i>Age Skill First Performed</i> | Birth to 10 years                                                                    |                                                  |                                                   |                                              |
|                                  | <b>Watches your face when you speak</b>                                              | <b>107</b>                                       | <b>78%</b>                                        | <b>1 year</b>                                |
| <i>Age Skill First Performed</i> | Birth to 12 years                                                                    |                                                  |                                                   |                                              |
|                                  | <b>Makes noise when talked to</b>                                                    | <b>97</b>                                        | <b>71%</b>                                        | <b>8 months</b>                              |
| <i>Age Skill First Performed</i> | Birth to 5 years                                                                     |                                                  |                                                   |                                              |
|                                  | <b>Turns head from side to side with sound at the level of the ear</b>               | <b>110</b>                                       | <b>80%</b>                                        | <b>7 months</b>                              |
| <i>Age Skill First Performed</i> | Birth to 6 years                                                                     |                                                  |                                                   |                                              |
|                                  | <b>Makes expressive noises, e.g. cooing in the presence of others</b>                | <b>113</b>                                       | <b>82%</b>                                        | <b>9 months</b>                              |
| <i>Age Skill First Performed</i> | Birth to 5 years                                                                     |                                                  |                                                   |                                              |
|                                  | <b>Says single syllables, e.g. ba, ka, ma</b>                                        | <b>113</b>                                       | <b>82%</b>                                        | <b>1 year 7 months</b>                       |
| <i>Age Skill First Performed</i> | 4 months to 10 years                                                                 |                                                  |                                                   |                                              |
|                                  | <b>Uses mama, or dada, with meaning</b>                                              | <b>113</b>                                       | <b>82%</b>                                        | <b>2 years 2 months</b>                      |
| <i>Age Skill First Performed</i> | 6 months to 16 years                                                                 |                                                  |                                                   |                                              |
|                                  | <b>Babbles 2 or 3 words repeatedly</b>                                               | <b>90</b>                                        | <b>66%</b>                                        | <b>2 years 4 months</b>                      |
| <i>Age Skill First Performed</i> | 4 months to 12 years                                                                 |                                                  |                                                   |                                              |
|                                  | <b>Combines two words in a phrase</b>                                                | <b>88</b>                                        | <b>64%</b>                                        | <b>3 years 2 months</b>                      |
| <i>Age Skill First Performed</i> | 10 months to 13 years                                                                |                                                  |                                                   |                                              |
|                                  | <b>Understands no-no</b>                                                             | <b>119</b>                                       | <b>87%</b>                                        | <b>2 years 2 months</b>                      |

|                                  |                                                               |            |            |                          |
|----------------------------------|---------------------------------------------------------------|------------|------------|--------------------------|
| <i>Age Skill First Performed</i> | 4 months to 15 years                                          |            |            |                          |
|                                  | <b>Tries to communicate by actions or gestures</b>            | <b>109</b> | <b>80%</b> | <b>2 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 1 month to 11 years                                           |            |            |                          |
|                                  | <b>Tries to repeat your sound</b>                             | <b>104</b> | <b>76%</b> | <b>2 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 4 months to 18 years                                          |            |            |                          |
|                                  | <b>Attends to a book or toy for about two minutes</b>         | <b>114</b> | <b>83%</b> | <b>2 years 3 months</b>  |
| <i>Age Skill First Performed</i> | 3 months to 18 years                                          |            |            |                          |
|                                  | <b>Follows simple directions accompanied by gestures</b>      | <b>102</b> | <b>74%</b> | <b>3 years 1 month</b>   |
| <i>Age Skill First Performed</i> | 6 months to 13 years                                          |            |            |                          |
|                                  | <b>Answers simple questions nonverbally</b>                   | <b>87</b>  | <b>63%</b> | <b>2 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 5 months to 10 years                                          |            |            |                          |
|                                  | <b>Points to objects, pictures, and family members</b>        | <b>93</b>  | <b>68%</b> | <b>2 years 10 months</b> |
| <i>Age Skill First Performed</i> | 6 months to 16 years                                          |            |            |                          |
|                                  | <b>Having someone read a story to them</b>                    | <b>102</b> | <b>74%</b> | <b>2 years</b>           |
| <i>Age Skill First Performed</i> | Birth to 12 years                                             |            |            |                          |
|                                  | <b>Tries to imitate simple words</b>                          | <b>97</b>  | <b>70%</b> | <b>2 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 3 months to 16 years                                          |            |            |                          |
|                                  | <b>Points to simple body parts such as nose</b>               | <b>106</b> | <b>77%</b> | <b>2 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 5 months to 9 years                                           |            |            |                          |
|                                  | <b>Identifies colors</b>                                      | <b>93</b>  | <b>68%</b> | <b>4 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 20 years                                           |            |            |                          |
|                                  | <b>Understands simple verbs such as eat, sit, sleep, etc.</b> | <b>116</b> | <b>85%</b> | <b>3 years 1 month</b>   |
| <i>Age Skill First Performed</i> | 3 months to 10 years                                          |            |            |                          |

|                                  |                                                                                                 |           |            |                          |
|----------------------------------|-------------------------------------------------------------------------------------------------|-----------|------------|--------------------------|
|                                  | <b>Correctly pronounces most vowels and n, m, p, h, especially in beginning syllables/words</b> | <b>73</b> | <b>53%</b> | <b>4 years 7 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 3 months to 15 years                                                                     |           |            |                          |
|                                  | <b>Says 8 to 10 words</b>                                                                       | <b>83</b> | <b>61%</b> | <b>3 years 7 months</b>  |
| <i>Age Skill First Performed</i> | Birth to 10 years                                                                               |           |            |                          |
|                                  | <b>Asks for common foods by name</b>                                                            | <b>80</b> | <b>58%</b> | <b>4 years 3 months</b>  |
| <i>Age Skill First Performed</i> | 1 year to 15 years                                                                              |           |            |                          |
|                                  | <b>Makes animal sounds, such as moo</b>                                                         | <b>96</b> | <b>70%</b> | <b>3 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 6 months to 21 years                                                                            |           |            |                          |
|                                  | <b>Combines words, such as more milk</b>                                                        | <b>79</b> | <b>58%</b> | <b>3 years 10 months</b> |
| <i>Age Skill First Performed</i> | 1 year to 10 years                                                                              |           |            |                          |
|                                  | <b>Uses pronouns, such as mine</b>                                                              | <b>70</b> | <b>51%</b> | <b>3 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 1 year to 10 years                                                                              |           |            |                          |
|                                  | <b>Says around 40 words</b>                                                                     | <b>71</b> | <b>52%</b> | <b>5 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 1 year to 15 years                                                                              |           |            |                          |
|                                  | <b>Knows about 50 words</b>                                                                     | <b>77</b> | <b>56%</b> | <b>5 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 2 months to 16 years                                                                     |           |            |                          |
|                                  | <b>Knows concepts such as in, on</b>                                                            | <b>82</b> | <b>60%</b> | <b>4 years 9 months</b>  |
| <i>Age Skill First Performed</i> | 7 months to 13 years                                                                            |           |            |                          |
|                                  | <b>Knows pronouns such as you, me, her, him, etc.</b>                                           | <b>70</b> | <b>51%</b> | <b>5 years</b>           |
| <i>Age Skill First Performed</i> | 1 year 4 months to 18 years                                                                     |           |            |                          |
|                                  | <b>Knows descriptive words such as big, happy</b>                                               | <b>82</b> | <b>60%</b> | <b>4 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 9 months to 14 years                                                                            |           |            |                          |

|                                  |                                                                                                                      |           |            |                          |
|----------------------------------|----------------------------------------------------------------------------------------------------------------------|-----------|------------|--------------------------|
|                                  | <b>Uses question inflection to ask for something (e.g., My ball?)</b>                                                | <b>68</b> | <b>49%</b> | <b>4 years 9 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 4 months to 18 years                                                                                          |           |            |                          |
|                                  | <b>Uses plurals such as shoes or socks and regular past tense verbs such as jumped</b>                               | <b>60</b> | <b>44%</b> | <b>5 years 10 months</b> |
| <i>Age Skill First Performed</i> | 2 years to 20 years                                                                                                  |           |            |                          |
|                                  | <b>Groups objects such as foods, clothes, etc</b>                                                                    | <b>65</b> | <b>47%</b> | <b>6 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 3 years to 23 years                                                                                                  |           |            |                          |
|                                  | <b>Uses most speech sounds but may distort some of the more difficult sounds such as l, r, s, sh, ch, y, v, z th</b> | <b>68</b> | <b>50%</b> | <b>6 years</b>           |
| <i>Age Skill First Performed</i> | 1 year 4 months to 18 years                                                                                          |           |            |                          |
|                                  | <b>Describes the use of objects such as fork, car, etc.</b>                                                          | <b>67</b> | <b>49%</b> | <b>5 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 18 years                                                                                                  |           |            |                          |
|                                  | <b>Enjoys poems and recognizes language absurdities such as, Is that an elephant on your head?</b>                   | <b>55</b> | <b>40%</b> | <b>5 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 21 years                                                                                                  |           |            |                          |
|                                  | <b>Expresses ideas and feelings rather than just talking about the world around him or her</b>                       | <b>55</b> | <b>40%</b> | <b>6 years 7 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 19 years                                                                                                  |           |            |                          |
|                                  | <b>Repeats sentences</b>                                                                                             | <b>60</b> | <b>44%</b> | <b>5 years 7 months</b>  |
| <i>Age Skill First Performed</i> | 1 year to 19 years                                                                                                   |           |            |                          |
|                                  | <b>Understands spatial concepts such as behind, under, etc.</b>                                                      | <b>73</b> | <b>53%</b> | <b>6 years</b>           |
| <i>Age Skill First Performed</i> | 2 years to 20 years                                                                                                  |           |            |                          |
|                                  | <b>Uses some irregular past tense verbs such as ran, fell</b>                                                        | <b>48</b> | <b>35%</b> | <b>6 years</b>           |
| <i>Age Skill First Performed</i> | Birth to 20 years                                                                                                    |           |            |                          |

|                                  |                                                                              |           |             |                          |
|----------------------------------|------------------------------------------------------------------------------|-----------|-------------|--------------------------|
|                                  | <b>Describes how to do things such as painting a picture</b>                 | <b>43</b> | <b>31%</b>  | <b>6 years 9 months</b>  |
| <i>Age Skill First Performed</i> | 3 years to 34 years                                                          |           |             |                          |
|                                  | <b>Lists items that belong in a category such as animals, etc</b>            | <b>57</b> | <b>42%</b>  | <b>6 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 4 years to 18 years                                                          |           |             |                          |
|                                  | <b>Answers “why” questions</b>                                               | <b>56</b> | <b>41%</b>  | <b>7 years 7 months</b>  |
| <i>Age Skill First Performed</i> | 8 months to 34 years                                                         |           |             |                          |
|                                  | <b>Asks “what” questions</b>                                                 | <b>63</b> | <b>46%</b>  | <b>7 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 4 month to 34 years                                                   |           |             |                          |
|                                  | <b>Asks “who” questions</b>                                                  | <b>64</b> | <b>47%</b>  | <b>7 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 4 months to 34 years                                                  |           |             |                          |
|                                  | <b>Asks “where” questions</b>                                                | <b>59</b> | <b>43%</b>  | <b>7 years 3 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 4 months to 34 years                                                  |           |             |                          |
|                                  | <b>Asks “when” questions</b>                                                 | <b>57</b> | <b>41%</b>  | <b>7 years 3 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 34 years                                                          |           |             |                          |
|                                  | <b>Understands more than 2,000 words</b>                                     | <b>54</b> | <b>39 %</b> | <b>7 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 20 years                                                          |           |             |                          |
|                                  | <b>Understands time sequences (what happened first, second, third, etc.)</b> | <b>50</b> | <b>37%</b>  | <b>7 years 7 months</b>  |
| <i>Age Skill First Performed</i> | 3 years to 34 years                                                          |           |             |                          |
|                                  | <b>Engages in conversation, taking turns on the topic</b>                    | <b>54</b> | <b>39%</b>  | <b>7 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 2 years 5 months to 36 years                                                 |           |             |                          |
|                                  | <b>Uses sentences with 8 or more words in length</b>                         | <b>51</b> | <b>37%</b>  | <b>7 years 10 months</b> |
| <i>Age Skill First Performed</i> | 2 years to 38 years                                                          |           |             |                          |

|                                  |                                                                                  |           |             |                          |
|----------------------------------|----------------------------------------------------------------------------------|-----------|-------------|--------------------------|
|                                  | <b>Describes objects</b>                                                         | <b>53</b> | <b>39%</b>  | <b>6 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 18 years                                                              |           |             |                          |
|                                  | <b>Constantly asks questions</b>                                                 | <b>64</b> | <b>47%</b>  | <b>6 years 5 months</b>  |
| <i>Age Skill First Performed</i> | 3 years to 34 years                                                              |           |             |                          |
|                                  | <b>Associates names with objects</b>                                             | <b>71</b> | <b>52%</b>  | <b>4 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 9 months to 21 years                                                             |           |             |                          |
|                                  | <b>Uses some personal pronouns i.e., I, me, mine</b>                             | <b>68</b> | <b>50%</b>  | <b>6 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 8 months to 36 years                                                             |           |             |                          |
|                                  | <b>Has understanding of on, under, and behind</b>                                | <b>73</b> | <b>53%</b>  | <b>5 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 2 years to 18 years                                                              |           |             |                          |
|                                  | <b>Answers questions like “what do you do when you are cold, hungry, tired?”</b> | <b>59</b> | <b>43%</b>  | <b>7 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 2 years 3 months to 35 years                                                     |           |             |                          |
|                                  | <b>Follows two-step commands, e.g. sit-down, and close the door</b>              | <b>89</b> | <b>65%</b>  | <b>5 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 1 year 6 months to 18 years                                                      |           |             |                          |
|                                  | <b>Understands rhyming</b>                                                       | <b>43</b> | <b>31%</b>  | <b>5 years 11 months</b> |
| <i>Age Skill First Performed</i> | 2 years to 40 years                                                              |           |             |                          |
|                                  | <b>Uses imagination to create stories verbally</b>                               | <b>39</b> | <b>28%</b>  | <b>7 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 4 years to 40 years                                                              |           |             |                          |
|                                  | <b>Uses imagination to create stories on paper</b>                               | <b>19</b> | <b>14%</b>  | <b>5 years 11 months</b> |
| <i>Age Skill First Performed</i> | 4 years to 13 years                                                              |           |             |                          |
|                                  | <b>Carries out a series of three directions</b>                                  | <b>40</b> | <b>29 %</b> | <b>8 years 4 months</b>  |
| <i>Age Skill First Performed</i> | 2 years 6 months to 34 years                                                     |           |             |                          |

|                                      |                                                                   |           |            |                             |
|--------------------------------------|-------------------------------------------------------------------|-----------|------------|-----------------------------|
|                                      | <b>Uses verbs that end in ing,<br/>"such as walking, talking"</b> | <b>53</b> | <b>39%</b> | <b>6 years 9<br/>months</b> |
| <i>Age Skill First<br/>Performed</i> | 2 years to 40 years                                               |           |            |                             |
|                                      | <b>Says about 200 - 300 different<br/>words</b>                   | <b>58</b> | <b>42%</b> | <b>6 years 7<br/>months</b> |
| <i>Age Skill First<br/>Performed</i> | 1 year 4 months to 40 years                                       |           |            |                             |

**5. Eating Problems.** In some cases, the same factors that cause delayed speech may also contribute to eating problems. Poor muscle tone may result in reduced control of fine motor movement of the tongue, lips, and jaws that are necessary for sucking, swallowing, and chewing. As a result, some individuals have difficulty making the adjustments from baby food to table food. An oral-motor treatment plan may be developed as part of the child's therapy program. By the age of four years, the majority of children with Lowe syndrome are able to eat table food (see Eating Difficulties under Special Health Concerns, Section III). An oral motor specialist or nutritionist may be able to provide beneficial advice and exercises.



| <b>MEALTIME</b>                      | <b>(Based on 137 individuals<br/>between the ages of 10 months to<br/>56 years)</b> | <b>Number of<br/>individuals<br/>performing<br/>activity</b> | <b>Percent of<br/>individuals<br/>performing<br/>activity</b> | <b>Average<br/>Age Skill<br/>was<br/>preformed</b> |
|--------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------|---------------------------------------------------------------|----------------------------------------------------|
|                                      | <b>Eats using a nasogastric feeding<br/>tube (NG tube)</b>                          | <b>13</b>                                                    | <b>9%</b>                                                     | <b>2 years 3<br/>months</b>                        |
| <i>Age Skill First<br/>Performed</i> | Birth to 18 years                                                                   |                                                              |                                                               |                                                    |
|                                      | <b>Eats using a viapercutaneous<br/>endoscopic gastrostomy (PEG<br/>tube)</b>       | <b>10</b>                                                    | <b>7%</b>                                                     | <b>1 year 6<br/>months</b>                         |
| <i>Age Skill First<br/>Performed</i> | 4 months to 6 years                                                                 |                                                              |                                                               |                                                    |
|                                      | <b>Eats table food, i.e. not baby<br/>food</b>                                      | <b>106</b>                                                   | <b>77%</b>                                                    | <b>3 years 1<br/>month</b>                         |
| <i>Age Skill First<br/>Performed</i> | 6 months to 16 years                                                                |                                                              |                                                               |                                                    |
|                                      | <b>Eats finger foods</b>                                                            | <b>79</b>                                                    | <b>58%</b>                                                    | <b>2 years 11<br/>months</b>                       |
| <i>Age Skill First<br/>Performed</i> | 1 month to 15 years                                                                 |                                                              |                                                               |                                                    |
|                                      | <b>Eats using a spoon</b>                                                           | <b>106</b>                                                   | <b>77%</b>                                                    | <b>4 years 1<br/>month</b>                         |
| <i>Age Skill First<br/>Performed</i> | 3 months to 16 years                                                                |                                                              |                                                               |                                                    |

|                                  |                                                                                   |            |            |                           |
|----------------------------------|-----------------------------------------------------------------------------------|------------|------------|---------------------------|
|                                  | <b>Eats using a fork for piercing food</b>                                        | <b>70</b>  | <b>51%</b> | <b>5 years 10 months</b>  |
| <i>Age Skill First Performed</i> | 1 year to 34 years                                                                |            |            |                           |
|                                  | <b>Eats meals with family</b>                                                     | <b>103</b> | <b>75%</b> | <b>2 years 10 months</b>  |
| <i>Age Skill First Performed</i> | Birth to 23 years                                                                 |            |            |                           |
|                                  | <b>Eats complete meal using all utensils correctly</b>                            | <b>41</b>  | <b>30%</b> | <b>6 years 7 months</b>   |
| <i>Age Skill First Performed</i> | 2 years 6 months to 16 years                                                      |            |            |                           |
|                                  | <b>Prepares a meal with assistance</b>                                            | <b>24</b>  | <b>18%</b> | <b>12 years 2 months</b>  |
| <i>Age Skill First Performed</i> | 5 years to 21 years                                                               |            |            |                           |
|                                  | <b>Assists with preparing a meal</b>                                              | <b>35</b>  | <b>26%</b> | <b>10 years 10 months</b> |
| <i>Age Skill First Performed</i> | 3 years to 21 years                                                               |            |            |                           |
|                                  | <b>Prepares a meal without assistance, no cooking involved</b>                    | <b>12</b>  | <b>9%</b>  | <b>13 years 1 month</b>   |
| <i>Age Skill First Performed</i> | 6 years to 20 years                                                               |            |            |                           |
|                                  | <b>Prepares a meal without assistance</b>                                         | <b>6</b>   | <b>4%</b>  | <b>14 years 10 months</b> |
| <i>Age Skill First Performed</i> | 12 years to 20 years                                                              |            |            |                           |
|                                  | <b>Measures a liquid substance using a measuring cup and / or measuring spoon</b> | <b>16</b>  | <b>12%</b> | <b>15 years 8 months</b>  |
| <i>Age Skill First Performed</i> | 9 years to 34 years                                                               |            |            |                           |
|                                  | <b>Measures a dry substance using a measuring cup and / or measuring spoon</b>    | <b>16</b>  | <b>12%</b> | <b>15 years 6 months</b>  |
| <i>Age Skill First Performed</i> | 9 years to 34 years                                                               |            |            |                           |

**6. Toileting and Self-Help Skills.** Toilet training can be quite challenging for individuals with Lowe syndrome. Although many begin training in the earlier years (and a few succeed), the majority achieve this major milestone between ages of five and ten years, and older in some cases. The table listed below on Toileting is based on data from the ***Report on the Lowe Syndrome Comprehensive Survey – 2008***, indicating that the majority of individuals were able to indicate when their pants were wet by the age of 5 years. The need to use the toilet before wetting was achieved by the majority of individuals by the age of 6 years.

| <b>TOILETING</b>                 | <b>(Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was preformed</b> |
|----------------------------------|-----------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
|                                  | <b>Indicates when pants are wet</b>                                         | <b>88</b>                                        | <b>64%</b>                                        | <b>5 years 2 months</b>                |
| <i>Age Skill First Performed</i> | Birth to 20 years                                                           |                                                  |                                                   |                                        |
|                                  | <b>Indicates need to use toilet before wetting</b>                          | <b>85</b>                                        | <b>62%</b>                                        | <b>6 years 2 months</b>                |
| <i>Age Skill First Performed</i> | 1 year 6 months to 20 years                                                 |                                                  |                                                   |                                        |
|                                  | <b>Stays dry all day, but is wet at night</b>                               | <b>60</b>                                        | <b>44%</b>                                        | <b>6 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 1 year 6 months to 25 years                                                 |                                                  |                                                   |                                        |
|                                  | <b>Stays dry all night</b>                                                  | <b>54</b>                                        | <b>39%</b>                                        | <b>9 years</b>                         |
| <i>Age Skill First Performed</i> | 2 years to 27 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Wipes self and flushes after toileting without assistance</b>            | <b>37</b>                                        | <b>27%</b>                                        | <b>9 years 9 months</b>                |
| <i>Age Skill First Performed</i> | 4 years to 22 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Finds appropriate toilet facilities when in an unfamiliar setting</b>    | <b>31</b>                                        | <b>23%</b>                                        | <b>8 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 3 years to 20 years                                                         |                                                  |                                                   |                                        |

Other self-help skills such as dressing and grooming may also be delayed. Most of the individuals have great difficulty with fine motor skills such as tying shoelaces, buttoning buttons, and writing. For some children, self-help skills can be achieved with modification to clothing and footwear. Adaptive clothing to encourage independence and self-help skills might include: Velcro on shoes, jackets with Velcro or snaps, rather than zippers, elastic waist pants, pullover shirts, socks with no heels, and one piece snowsuits. These can make getting dressed less frustrating and allow more independence. In some cases, computers for writing may be useful in the school environment; Zoom text is one example of software that can be used in the school environment to enlarge materials for a student's use. Achievement of Dressing Skills varies from one individual to another. The data reflected below from the ***Report on the Lowe Syndrome Comprehensive Survey – 2008***, indicated that less than a third of the individuals were able to accomplish dressing skills at the time of the survey.

| <b>DRESSING</b>                  | <b>(Based on 137 individuals between the ages of 10 months to 56 years)</b> | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was preformed</b> |
|----------------------------------|-----------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
|                                  | <b>Dresses or undresses without assistance</b>                              | <b>45</b>                                        | <b>33%</b>                                        | <b>9 years 6 months</b>                |
| <i>Age Skill First Performed</i> | 4 years to 20 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Buttons without assistance</b>                                           | <b>14</b>                                        | <b>10%</b>                                        | <b>9 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 5 years to 18 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Zippers without assistance</b>                                           | <b>24</b>                                        | <b>18%</b>                                        | <b>8 years 3 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 15 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>“Velcros” without assistance</b>                                         | <b>41</b>                                        | <b>30%</b>                                        | <b>7 years 8 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 20 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Snaps without assistance</b>                                             | <b>20</b>                                        | <b>15%</b>                                        | <b>9 years 5 months</b>                |
| <i>Age Skill First Performed</i> | 4 years to 34 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Ties shoes without assistance</b>                                        | <b>4</b>                                         | <b>3%</b>                                         | <b>12 years 6 months</b>               |
| <i>Age Skill First Performed</i> | 6 years to 21 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Ties a bow without assistance</b>                                        | <b>3</b>                                         | <b>2%</b>                                         | <b>14 years 8 months</b>               |
| <i>Age Skill First Performed</i> | 7 years to 21 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Puts on socks without assistance</b>                                     | <b>43</b>                                        | <b>31%</b>                                        | <b>10 years 10 months</b>              |
| <i>Age Skill First Performed</i> | 4 years to 21 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Selects appropriate clothes, i.e. coat when cold out</b>                 | <b>35</b>                                        | <b>26%</b>                                        | <b>9 years 5 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 20 years                                                         |                                                  |                                                   |                                        |
|                                  | <b>Refines appearance, i.e. tucks shirt in</b>                              | <b>18</b>                                        | <b>13%</b>                                        | <b>10 years 5 months</b>               |
| <i>Age Skill First Performed</i> | 7 years to 20 years                                                         |                                                  |                                                   |                                        |

|                                  |                      |           |            |                          |
|----------------------------------|----------------------|-----------|------------|--------------------------|
|                                  | <b>Wears a watch</b> | <b>19</b> | <b>14%</b> | <b>12 years 3 months</b> |
| <i>Age Skill First Performed</i> | 8 years to 19 years  |           |            |                          |

|                                  | <b>(Based on 137 individuals between the ages of 10 months to 56 years</b>   | <b>Number of individuals performing activity</b> | <b>Percent of individuals performing activity</b> | <b>Average Age Skill was preformed</b> |
|----------------------------------|------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------|----------------------------------------|
| <b>GROOMING</b>                  |                                                                              |                                                  |                                                   |                                        |
|                                  | <b>Knows when they need to wash hands when soiled</b>                        | <b>64</b>                                        | <b>47%</b>                                        | <b>6 years 8 months</b>                |
| <i>Age Skill First Performed</i> | 2 years to 34 years                                                          |                                                  |                                                   |                                        |
|                                  | <b>Washes and dries hands and face (with assistance in regulating water)</b> | <b>65</b>                                        | <b>47%</b>                                        | <b>7 years 7 months</b>                |
| <i>Age Skill First Performed</i> | 2 years 3 months to 34 years                                                 |                                                  |                                                   |                                        |
|                                  | <b>Bathes self with help for hair, neck and back</b>                         | <b>50</b>                                        | <b>37%</b>                                        | <b>9 years 8 months</b>                |
| <i>Age Skill First Performed</i> | 2 years 5 months to 40 years                                                 |                                                  |                                                   |                                        |
|                                  | <b>Bathes without assistance</b>                                             | <b>20</b>                                        | <b>15%</b>                                        | <b>8 years 8 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 14 years                                                          |                                                  |                                                   |                                        |
|                                  | <b>Places toothpaste on the tooth brush without assistance</b>               | <b>31</b>                                        | <b>23%</b>                                        | <b>7 years 10 months</b>               |
| <i>Age Skill First Performed</i> | 3 years to 15 years                                                          |                                                  |                                                   |                                        |
|                                  | <b>Brushes teeth with assistance</b>                                         | <b>65</b>                                        | <b>47%</b>                                        | <b>7 years 6 months</b>                |
| <i>Age Skill First Performed</i> | 1 year to 40 years                                                           |                                                  |                                                   |                                        |
|                                  | <b>Brushes teeth completely without assistance</b>                           | <b>34</b>                                        | <b>25%</b>                                        | <b>8 years 5 months</b>                |
| <i>Age Skill First Performed</i> | 3 years to 16 years                                                          |                                                  |                                                   |                                        |
|                                  | <b>Cuts / files nails without assistance</b>                                 | <b>1</b>                                         | <b>1%</b>                                         | <b>unknown</b>                         |
| <i>Age Skill First Performed</i> | age range unknown                                                            |                                                  |                                                   |                                        |
|                                  | <b>Uses a hair dryer without assistance</b>                                  | <b>5</b>                                         | <b>4%</b>                                         | <b>9 years 4 months</b>                |

|                                  |                                                                                           |           |            |                          |
|----------------------------------|-------------------------------------------------------------------------------------------|-----------|------------|--------------------------|
| <i>Age Skill First Performed</i> | 6 years to 13 years                                                                       |           |            |                          |
|                                  | <b>Uses hair products, such as mousse, hair gel and / or hairspray without assistance</b> | <b>5</b>  | <b>4%</b>  | <b>10 years 4 months</b> |
| <i>Age Skill First Performed</i> | 9 years to 15 years                                                                       |           |            |                          |
|                                  | <b>Uses deodorant</b>                                                                     | <b>31</b> | <b>23%</b> | <b>13 years 8 months</b> |
| <i>Age Skill First Performed</i> | 6 years to 45 years                                                                       |           |            |                          |
|                                  | <b>Shaves without assistance</b>                                                          | <b>7</b>  | <b>5%</b>  | <b>20 years 1 month</b>  |
| <i>Age Skill First Performed</i> | 15 years to 24 years                                                                      |           |            |                          |

#### D. PRIMARY AND SECONDARY SCHOOL SETTING

For children with Lowe syndrome there have been many different types of educational settings reported. Individualized Education Plans and classroom settings vary from state to state and town to town and by country. It is important for parent's to know what services are available in the home state or country to provide the most appropriate education possible.

In 1975, the United States Congress passed the Education for All Handicapped Children's Act (Public Law 94-142). This law requires all states to provide a "free, appropriate public education" to school-age children with disabilities (See Paragraph on Adulthood for information on Guardianship).



| <b>School Setting</b> | <b>TOTAL NUMBER IN SCHOOL SETTING<br/>(Based on 114 OUT OF 137 RESPONDENTS)</b> | <b>Number of individuals reporting school setting<br/>114</b> | <b>Percent of individuals reporting school setting<br/>83%</b> |
|-----------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------|----------------------------------------------------------------|
|                       | Students with multiple disabilities                                             | 82                                                            | 72%                                                            |
|                       | Students with all disabilities                                                  | 67                                                            | 59%                                                            |
|                       | Students with physical disabilities                                             | 44                                                            | 39%                                                            |
|                       | Students with visual disabilities                                               | 36                                                            | 32%                                                            |
|                       | Students with behavioral issues                                                 | 22                                                            | 18%                                                            |
|                       | One on one separate class, can view other students                              | 1                                                             | 1%                                                             |

#### E. MIDDLE CHILDHOOD AND ADOLESCENCE.

Public school programming for individuals with disabilities depends upon several factors, including the child's individual needs and community resources. Some individuals are enrolled in



classes for students with multiple, physical or visual disabilities. While some individuals participate in regular classrooms with support, for other individuals, programming is geared toward self-help and pre-vocational skills. Just as the presence and severity of symptoms varies from child to child with Lowe syndrome, the educational plans also vary. The table below lists the many types of academic/school classroom settings that individuals with disabilities may be enrolled. The data in the table is based on the ***Report on the Lowe Syndrome Comprehensive***

**Survey – 2008.** Individuals with Lowe syndrome may participate in one, two or many different school settings through their school age years. Placement in a school setting may be dependent on the individual's cognitive, medical, emotional, physical and visual needs. As a parent, it is your role, along with the school district, to determine the most appropriate school environment for your child.

| <b><i>Academic/<br/>classroom<br/>school setting</i></b> | <b>TOTAL NUMBER IN ACADEMIC /<br/>SCHOOL SETTING (Based on 113 OUT OF<br/>137 RESPONDENTS)</b>               | <b>113</b> | <b>82%</b> |
|----------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|------------|------------|
|                                                          | Special education classroom                                                                                  | 87         | 77%        |
|                                                          | General education (regular / inclusion) classroom with services OT, PT, speech, etc. in a separate classroom | 49         | 43%        |
|                                                          | General education (regular / inclusion) classroom                                                            | 31         | 27%        |
|                                                          | (Sheltered) Workshop                                                                                         | 13         | 12%        |
|                                                          | Residential school                                                                                           | 10         | 9%         |
|                                                          | Trade School                                                                                                 | 1          | 1%         |
|                                                          | School for the Blind                                                                                         | 1          | 1%         |
|                                                          | Community / Junior College University                                                                        | 1          | 1%         |
|                                                          | Transition program/life skills                                                                               | 1          | 1%         |
|                                                          | Rehabilitation center                                                                                        | 1          | 1%         |

**F. ADULTHOOD.** In 1973, the United States Congress passed the Vocational Rehabilitation Act, Public Law 93-112. Section 504 of the Rehabilitation Act prohibits discrimination against people with disabilities and protects their rights relating to voting, education, accessibility, and employment. The fundamental purpose of this law is the development and implementation of a comprehensive and coordinated program of vocational rehabilitation and independent living.

Throughout life, most individuals with Lowe syndrome live at home with their families. A few families, however, have decided that placement in a residential setting is appropriate due to the complexities of medical management, educational needs, or severe behavior problems. As adults, some individuals have successfully made the move into a group home and a few live independently. Some work in sheltered workshops or participate in other special programs for adults with disabilities. Parents should consider establishing legal guardianship of their child when

they turn 18 years old. In the United States, it is appropriate for families to begin exploring guardianship options for their individual with disabilities. Generally, the process begins around the age of 17 years. Guardianship is a legal process that enables a person or agency to assist in the management of daily decisions for an individual with disabilities. There are a few different types of guardianship and each family should research what type of guardianship best suits their individuals' needs. Below is a list of different Work Settings in which individuals with Lowe syndrome have participated. The statistics are a reflection of the data reported in the ***Report on the Lowe Syndrome Comprehensive Survey – 2008***.

| Work Setting                                                          | TOTAL NUMBER IN ANY FORM OF WORK SETTING / ENVIRONMENT (19 OUT OF 137 RESPONDENTS) | Number of individuals reporting participation in a work setting 19 | Percent of individuals reporting participation in a work setting 14% |
|-----------------------------------------------------------------------|------------------------------------------------------------------------------------|--------------------------------------------------------------------|----------------------------------------------------------------------|
| <b>Percentages in this Section of Questions Based on 19 Responses</b> |                                                                                    |                                                                    |                                                                      |
|                                                                       | Unsupervised employment for pay                                                    | 2                                                                  | 11%                                                                  |
|                                                                       | Supervised employment for pay                                                      | 6                                                                  | 32%                                                                  |
|                                                                       | Sheltered workshop for individuals with disabilities for pay                       | 10                                                                 | 53%                                                                  |
|                                                                       | Sheltered workshop for individuals with disabilities without pay                   | 3                                                                  | 16%                                                                  |
|                                                                       | Volunteer without pay                                                              | 8                                                                  | 42%                                                                  |
|                                                                       | Education / School work program for pay                                            | 3                                                                  | 16%                                                                  |
|                                                                       | Education / School work program without pay                                        | 7                                                                  | 37%                                                                  |



## VII. B E H A V I O R

As mentioned previously (see Behavior Problems under Medical Features, Section III), some individuals develop severe behavior problems, especially during the school age years. As a result, parents and school staff spend significant amounts of time and attention dealing with these problems because they can interfere with learning, social interaction, and family functioning. In the Report on the Lowe Syndrome Comprehensive Survey - 2008, some individuals between the ages of 9 months and 27 years reported being formally diagnosed with a specific behavior disorder. Some individuals have taken part in a behavioral modification program with a behavioral specialist. A behavioral psychologist may work with parents and teachers to develop appropriate and effective methods for dealing with the behavioral issues and helping the child to maximize their capacity for learning. A Behavior Intervention Plan developed by a school may also be beneficial. Of the survey participants, some individuals reported using a behavior improvement plan with the ages ranging between 8 months and 17 years. Behavior problems in Lowe syndrome are believed to have an organic origin. That is, they are caused by a problem in brain function due to the syndrome. As a result, parents and teachers may find it helpful to consider the behavior problems as another one of the child's disabilities. Also, because medications are often helpful in treating the behavior problems, a physician may be involved in the treatment and educational plan.

### A. FORMAL DIAGNOSIS

| <b>Formal Diagnosis</b><br><b>(based on 137 survey participants)</b>    |                      | <b>Number of<br/>individuals<br/>reporting formal<br/>diagnosis</b> | <b>Percent of<br/>individuals<br/>reporting formal<br/>diagnosis</b> |
|-------------------------------------------------------------------------|----------------------|---------------------------------------------------------------------|----------------------------------------------------------------------|
| Formal<br>Diagnosis                                                     |                      | <b>29</b>                                                           | <b>23%</b>                                                           |
| Age First<br>Diagnosed                                                  | 9 months to 27 years |                                                                     |                                                                      |
| Specific Behavior Disorder(s) Which Have Been<br>Formally Diagnosed     |                      | Total number of<br>Individuals<br>diagnosed                         | Percent of<br>Individuals<br>diagnosed                               |
| Pervasive Developmental Disorder - Total                                |                      | 18                                                                  | <b>13%</b>                                                           |
| Autism Spectrum Disorder                                                |                      | 13                                                                  | <b>9%</b>                                                            |
| Pervasive Developmental Disorder - not<br>otherwise specified (PDD-NOS) |                      | 5                                                                   | <b>4%</b>                                                            |
| Obsessive-Compulsive Disorder (OCD)                                     |                      | 14                                                                  | <b>10%</b>                                                           |
| Attention Deficit / Hyperactivity Disorder (ADHD)                       |                      | 4                                                                   | <b>3%</b>                                                            |
| Impulse Control Disorder                                                |                      | 4                                                                   | <b>3%</b>                                                            |
| Intermittent Explosive Disorder                                         |                      | 4                                                                   | <b>3%</b>                                                            |
| Generalized Anxiety Disorder (GAD)                                      |                      | 3                                                                   | <b>2%</b>                                                            |
| Specific or Social Phobias                                              |                      | 3                                                                   | <b>2%</b>                                                            |
| Emotional and Behavioral Disorders                                      |                      | 2                                                                   | <b>1%</b>                                                            |

|                     |   |    |
|---------------------|---|----|
| Panic Disorder      | 2 | 1% |
| Psychosis           | 1 | 1% |
| Behavioral Seizures | 1 | 1% |

## B. SPECIFIC BEHAVIORS

The 2008 Comprehensive Survey looked at 54 behaviors. In this section we have compiled the behaviors into 14 behavior specific categories. Some individuals may exhibit none, one or many of the behaviors listed. The behaviors exhibited by individuals with Lowe syndrome may also overlap with behaviors in other categories. For all the behaviors listed in this section, the type of behavior may vary depending on the type of environment the individual is in. For example, behavior at school might be different from behavior exhibited at home or in the work setting. There may also be varying levels of the behavior depending on the child's temperament, personality, and environment. The types of behaviors may include, but are not limited to the examples in this section.

In this section the behaviors are separated by category. Consultation with medical and behavioral professionals is advised when determining if a child is exhibiting a behavior that is inappropriate and needs further investigation, treatment or a formal diagnosis.

The below behaviors are listed in the order in which they were reported in the **2008 Comprehensive Study Lowe Syndrome**.

**1. Self Abusive/Self Injurious.** Self-injurious behavior is defined as injury to one's own body that causes tissue damage or leaves marks for more than a few minutes or which is done to cope with an overwhelming or distressing situation. In individuals with Lowe syndrome the self injurious behavior is often due to underlying reasons, such as frustration, inability to communicate needs or inappropriate means of expressing anger. Sometimes anticipating a child's needs, redirecting the behavior or anticipating triggers may help to decrease the self injurious behavior (see Positive Reinforcement Techniques, Section VIII).

| Numbers are based on 137 survey participants       |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Hits, scratches or bites self</b>            |                      | 77                                                | 56%                                                |
| Age at which behavior began occurring              | 6 months to 40 years |                                                   |                                                    |
| <b>2. Strikes body parts against hard surfaces</b> |                      | 50                                                | 37%                                                |
| Age at which behavior began occurring              | 6 months to 40 years |                                                   |                                                    |

**2. Stereotypic Behaviors/Anxiety Disorders.** Anxiety disorders involve excessive fear or worry. Anxiety disorders include phobias and unrealistic fear of objects or situations. They may also include generalized anxiety disorder causing a pattern of excessive, unrealistic worry that cannot be associated with an event or experience in their lives. Anxiety can also cause panic disorders resulting in "panic attacks" that include physical symptoms such as a rapid heartbeat and dizziness. Some anxiety disorders may include obsessive compulsive behavior that causes an

individual to be “trapped” in a pattern of repetitive thoughts and behaviors, for example counting, hand washing or unusually strong attachments to objects.

| Numbers are based on 137 survey participants                                                          |                             | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|-------------------------------------------------------------------------------------------------------|-----------------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Exhibits incapacitating fear of normally neutral objects, noises, places, animals or people</b> |                             | <b>48</b>                                         | <b>35%</b>                                         |
| Age at which behavior began occurring                                                                 | 3 months to 13 years        |                                                   |                                                    |
| <b>2. Twirls, rubs, shakes or otherwise repetitively moves own body parts</b>                         |                             | <b>67</b>                                         | <b>49%</b>                                         |
| Age at which behavior began occurring                                                                 | 1 year 9 months to 20 years |                                                   |                                                    |
| <b>3. Ingests inedible objects, e.g., paper, rocks, dirt or non-nutritive substances</b>              |                             | <b>9</b>                                          | <b>7%</b>                                          |
| Age at which behavior began occurring                                                                 | 8 months to 16 years        |                                                   |                                                    |
| <b>4. Unusually strong attachment to or fascination with certain things or objects</b>                |                             | <b>60</b>                                         | <b>44%</b>                                         |
| Age at which behavior began occurring                                                                 | 6 months to 20 years        |                                                   |                                                    |

**3. Stereotypic Behaviors/Sexual Behavior Problems.** Some sexual behavior is appropriate at all ages when the behavior is typical of age related development. In cases of sexual behavior problems, individuals exhibit developmentally inappropriate behavior or aggressive sexual behavior. This type of behavior includes self-focused sexual behavior, such as masturbation and sexual behavior towards others. The term “sexual” is used to describe the type of behavior, but the motivations or intentions of the individual may not be related to sexual gratification. In situations involving sexual behavior, it is advisable for parents not to overreact because some sexual behaviors are typical within specific age ranges. Parents, however, should consult medical or behavioral professionals to determine whether the behavior needs to be further investigated. Most children can be encouraged to stop the behavior with limiting time in the setting in which it occurs, being told the rules, being carefully monitored and praising for appropriate behavior. In some cases sexual behavior is not typical of normal development and a referral to a mental health professional will be necessary.

| Numbers are based on 137 survey participants                  |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|---------------------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Publicly or excessively manipulates their genitalia</b> |                      | <b>14</b>                                         | <b>10%</b>                                         |
| Age at which behavior began occurring                         | 8 months to 17 years |                                                   |                                                    |

|                                                                                                    |                      |           |            |
|----------------------------------------------------------------------------------------------------|----------------------|-----------|------------|
| <b>2. Touches or grabs others' sexual body parts or rubs against others causing sexual arousal</b> |                      | <b>2</b>  | <b>1%</b>  |
| Age at which behavior began occurring                                                              | 15 years to 20 years |           |            |
| <b>3. Inserts finger(s) or objects into their rectum</b>                                           |                      | <b>6</b>  | <b>4%</b>  |
| Age at which behavior began occurring                                                              | 3 years to 14 years  |           |            |
| <b>4. Smears fecal matter or urine on self or objects</b>                                          |                      | <b>16</b> | <b>12%</b> |
| Age at which behavior began occurring                                                              | 1 year to 16 years   |           |            |

**4. Specific Behavior/Repetitive Motor Behavior.** Repetitive motor behaviors or “stimming” involve recurring and repetitive behaviors such as, speaking a word, phrase or sound over and over again, flapping hands, flicking fingers, banging the head, grinding the teeth and other behavioral acts that appear to be random in nature.

| Numbers are based on 137 survey participants                                                       |                             | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------------------------------------------------|-----------------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Sudden, rapid, recurrent, non-rhythmic, stereotyped motor movement(s) or vocalization(s)</b> |                             | <b>43</b>                                         | <b>31%</b>                                         |
| Age at which behavior began occurring                                                              | 4 months to 19 years        |                                                   |                                                    |
| <b>2. A voice louder than required for the situation(s)</b>                                        |                             | <b>51</b>                                         | <b>37%</b>                                         |
| Age at which behavior began occurring                                                              | 5 months to 40 years        |                                                   |                                                    |
| <b>3. Uses repetitive language</b>                                                                 |                             | <b>44</b>                                         | <b>32%</b>                                         |
| Age at which behavior began occurring                                                              | 1 year 2 months to 20 years |                                                   |                                                    |
| <b>4. Flaps hand(s) and/or waves finger(s) in front of eyes</b>                                    |                             | <b>79</b>                                         | <b>58%</b>                                         |
| Age at which behavior began occurring                                                              | 3 months to 12 years        |                                                   |                                                    |

**5. Physical/Verbal Aggression.** Physical and verbal aggression cause acting out feelings or impulses in destructive ways, either by physically harming someone or by being verbally aggressive towards others.

| Numbers are based on 137 survey participants             |  | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------|--|---------------------------------------------------|----------------------------------------------------|
| <b>1. Hit(s), scratch(es), kick(s) or bite(s) others</b> |  | <b>65</b>                                         | <b>47%</b>                                         |

|                                                                      |                             |           |            |
|----------------------------------------------------------------------|-----------------------------|-----------|------------|
| Age at which behavior began occurring                                | 1 year to 18 years          |           |            |
| <b>2. Verbally threaten(s) others with harm or misfortune</b>        |                             | <b>11</b> | <b>8%</b>  |
| Age at which behavior began occurring                                | 6 years to 34 years         |           |            |
| <b>3. Makes threatening physical gestures, e.g. with closed fist</b> |                             | <b>12</b> | <b>9%</b>  |
| Age at which behavior began occurring                                | 5 years to 20 years         |           |            |
| <b>4. Intentionally throws objects at others</b>                     |                             | <b>26</b> | <b>19%</b> |
| Age at which behavior began occurring                                | 1 year 6 months to 21 years |           |            |
| <b>5. Uses profane language on a regular basis</b>                   |                             | <b>23</b> | <b>17%</b> |
| Age at which behavior began occurring                                | 5 years to 24 years         |           |            |
| <b>6. Tease(s), boss(s), or bullies others</b>                       |                             | <b>18</b> | <b>13%</b> |
| Age at which behavior began occurring                                | 4 years to 34 years         |           |            |

**6. Disruptive Behavior.** Disruptive behavior disorder characteristically involves consistent patterns of behavior that “breaks the rules.” Some disruptive behavior is typical in the preschool years and in adolescence, and is often labeled as a tantrum. Other times the disruptive behavior may carry a clinical diagnosis of Attention-Deficient/Hyperactivity Disorder, Oppositional Defiant Disorder or Conduct Disorder.

| Numbers are based on 137 survey participants                                              |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|-------------------------------------------------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Engages in episodes of disruptive behavior(s) in an effort to get their own way</b> |                      | <b>64</b>                                         | <b>47%</b>                                         |
| Age at which behavior began occurring                                                     | 1 year to 34 years   |                                                   |                                                    |
| <b>2. Engages in episodes of disruptive behavior(s) for no apparent reason</b>            |                      | <b>39</b>                                         | <b>28%</b>                                         |
| Age at which behavior began occurring                                                     | 6 months to 34 years |                                                   |                                                    |
| <b>3. Actively resists requests or demands</b>                                            |                      | <b>57</b>                                         | <b>42%</b>                                         |
| Age at which behavior began occurring                                                     | 1 year to 19 years   |                                                   |                                                    |

**7. Social Development/Frustration Tolerance.** Social development involves a set of unspoken rules or guidelines that are usually learned through normal development. Individuals who engage in social avoidance have a tendency to ignore social cues and have not learned how to read, reach out to, or interact with the individuals around them. An individual may focus on an object rather than the person with whom they are speaking, in order to avoid eye contact.

| Numbers are based on 137 survey participants                                                               |                    | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|------------------------------------------------------------------------------------------------------------|--------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Avoids social interaction(s), i.e. avoids eye contact, hides, moves away, etc.</b>                   |                    | <b>23</b>                                         | <b>17%</b>                                         |
| Age at which behavior began occurring                                                                      | 1 year to 15 years |                                                   |                                                    |
| <b>2. Avoids engaging in reciprocal social interaction(s), i.e. turn taking, conversational turns, etc</b> |                    | <b>26</b>                                         | <b>19%</b>                                         |
| Age at which behavior began occurring                                                                      | 1 year to 9 years  |                                                   |                                                    |

**8. Property Destruction.** Property destruction involves behaviors that intentionally destroy property. More serious behaviors include Conduct Disorder Behaviors which involve acting on feelings or impulses in destructive ways and aggressive behavior which involves threats or harm to people or animals, and stealing, bullying or telling lies to get something.

| Numbers are based on 137 survey participants                                 |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|------------------------------------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Purposefully destroys other individuals and / or household objects</b> |                      | <b>21</b>                                         | <b>15%</b>                                         |
| Age at which behavior began occurring                                        | 2 years to 20 years  |                                                   |                                                    |
| <b>2. Intentionally takes the possessions of others without permission</b>   |                      | <b>19</b>                                         | <b>14%</b>                                         |
| Age at which behavior began occurring                                        | 2 years and 16 years |                                                   |                                                    |
| <b>3. Intentionally keeps and / or hides excessive amounts of objects</b>    |                      | <b>12</b>                                         | <b>9%</b>                                          |
| Age at which behavior began occurring                                        | 5 years to 30 years  |                                                   |                                                    |

**9. Hyperactive and Inattentive Behaviors.** Hyperactive/inattentive behaviors also known as Attention-Deficit/Hyperactivity Disorder is a behavior where individuals have difficulty focusing attention; they can often be impulsive and distractible. Individuals have difficulty sitting still, taking turns, and remaining quiet.

| Numbers are based on 137 survey participants |                    | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------|--------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Talks and chatters excessively</b>     |                    | <b>44</b>                                         | <b>32%</b>                                         |
| Age at which behavior began occurring        | 1 year to 20 years |                                                   |                                                    |
| <b>2. Exhibits hyperactive behavior(s)</b>   |                    | <b>52</b>                                         | <b>38%</b>                                         |

|                                                                                                                                                                  |                    |           |            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------|------------|
| such as having difficulty sustaining attention in tasks or play, being easily distracted, or having difficulty remaining seated and quiet when required to do so |                    |           |            |
| Age at which behavior began occurring                                                                                                                            | 1 year to 24 years |           |            |
| <b>3. Exhibits impulsive and dangerous activities without awareness of the danger(s), such as walking into the street without looking</b>                        |                    | <b>32</b> | <b>23%</b> |
| Age at which behavior began occurring                                                                                                                            | 1 year to 14 years |           |            |

**10. Tactile Sensory Defensiveness.** Sensory processing is the process in which individuals take in and interpret information from the environment. An individual who exhibits tactile defensiveness has difficulty interpreting sensory information. The senses of touch, movement, sound, taste, smell, sight and body position can all be affected by this inability to process the information being received. Results include a dislike of being touched, resistance to feeling different textures through all the senses, not liking loud noises and other adverse reactions to environmental stimuli.

| Numbers are based on 137 survey participants                                           |                              | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------------------------------------|------------------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Dislikes being touched</b>                                                       |                              | <b>34</b>                                         | <b>25%</b>                                         |
| Age at which behavior began occurring                                                  | Birth to 16 years            |                                                   |                                                    |
| <b>2. Resists feeling various textures, e.g. clay, finger paints, play-do, or sand</b> |                              | <b>62</b>                                         | <b>45%</b>                                         |
| Age at which behavior began occurring                                                  | Birth to 10 years            |                                                   |                                                    |
| <b>3. Removes their clothes at inappropriate times</b>                                 |                              | <b>18</b>                                         | <b>13%</b>                                         |
| Age at which behavior began occurring                                                  | 2 years 6 months to 43 years |                                                   |                                                    |

**11. Need for Sameness.** The Need for Sameness causes individuals to desire routine or order in their environment. There is a tendency to engage in repetitive behavior, doing and thinking about the same thing over and over. This type of behavior may appear to be a comfort or compulsion. Individuals exhibiting a need for sameness become upset when there is disruption in routine, or when transitioning from one activity to another. Some individuals have specific “rituals” that need to be performed precisely the same way every time.

| Numbers are based on 137 survey participants                                                                                     |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------------------------------------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Spends time arranging objects / items in an orderly way</b>                                                                |                      | <b>26</b>                                         | <b>19%</b>                                         |
| Age at which behavior began occurring                                                                                            | 1 year to 17 years   |                                                   |                                                    |
| <b>2. Spends time making the environment appear orderly which interferes with learning, daily routine, or social interaction</b> |                      | <b>9</b>                                          | <b>7%</b>                                          |
| Age at which behavior began occurring                                                                                            | 2 years to 9 years   |                                                   |                                                    |
| <b>3. Maintains rigid rituals and routines</b>                                                                                   |                      | <b>44</b>                                         | <b>32%</b>                                         |
| Age at which behavior began occurring                                                                                            | Birth to 18 years    |                                                   |                                                    |
| <b>4. Has restricted interests and attention span like watching the same video(s) over and over</b>                              |                      | <b>57</b>                                         | <b>42%</b>                                         |
| Age at which behavior began occurring                                                                                            | 6 months to 20 years |                                                   |                                                    |
| <b>5. Appears obsessed with object(s) and / or topic(s), e.g., elevator(s), car(s), and plane(s)</b>                             |                      | <b>64</b>                                         | <b>47%</b>                                         |
| Age at which behavior began occurring                                                                                            | 9 months to 12 years |                                                   |                                                    |

**12. Hyper Vigilant to Correctness.** Individuals who are Hyper Vigilant demand perfection from themselves and from people around them. Unable to achieve perfection causes frustration and may cause the individual to not try an activity or task for fear of failing. There is also a need for constant reassurance for doing a task or activity correctly.

| Numbers are based on 137 survey participants                                                              |                     | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|-----------------------------------------------------------------------------------------------------------|---------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Fails to engage in activities or perform tasks that they are capable of doing</b>                   |                     | <b>49</b>                                         | <b>36%</b>                                         |
| Age at which behavior began occurring                                                                     | 2 years to 34 years |                                                   |                                                    |
| <b>2. Needs to "confess" or repeatedly asks for reassurance that they said or did something correctly</b> |                     | <b>21</b>                                         | <b>15%</b>                                         |
| Age at which behavior began occurring                                                                     | 3 years to 34 years |                                                   |                                                    |

**13. Oppositional Defiant.** Oppositional Defiant Disorder is characteristic of breaking rules at home and at school, but may occur in other environments as well and may differ from one environment to another. This type of behavior can occur in children of any age and in adolescents. Types of behaviors include, but are not limited to, defiance of authority, including

but not limited to, parents and teachers, arguing and refusing to obey home and school rules, and refusal to take responsibility for bad behavior or mistakes. It is possible that individuals may exhibit resentment and seek revenge towards others. Regular temper tantrums in individuals may also be characteristic of this type of behavior.

| Numbers are based on 137 survey participants                                           |                       | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------------------------------------|-----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Refuses to attend school or work, with no indication of illness</b>              |                       | <b>10</b>                                         | <b>7%</b>                                          |
| Age at which behavior began occurring                                                  | 3 years to 34 years   |                                                   |                                                    |
| <b>2. Refuses to eat meals, with no indication of illness</b>                          |                       | <b>20</b>                                         | <b>15%</b>                                         |
| Age at which behavior began occurring                                                  | Birth to 18 years     |                                                   |                                                    |
| <b>3. Refuses to take medications, with no indication of illness</b>                   |                       | <b>16</b>                                         | <b>12%</b>                                         |
| Age at which behavior began occurring                                                  | 2 years to 34 years   |                                                   |                                                    |
| <b>4. Tells lies</b>                                                                   |                       | <b>7</b>                                          | <b>5%</b>                                          |
| Age at which behavior began occurring                                                  | 7 years to 15 years   |                                                   |                                                    |
| <b>5. Refuses to go to bed</b>                                                         |                       | <b>22</b>                                         | <b>16%</b>                                         |
| Age at which behavior began occurring                                                  | 1 year to 18 years    |                                                   |                                                    |
| <b>6. Awakens in the night complaining of nightmares and refuses to go back to bed</b> |                       | <b>8</b>                                          | <b>6%</b>                                          |
| Age at which behavior began occurring                                                  | 10 months to 25 years |                                                   |                                                    |
| <b>7. Refuses to sleep alone</b>                                                       |                       | <b>11</b>                                         | <b>8%</b>                                          |
| Age at which behavior began occurring                                                  | 1 year to 20 years    |                                                   |                                                    |

**14. Obsessive/Compulsive Behavior.** Obsessive-Compulsive disorder is an anxiety disorder, characterized by recurrent, undesired thoughts (obsessions) and/or repeated behaviors (compulsions). Some individuals may express an urgent need to engage in specific ritual activities and/or behaviors which they are unable to control and are compelled to act on.

| Numbers are based on 137 survey participants                   |                      | Number of individuals reporting specific behavior | Percent of individuals reporting specific behavior |
|----------------------------------------------------------------|----------------------|---------------------------------------------------|----------------------------------------------------|
| <b>1. Repeatedly checks light switches, water faucet, etc.</b> |                      | <b>25</b>                                         | <b>18%</b>                                         |
| Age at which behavior began occurring                          | 7 months to 24 years |                                                   |                                                    |

|                                                                                                                                                                                                                                                                                       |                       |           |            |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-----------|------------|
| <b>2. Has difficulty controlling worry or anxieties</b>                                                                                                                                                                                                                               |                       | <b>30</b> | <b>22%</b> |
| Age at which behavior began occurring                                                                                                                                                                                                                                                 | 2 years to 17 years   |           |            |
| <b>3. Has fear of contamination or dirt</b>                                                                                                                                                                                                                                           |                       | <b>12</b> | <b>9%</b>  |
| Age at which behavior began occurring                                                                                                                                                                                                                                                 | 10 months to 18 years |           |            |
| <b>4. Obsesses about a scratch or injury(s)</b>                                                                                                                                                                                                                                       |                       | <b>16</b> | <b>12%</b> |
| Age at which behavior began occurring                                                                                                                                                                                                                                                 | 7 months to 10 years  |           |            |
| <b>5. Engages in uncontrollable crying or laughing</b>                                                                                                                                                                                                                                |                       | <b>18</b> | <b>13%</b> |
| Age at which behavior began occurring                                                                                                                                                                                                                                                 | 6 months to 13 years  |           |            |
| <b>6. Engages in repetitive behavior(s) (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating word silently) that the individual feels driven to perform in response to an obsession(s), or according to rules that must be applied rigidly</b> |                       | <b>22</b> | <b>16%</b> |
| Age at which behavior began occurring                                                                                                                                                                                                                                                 | 6 years to 18 years   |           |            |



## **VIII. BEHAVIOR EDUCATION AND TREATMENT**

There are a number of treatments available for behavior disorders. Some, concentrate on treating the underlying causes of the behavior and others on treating the behavior itself. Medication is also an option. Other approaches include avoidance or redirection techniques, which involve keeping the individual occupied with other activities, or replacing the behavior, if it is considered harmful or inappropriate, with safer or more appropriate behaviors. Positive reinforcement is also one method in which parents and caregivers can encourage appropriate behavior in individuals with Lowe syndrome.

### **A. BEHAVIOR MANAGEMENT**

As behavior varies in individuals with Lowe syndrome so do the techniques that may work for each individual. Parents are usually the best judges of how an individual will respond to different behavior management approaches.

Behavior management is more frequently used with younger children to teach and encourage appropriate behaviors, but it can be used in adolescents and adults to improve or change an undesirable behavior.

There are two basic principles to behavior management. The first includes modeling appropriate behavior and using positive reinforcement. These work by encouraging appropriate behavior by giving praise or rewards immediately following the desired behavior. The second technique uses negative reinforcement by following the inappropriate behavior with a natural undesirable consequence.

In young children (age five years and younger) it is important to provide consistent routines and structure to the child's day. If there needs to be a change in routine, the child should know this will occur. Children who have difficulty with change and transitions may still have difficulty with the change in their routine, but with consistency and time they may be better able to cope with necessary changes. Boundaries for children should be clear, with expectations for behavior stated prior to an activity or situation. A reward system for good behavior or for completing a specific number of positive behaviors works also. (See Behavior Techniques for examples of rewards) Engaging or redirecting a child to constructive activities, such as games, puzzles and toys that stimulate activity, will encourage them to focus on positive behaviors. (See Positive Reinforcement Techniques) Some parents have used a timer for activities to encourage and reinforce structure. Setting a reasonable time limit for an activity helps to teach children that there are limitations to activities, even ones they may find pleasurable. Giving a time limit for an expected activity that is then followed by a reward gives a child the feeling of accomplishment and reinforces the behavior with a positive outcome.

In older children (ages 6 years to 12 years) behavior management can also be used to encourage and reinforce appropriate behavior. Older children need clear, consistent instructions and explanations for tasks throughout the day. If a task is complex in length, break it down to more manageable steps. Visual charts are a good way to show steps and can be used to encourage appropriate behavior. (See Visual Charts) Rewarding a child for good behavior and completed tasks can encourage the behavior to reoccur. Setting up a system for rewards that is clear and consistent may help the child understand what is expected. At a young age children often do not like to be disciplined in front of others. It is important to have a plan for misbehavior that does not require discipline in front of others. Regular communication with teachers and

doctors regarding behavior and behavior patterns can potentially prevent or control behaviors before they become a major problem. Parents are the most important role models for their children. Children, especially children with disabilities, need good role models and parents are very important role models in their lives.

Behavior management techniques for teenagers are also very important. As children mature it is important to involve them in setting rules, expectations, rewards and consequences. Giving adolescents some power will improve their self-esteem and reinforce that they have control of their behavior and can create positive results with positive behavior. Most teenagers are often sensitive with their appearance, especially in front of others. As they are experiencing hormonal changes and sexual development, it is important to be gentle and understanding. Open communication regarding physical and sexual changes is necessary. Teachers and doctors also play an important role at this stage of development and keeping open communication with professionals about behavior and changes in behavior will assist in appropriate management should the need arise. Consistency in your parenting style, being a predictable, reasonable and fair parent is always important when working with behavior management techniques. Parents are the most important role model for their developing teens. In learning to manage a child's behavior it is important for parents to know that they are not alone and if the situation becomes overwhelming, they can speak to a professional. It is natural to have questions and needs when learning to manage a child's behavior.

## **B. BEHAVIOR IMPROVEMENT PROGRAM**

A Behavior Improvement Program is a program established to improve a behavior through behavioral techniques, such as positive reinforcement, behavior modification, rewards, and behavior therapies. There are many different kinds of assessments used to determine the underlying causes and potential treatment for a behavior. Some of the assessments might include, but are not limited to, the assessments listed in this section.

An Environmental Assessment is an evaluation of the physical setting, where the child lives or learns. This type of assessment is intended to determine factors in the individual's learning environment that might be interfering with daily functioning or behavior. For example the noise level in a classroom may contribute to adverse behaviors. Adjustments then can be made to change the classroom environment to change the observed behavior.

A Functional Behavioral Assessment is an evaluation of the behavior patterns or problematic behaviors that are causing problems either at home or in school. The assessment is often in conjunction with the child's Individual Education Plan (IEP). The assessment looks at the behavior, the motivation for the behavior and the function the behavior serves. The purpose of determining the function is to address the situation that drove the behavior.

## **C. POSITIVE REINFORCEMENT TECHNIQUES**

The *Report on the Lowe Syndrome Comprehensive Survey – 2008*, documented different types of positive reinforcement techniques. The positive reinforcement examples found in quotes are actual examples taken from written responses provided by families who participated in the *2008 Comprehensive Study on Lowe Syndrome*. Positive reinforcement techniques may be duplicated in more than one section given the nature of the behavior and the usefulness of the techniques.

**1. Redirection.** Redirection is a technique used to turn a child's attention away from the behavior that is currently happening. Redirection can be provided in many ways/forms. It can be verbal by asking your child to choose a new activity, non-verbal handing a child a toy to distract them from the behavior, and physical if a child needs to be physically guided to a new activity. Whichever method a parent uses, redirection is meant to be a positive transition from an activity that is inappropriate, to a more desired activity.

- "When he is disruptive I redirect the behavior into something else. He loves trains, Legos, TV and puzzles. We don't let him get away with the behavior, the behavior is acknowledged and then he is redirected to something else. If he is unable to get himself under control, I will take him upstairs to talk to him about the behavior and then get him started in a new activity."

- "We try to sing songs when brushing teeth or use encouraging language when having procedures or eye drops. If he is resisting or trying to wriggle away from being examined sometimes laughing loudly works and he will laugh too."

- "He feels very secure with his rituals and routines. We try to give him more and more experiences to enrich his interests. We do everything possible to break his routines and expose him to new pleasant conditions. We offer him types of rewards to make him motivated to skip his ritual in order to get his rewards quicker. Some other times he looks so happy with his ritual that we let him go through with it when it is not harmful to himself or others."

- "We encourage change, choices and let him know he does have choices. He sees others making different choices and wants to be a part of that and this encourages him to make different choices, at times, too."

- "We remind him when we have to do something different and that those things will be there later. We introduce new things to him as well and frequently and try not to do the same things all the time, so he does not to establish a routine of doing the same things constantly."

- "We try to redirect him as much as possible, give him soft toys to hold. We also are trained in holding him ourselves so that he isn't hurting himself or others. We use nickels as rewards, the Weather Channel as reward, or taking walks outside. Visual charts include his schedule for the day and any very fun or funny words that he enjoys."

- "We use distraction, such as exploring the fascination with him to broaden it out, using it as a tool or path to other things. We challenge/reframe obsessions by helping him explore more about the topic. We use all his obsessions to lead to other areas and as a way to develop other skills around it."

- "Mostly when he is agitated we redirect, redirect, redirect till we find something that works. We get his attention focused on something else, like handing him something and asking him to tell me what it is, or by asking, what's the next activity. He loves to carry quarters in his pocket and takes them to work for break. Also he does not want you to talk on the phone. I find warning him ahead of time when the phone rings before I answer it that he needs to be quiet. We

constantly reinforce not talking when someone else is talking. Quietly and gently we tell him he will get a turn. We are working on him to whisper to me if he wants to say something when someone else is talking.”

- “We reinforce appropriate language by saying those words are not acceptable, because they are not nice, hurt people’s feelings, etc. When he does not stop he is asked to go upstairs until he is ready to be with us again. Sometimes just a change of scenery for him changes the behavior. He does not always know how to express his frustration in words and the use of unkind words or threats is how he expresses his frustration. At that point I will acknowledge his feelings and try to give him the right words to use to express what he wants to say.”

- “This behavior occurs mostly during transitions from one thing to another. So we try very hard to let him know what’s going to happen next. Or if he’s had a bad day the next day he has to try again and we remind him that this is the try again day. We redirect, redirect, redirect and get quickly to something he does that can be positively reinforced.”

- “We separate him from the situation, positive reinforcement such as praise for being a part of the group/game in an appropriate manner or sitting quietly with the rest of the group, social stories for hard situations, selectively ignoring of behaviors.”

**2. Natural and Logical Consequences.** A natural or logical consequence is a consequence that occurs without parent involvement. Consequences occur through nature, society or by another person, generally someone in authority. For example, if you go outside in the cold weather without a jacket the consequence is that you get cold. Next time you will remember to put on a jacket when it’s cold out. Laws are considered natural consequences, if you break the law there is a consequence for breaking it. Another type of consequence is a logical consequence. Logical consequences are situations engineered by the person in authority and they are logically connected to the wrong. It is logical because it "fits" the offense.

- “When he is frustrated he bites his arm. I have to remind him that won’t help and it will cause a bruise on his arm which he doesn’t like at all.”

- “At school when he does not do his work, he has privileges revoked and discussions with school authority figures.”

- “When he does not come to dinner when everyone else is ready, I don’t make a big deal; I just tell him once we are now having dinner. I then leave his dinner at the table and he eats a cold dinner by himself. If he argues about eating alone or his dinner is cold, I remind him that we already ate and if he wants to have a hot meal with others, he needs to come to the table when I call him.”

- “We just tell him he is not allowed to use that sort of language and if he continues, we remove privileges like TV or the phone.”

**3. Rewards.** Rewards are given when your child does a good job, has made progress on a

problem or has reached a goal or achievement. Rewards are a good way to reinforce positive behavior or prevent problem behavior. Rewards are not used as bribes, but rather as reinforcement for positive behavior.

- "We have to give him verbal prompts to keep him on task. He needs several different breaks between activities. Stickers works as a reward and doing the things he likes best or taking them away if he is not on task. He needs to be told what is going to happen before things happen to keep him from acting out. That seems to help when he knows beforehand."

- "We try to give him more and more experiences to enrich his interests. We do everything possible to break his routines (expose him in new pleasant conditions), we offer him types of rewards to make him motivated to skip his ritual in order to get his rewards quicker. Other times he looks so happy with his ritual that we let him go through with it."

- "We give him opportunities to enjoy appropriate activities and objects. We use his obsessions as rewards. He has to accomplish other tasks before he can enjoy these things. He does daily tasks, i.e., clean room, put clothes away, make bed, exercises, clean his plate and put it in the dishwasher. He gets rewarded with swinging and watching his favorite movies."

- "When appropriate we ignore, redirect or ask questions about situations that could get more conversation about the topic and when it's appropriate to say what he's saying, engaging him. Again rewards have to be immediate, which is praise for doing the right thing."

- "We made a chart and rewarded good behavior with stars. When he earned a certain amount of stars he could trade them for a treat."

- "He is obsessed with trains. This fascination with trains enables us to use the trains as a reinforcement tool for behavior. I can use the train to encourage appropriate behavior, by saying to him when we are done at the doctors we can go see the train, but seeing the train is contingent on good behavior and I explain that he needs to listen to the doctor and do what is asked."

- "Rewards have to be immediate, which is praise for doing the right thing."

- "Give him opportunities to enjoy appropriate activities and objects. Use his obsessions as rewards. He loves changing sweatshirts and drinking out of water fountains. He has to accomplish other tasks before he can enjoy these things."

- "We use a Token system. After he gets 10 tokens for being good, he gets a reward. We also use behavior modification."

- "We use gentle prompting. We use encouraging words that he needs his sleep/rest. We use patience in his bed time routine. We use music and stories to encourage him to get ready for bed and say that these are rewards for his being helpful. We use positive words of encouragement for him being helpful."

**4. Visual Charts/Routine/Set Schedules.** Visual charts and schedules help to keep your child on task and can show or tell a child what needs to be done and when it should be done. This type of behavior modification technique can also take the pressure off you as a parent, by referring to the chart or check list of what needs to be done, the list becomes the rule enforcer (the bad guy). This also works well for individuals with obsessive behaviors who feel the need to constantly ask what's next or when are we going. Refer them to the list, the chart or the calendar every time they ask. Like all positive reinforcement techniques, routines need to be consistent and when there is a change in routine, prepare your child in advance for the change in routine. Charts can be a collaboration with your child, depending on their age and understanding of what the chart is. Younger children may comprehend better with charts that have pictures, whereas older children would understand charts with pictures and words or just words. Post the chart in a place where your child can see it and you can send them to look at it. To further reinforce following a routine use additional reinforcements such as praise or rewards to reinforce the behavior.

- "Talk to him, show him a visual chart of appropriate place for behavior to occur, such as a child removing clothes for a bath."
- "He keeps a daily schedule of events for that day so he knows what's going on, it helps him stay organized."
- "Daily timetable (wall chart) to set agenda in advance and reassure."
- "Reminder of when activity is appropriate, scheduling when he gets to do these things with a visual list of what has to happen or come first before preferred activity/object."
- "Visual charts include his schedule for the day and any very fun or funny words that he enjoys."
- "ABC charts to identify triggers to challenging behaviors. Reward charts to encourage specific behaviors."
- "We use PEC cards." (PEC cards are picture cards used to teach specific concepts/skills and assist with nonverbal communication)
- "We have a chart and reward good behavior with stars. When he earned a certain amount of stars he could trade them for a treat."
- "Having forced choices and a daily schedule has helped with this. Telling him what is coming next and whom he will be with and when he is going."
- "Visual charts - timetable that sets out the plan for the day and the people that he is going to be with, mode of transport, places etc. Lots of reassurance needed."

**5. Verbal/Nonverbal Cues for Appropriate Behavior (Praise and Positive Words Included In This Section).** Verbal and nonverbal cues are words or gestures used to remind your child what type of behavior you expect from them. Praise and positive words have been included in this section because praise can be a very strong verbal reinforcement tool when encouraging the

behavior you want to see. All words of encouragement need to be descriptive, so that your child understands exactly which behavior you are giving them praise for and that you are encouraging that behavior to happen again. Verbal reinforcements, like rewards, are most effective when given immediately. **CATCH YOUR CHILD BEING GOOD** and give extra praise for those behaviors you want to increase.

- “With a Behavior therapist we have worked on him answering the what, why and when questions. He then has to ask questions on a 1-1 basis. He is getting much better at this and not asking the same thing over and over. We have to help him expand his words and concepts with a 1-1 drill like structured setting and then he generalizes it in school with others.”

- “He is involved in social groups with the school psychologist, and his special ed. teachers work with him on social interaction. We are an active family and encourage him to talk to others when we are out.”

- “We have to give him verbal prompts to keep him on task, He needs several different breaks in between activities, mostly at school. Stickers work as a reward and doing the things he likes best or taking them away if not on task.. He needs to be told what is going to happen before things happen to keep him from acting out. That seems to help when he knows beforehand.”

- “Use a timer to keep him at his task until the timer is finished. Verbally tell him what sequence of events will take place. He is motivated by what activity/event comes next.”

- “He became increasingly wary of being touched in certain places, especially his head, hair and shoulders. We are very gentle with him and careful about the way we touch him. We warn him when we were going to touch him and how we were going to touch him, warning and explaining before doing seems to help.”

- “He often will avoid things he is capable of doing- toileting, some dressing skills, putting items away. We use behavior modification, positive praise for little steps, and incentives for achieving tasks.”

- “When there is a situation involving an unfamiliar animal, he is given reassurance that he is safe. We have taught him techniques on how to be safe around animals, such as standing still and keeping his hands fisted and out of reach. We have also slowly exposed him to animals of different varieties through friends who have pets and outing to places that have animals.”

- “Whispering to him and sharing with him the places where we use a quiet voice like church, quiet restaurant, movies, etc. and he has learned to pick up that we are in a place where we need to use a quiet voice.”

- “Forced choices. He doesn't like open-ended requests. We give him two choices and he usually picks one. We try to give him as much control over his choices as possible.”

- “He understands the concept of First/Then. He usually is easy to distract or redirect.”

- “Discuss appropriate words and mostly try not to draw attention to it as it will just escalate.”

- “Our son will raise his voice, walk away, and repeat things to get his way. We answer his request once and then give him two choices on what he can do and he has to pick once thing. Having a set schedule and forced choices helps out tremendously.”

## **6. Replacement of Behavior with another Appropriate Behavior/ Exposure to Activities**

**They Resist.** When using this technique, think about the appropriate activities your child enjoys and when an inappropriate behavior occurs, replace what they are doing with the new activity. A sensory box is a replacement tool that can be used to replace the offending behavior. A sensory box can be filled with rice, sand or water and toys that your child can manipulate are placed inside the box. Be sure to place items in the box that are safe for your child to handle. Many children with Lowe syndrome are resistant to feeling different textures. A sensory box can also be used to slowly expose children to new textures.

- “Patience and gradually introducing and re-introducing textures.”

- “Bought different textured fabrics and introduced them to him slowly every day. Took him in the yard and carefully touched his bare feet to the grass and sandbox. Over time he became use to different textures, about 6 months to a year.”

- “Brushing techniques. Exposure to new textures.”

- “He is very tactile defensive. We work with him all the time; have him carry something (textures) for you, making it his job.”

- “Introduce him to various objects for short periods of time. Reward him for allowing it to happen. Give extra drinks or time with something of his choosing.”

- “We continue to do OT to desensitize him.”

- “Trade off time with what he wants for things that he needs to be doing.”

- “Remind him when we have to do something different that those things will be there later, introduce new things to him as well and frequently, try not to do the same things all the time and not to establish a routine of doing the same things constantly.”

- “Redirection when needed and/or a diversified routine. Over time offer many new experiences. Replace objects he is holding and obsessing about.”

- “Give him opportunities to enjoy appropriate activities and objects. Use his obsessions as rewards. He loves changing sweatshirts and drinking out of water fountains. He has to accomplish other tasks before he can enjoy these things. He does daily tasks i.e. clean room, put sweatshirts away, make bed, write a letter, routine physical exercise, clean his plate and put in

dishwasher etc. He gets rewarded with swinging and watching his favorite movies also.”

- “Verbal cues to put hands down. Give him an object he would prefer to shake. Distract with music, scenery, etc.”

- “When he is using a louder than normal voice, I lower my voice to a whisper and that encourages him to lower his voice. If he does not pick up on me lowering my voice than I say we need to whisper so that we do not disturb others.”

**7. Ignore Behavior/ Let Behavior Happen.** To use this technique effectively you must ignore the behavior completely and consistently. That means no eye contact, no physical contact and no verbal contact with your child when the behavior occurs. Make sure your child is in a safe place when using this technique and if necessary walk away from your child if you are unable to ignore the behavior. In some children the behavior will get worse before it gets better, but by being consistent and ignoring the behavior every time it happens the negative behavior will decrease. This type of behavior modification can be used with praise, so as you ignore the inappropriate behavior, praise the behavior you want to increase. This allows your child to get attention for appropriate behavior and lets a child know what behavior you expect.

- “We put him in a safe place and ignored him, because the harder we tried to get him to stop, the worse it got.”

- “Not reacting dramatically to reinforce the behavior. Calmly and without speaking take his hand from his face and push gently towards lap. Making a better effort to prevent frustrations building up ( i.e. avoiding thirst, hunger, boredom ) and avoid saying "no" which often sparks an attack, so finding other ways of turning him down without saying no.”

- “We use positive words/phrases of encouragement. At times we ignore it and it improves. We evaluate the current situation at the time of the behavior.”

- “Discuss proper indoor verses outdoor voice. If he is not hurting himself or others then we just let the behavior pass, by ignoring the behavior. If we were to make it an issue the behavior worsens.”

- “No reinforcement for loud voices. Ignore and respond when he stops or uses soft voices.”

- “Discuss appropriate words and mostly try not to draw attention to behavior, as it will just escalate.”

**8. Anticipating Behavior/Triggers.** Triggers are situations or behaviors that cause distress in your child. When anticipating the behavior or trigger it is important to know what causes your child to act out or lose control. Be ready to remove your child from these types of situations. By verbally acknowledging your child’s feelings in these situations you can help your child become aware of their own triggers. Start developing strategies with your child to reduce frustrations, covering their ears when a noise is too loud, preparing for school the night before by making

lunch or laying out clothes to avoid morning “melt downs.” Be prepared to offer alternative activities to either soothe them, such as rocking, a warm bath, quiet music or a more active activity, bouncing on a ball, going to the playground, pushing against the wall or other physical activities to redirect anger or frustration.

- “We are as physical as we can be in terms of rough and tumble play etc. but we utterly respect when he doesn't want to be touched/hugged. Things like face and hair washing, brushing teeth, cutting nails, hair etc we just try and do with as little fuss and as quickly as we can and praise him for his tolerance.”

- “Try to prevent event from occurring in first place - remove triggers. Praise him for appropriate behavior.”

- “We learned to use the things he obsesses about as reinforcement, i.e. - water fountains. Or we try to stay away from things he obsesses about that he hates.”

- “ABC charts to identify triggers to challenging behaviors. Reward charts for good behavior.”

- “Redirection. Avoiding things that frustrate him. Reading his signals (he doesn't speak) as to when he is hungry or uncomfortable.”

- “When he hits his hands on his head in frustration. I try to avoid the frustration as often as possible. I will pull his hands down and to tell him to be nice to himself. Taking him out for rewards often works. I try to keep him distracted and to move away from whatever is frustrating him.”

- “We have found letting him know what will be expected and giving him a minute or two to think about it before he is expected to actually do it has helped a lot. This gives him time to shift gears so to speak. He is very routine oriented so if he has a schedule it also helps him to know what to expect.”

- “Having forced choices and a daily schedule has helped with this. Telling him what is coming next and whom he will be with and when he is going.”

**9. Additional Positive Reinforcement Techniques.** This section is a list of additional behavior techniques that were placed in a paragraph of their own either because the techniques overlapped into many of the positive reinforcement sections, provided a specific type of therapy to encourage appropriate behavior or because the technique itself was unique from all the rest.

- “He is involved in social groups with the school psychologist, and his special education teachers work with him on social interaction. Plus, we are an active family and encourage him to talk to others when we are out.”

- “Direct him to respond and use a verbal prompt to help him respond. When encouraging social interactions, we place him in close proximity to the individual. We encourage doing favorite

activities with his peers.”

- “We have to give him verbal prompts to keep him on task. He needs several different breaks in between activities. Stickers works as a reward and doing the things he likes best or taking them away if not on task. He needs to be told what is going to happen before things happen to keep him from acting out.”

- “Positive reinforcement for staying a part of activity, social stories, working up to keeping him involved for a certain time period, giving him a choice in the activity, reminders to have a quieter voice, quiet game-who can stay quiet the longest.”

- “To help our son be less sensitive to touch, we do a lot of touching while talking to him or when playing with his favorite objects.”

- “We exposed him to lots of different texture through PT, OT, Vision Therapy and general exposure to textures he did not like. We also placed him in a small home daycare setting with typical children and moved him to a regular preschool setting that exposes him to a variety of activities that encouraged him to be more comfortable with different textures and sensory experiences.”

- “PECS, Simple sign language and gestures for communication. Music as rewards.”

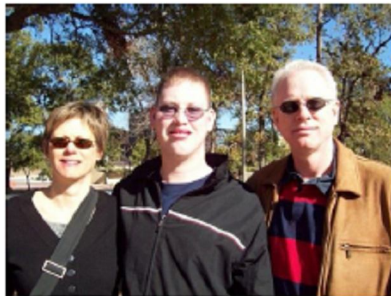
- “We usually try to keep his routine about the same on a daily basis so he knows what to expect. We try to stay away from things that would scare him. If we can’t control it, we just keep him close with hugs and it usually calms him down.”

- “We give him reassurance when he is afraid of something, pick him up, hold him, hug him. We provide repetition by going to the same places. We give him strategies such as, cover ears when loud noises scare him, wear ear plugs, and expose him to different objects until he got over his fear of touching them. We introduced him to different things that scared him and kept revisiting them.”

- “We are using a problem solving technique with him to give him some control over the situation at the same time maintaining the control I need. It takes a lot of effort and time to problem solve, but most of the time it avoids the power struggles. I also use “If...then” statement or “First...then” statements. Such as “If you are dressed, then you can watch TV.” This puts the control in his hands, rather than my constantly telling him to do something.”

#### **D. OTHER BEHAVIOR MANAGEMENT TECHNIQUES**

Applied Behavior Analysis is a teaching style that involves using a series of trials to encourage the desired behavior or response. Each behavior or skill is broken down to its simplest form and then re-taught to the child using a system of repetition and reinforcement. Sensory Integration Therapy is used to treat children with sensory, motor and perceptual difficulties. Sensory integration therapists believe that by changing experiences you can change the brain. Occupational therapists are most often providers of sensory integration therapy.



## IX. PARENTS AND FAMILIES: LIVING WITH LOWE SYNDROME

Raising a child with a disability presents challenges and when the disability is Lowe syndrome the challenges are many. Parents must deal with complex and frightening medical problems, with complicated special education choices and with raising a child whose development may be slow and erratic and whose behavior may disrupt family life. And, all the while, parents must manage their own feelings of grief, fatigue, inadequacy, and fear for the future.

It all begins when families learn something is ‘wrong’ with their child. This usually happens shortly after birth when they learn that their son has eye problems. Because most doctors are not familiar with Lowe syndrome, many families (especially those with no history of Lowe syndrome) experience long and frustrating delays before receiving the diagnosis and the beginning of treatment. Fortunately, due to the LSA website and continuing research and numerous published papers on Lowe syndrome comprehensive information is now available to families and doctors. Additionally, genetic testing is available to verify a diagnosis.

After securing needed medical care, parents must turn their attention to the education of the child and his place in the family. Having a child with so many disabilities places extra demands on everyone’s time, energy, and financial resources. A family can easily become socially isolated and emotionally drained, focusing all its attention and energies on caring for the child. Boys with Lowe syndrome are often warm and loving but they can also be distant and rejecting. They are wonderfully curious but can be exhaustive questioners and talkers. Often happy and cheerful, they can also be obstinate and forceful in trying to get what they want and can provoke a crisis at any moment and at any place.

While parents continue to have emotional ‘ups and downs’ over the years, experience helps them make the adjustments needed to meet the needs of their son, their family, and themselves. Experienced parents offer the following bits of advice to help new parents keep things in perspective and maintain a healthy and realistic attitude.



“! Become knowledgeable about Lowe syndrome. Learn as much as you can because chances are you will be assisting and your doctor will be learning about Lowe syndrome and in some cases, learning together. Reading this book and the LSA newsletters along with talking to other parents will be a good start. If you have other children, they need to understand their sibling’s condition as well. They should know its name and the fact that it is not contagious. As they get older they should be told how Lowe syndrome is inherited and the possible genetic implications it could pose for their own children. Also, share the information you learn with members of your extended family. Grandparents, aunts and uncles can be a rich source of help and support for years to

come. Help to keep them involved and informed.”

“! If you have a young child, find an early intervention program to provide the stimulation and assistance your child needs in the crucial early years. Remember that progress may at times be slow, but never give up because you are your child’s best advocate.”



“! Listen to the concerns that other family members have and keep them informed. Involve the whole family in caring for the child. If you have other children, you may find yourself feeling guilty and torn because of the extra attention required to care for your individual with Lowe syndrome. Talk to your other children and help them understand that this inequity doesn't mean you love them any less than their sibling. Giving them opportunities to help can make them feel grown up and an

important part of the family. Siblings can provide wonderful stimulation and companionship and, because of their unique perspective, are sometimes able to offer surprisingly helpful suggestions.”

“! Get to know other parents in the LSA. Even though you may be separated by hundreds or thousands of miles, you can use the telephone, e-mail or regular mail, or share letters in *On the Beam* and attend conferences. Your life will be greatly enriched by these mutually supportive and very special friendships.”

“! Participate in a local parent support group. Getting to know other parents who have children with disabilities or chronic illness can help overcome feelings of isolation and lift some of the burden we all feel. In addition, a community group is a valuable resource in finding out about local programs and services.”





“! Learn about the rights of people with disabilities. You can be your child's best advocate as well as an advocate for other children.”

“! As much as possible, try to keep a sense of humor. Sometimes the most effective way of dealing with a difficult situation is to try to find something funny in it.”

“! Understand that the many emotions you feel are normal, including grief, fear, anger, and despair. Help your other children understand that mixed emotions are normal and perfectly understandable. There is no right or wrong way to feel. What is important is how you choose to cope with your feelings. Fear and anger, for instance, can lead to paralysis or they can lead to productive action. If needed, seek professional counseling to help you cope with the many emotions you will have dealing with a child with a disability.”

“!To quote a doctor I know, think of the airplane safety warning, “Parents, put on your oxygen mask first.” Remember to take care of yourself so that you can be there for your child.”

“!Confidence in your ability to handle the challenge of having a child with Lowe syndrome can be found in the knowledge that other families have traveled the same path and have found ways to cope successfully.”



## X. WORDS OF EXPERIENCE AND ENCOURAGEMENT FROM LSA PARENTS

Following are selected quotes from letters published in *On the Beam* and messages posted on LSA-Talk.

### **On Feelings...**

“Since his birth we have experienced every conceivable emotion.”

“I can remember feeling so lucky that my son was very high functioning mentally when he was younger. I figured, if we have to have this Lowe syndrome, at least it is not too bad. As all of these nasty manifestations are hitting him and his kidney problem seems to be worsening, I don’t feel so lucky anymore.”

“My son is 2 years old. I have so many people come up to say what a cute baby. He still has a lot of his baby fat and because he isn’t walking they assume he’s a baby. I usually just smile and say thank you. I can never bring myself to get into the real story with strangers.”

“When I see other children that go through horrible surgeries and almost die, but then they come out healthy and lead normal lives, I wish they could do that for my son. It is so hard to deal with most of the time.”

“I am always running about going here and there and never can relax. I am wiped out, mentally more than anything. A friend told me to have a glass of wine and relax, so I am off to do just that.”

### **On day-to-day life...**

“From the age of two until time for kindergarten, I drove him year round 35 miles each way to the Rehab Center, hauling three youngsters besides in the summer.”

“The visits to doctors and clinics and the surgeries and tests which drain even the strongest, are very vivid for me.”

“My son’s behavior was so bad in the mall a couple of weeks ago, someone called security. He was yelling, cussing and biting himself. The security guard came and asked what the problem was. I said, ‘Well, we have behavior problems.’ He asked my son what was wrong. He said he was hungry. I had bought some French fries and he wouldn’t eat them. Anyway, I thought this man has NO clue. No idea at all. Looking back now, I laugh. Didn’t think it was so funny then.”

“It hasn’t always been easy but with guidance and structure, our son leads a productive life and enjoys his friends, school and family even though he has Lowe syndrome.”

“When our son was younger, from about the age of 2 until 6, we spent a lot of time in the hospital with minor illnesses becoming major illnesses. As his immune system matured, his illnesses are more typical and less stressful on him and our family.”

“I was thinking of putting him in a special center when he gets in his teens because I don’t know if I’ll be able to handle him on my own.”

### **On dealing with doctors and other professionals...**

“I always question the doctors. They don’t know what we have to go through until they walk a mile in our shoes. So I always stress MY STRESS!”

“As brilliant as our doctors are, and as caring and honest as they have been, it can be discouraging to hear answers to our questions about Lowe syndrome by hearing ‘we don’t know’.”

“We can’t stress enough how important it is for parents to be firm about what they believe is right for their child. If you really feel something is not being dealt with properly, you have to let the professionals know.”



“In dealing with educational issues, parents need to be constant advocates and persistent in obtaining services and/or advocating for their child’s education plan and objectives.”

“We have changed medical professional when needed, for a variety of reasons.”

“I have shared the newsletter with everyone who cares for and works with him. It has helped a lot of people understand what I have been trying to tell them.”

“Our medical insurance refused to allow refills on any of my son’s meds. They said the doctor has to call and authorize them again and they would like him to choose different meds because his are too expensive. So, in addition to the roller coaster of so many problems we need to watch out for, we need to fight with insurance companies too.”

### **On siblings and family life...**

“My typical son is having difficulty sleeping in the same room as his brother. He is afraid of seeing him have seizures. The school called today because he was telling the teacher about his brother and burst into tears. He is seeing a school counselor and we are helping him here at home too.”

(From a sister) “As his sister, I had problems, frustrations, and yes, joys, which I felt no one would ever understand.”

(From a brother) “My friends all say he is the coolest kid they know. He’s funny, does his crazy projects and makes us laugh when he hangs out with us.”

(From a grandparent) “Attending the conference has given us a better understanding of Lowe syndrome and renewed hope for our grandson’s future. Seeing others much older than him, we have a better idea of how he will cope in the future, and we see he has a promising future, even though there will be many bumps along the way.”

(From a grandparent) “The most outstanding aspect from the conference was our observation of the parents of individuals affected with Lowe syndrome. We are so tremendously impressed with you. Not only do you handle all the day-to-day problems with your individuals, but somehow you manage to find the time to learn all you possibly can about Lowe syndrome and its various aspects and treatments. This is exhibited by the respect accorded you by the physician and researchers involved in the conference. They obviously value your input, insights and opinion.”

“You have unending love and patience with your individuals and it shows in everything you do, even to the casual observer. You have problems, challenges and difficult decisions to deal with everyday and you are doing it well.”

“Just went to our second daughter’s high school graduation, so even with all we go through with our individuals, life still goes on.”

(From a sister) “Because of my biology class, I have lots of questions and look forward to acquiring answers to them. I thought I would share this information with my biology classmates. Everyone loves my brother and, who knows, maybe someone in the class will be able to find a cure.”

### **On parent-to-parent support...**

“I was so happy to learn that I am not totally alone. It makes me feel very warm inside to think we have found a new ‘family’.”

“I am so grateful we have each other to lean on. If there wasn’t such a thing as the Internet I think I would go crazy! It has helped so much to be able to talk with everyone.”

“I just wanted to thank everyone for their letters of encouragement and support. I treasure every piece of advice that is given or shared in our support group. This is a very stressful time. Without you guys I don’t know how I would cope. It helps immensely that there is actually someone out there who knows exactly what we are going through.”

“I was very discouraged and very upset because I felt so alone in this. This was something new for us to deal with and I was frightened. I wrote a letter to the list and shared our day with you. I have gotten back many letters of support, encouragement and love and it just overwhelmed my heart to know that there is so much love out there among other Lowe syndrome families to share with others.”

### **On hope, courage, joy and humor...**

“When people ask me how I am doing I almost always say ‘hanging in there!’ It may not be the strongest piece of rope but we’re hanging in there, right?”

“Miracles don’t pop out of the blue; rather you have to make them happen.”

“For all of you who have doubts that your child will walk, don’t! Because no one could have doubted it more than I.”

“I have informed the people at the agency that provides services for my son that I am sick of the word ‘frustration’ and they came up with some new ones for me. Here is the list: exasperated, exhausted, done, overly challenged, tired, distraught, fatigued, weary, annoyed, tormented, anguished, disappointed, confused, distressed, frantic, thwarted, hindered, and my most favorite: EMOTIONALLY SPENT! Yes, I have spent all my emotions! (Is this the Lowe syndrome parental sense of humor?)”

“Being the parent of a sick child with such a disease as our individuals ... it does leave one quite ‘spent’ as one of our moms said. I am so spent I have no change left!”

“My son is 10, but about the size of a 6 year old, so when somebody asks how old he is, and I say 10....they look at me for a minute, like WHAT’S WRONG WITH HIM? I just say he has a rare syndrome, and is small for his age. Most folks are fine, but once in awhile you get a rude one that stares, but we’re the fortunate ones because we have learned so much, and have been blessed!”

“He has taught us as parents, as well as his sister, what life is really all about. Because of him we have experienced parenthood, family life and loving to the fullest degree. We have learned to never take anything for granted.”

“I had a little tag made up for his jacket that says: Contents: One Terrific Kid, and that’s the way we all feel about him.”

“I’ve come to realize, getting a diagnosis of Lowe syndrome is not the end, only the beginning. With new therapies and medications, our individuals can lead happy, productive lives. I truly believe the possibilities are endless.....”

**And, on getting credit...**

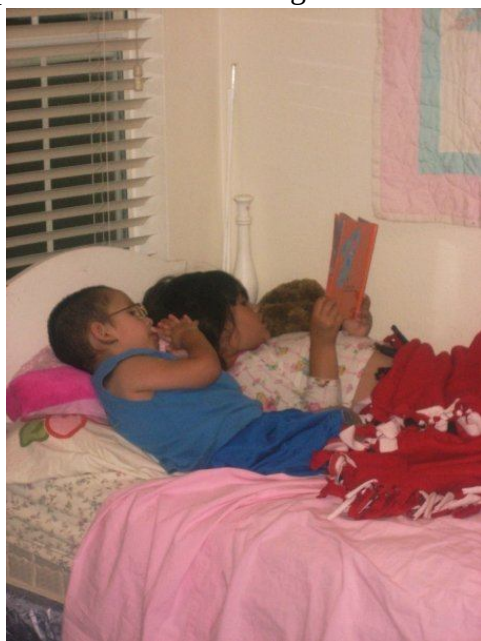
“Sometimes I feel like we have all earned a PhD in the school of life with Lowe syndrome. Do you think anyone would give us a degree or at least an honorary degree in the field of Lowe Syndromology?”

“I feel as if I’ve earned my Master’s degree in disabilities law and advocacy on behalf of my son.”

## XI. THE LOWE SYNDROME ASSOCIATION

In 1983 a handful of parents founded the Lowe Syndrome Association (LSA). The LSA is an international, voluntary, non-profit organization made up of parents, friends, professionals, and others who are interested in Lowe syndrome. We now have members from 22 countries on five continents. The primary purposes of the LSA are to foster communication among families, promote a better understanding of the syndrome, provide medical and educational information, and encourage and support research.

The LSA newsletter, *On the Beam*, is published three times a year. It contains letters from parents and pictures of their children, medical and educational articles, and other helpful and interesting features. The LSA sponsors a web site ([www.lowesyndrome.org](http://www.lowesyndrome.org)) and an e-mail discussion list for members called LSA-Talk. (To subscribe, go to <http://www.lowesyndrome.org/LSA/LSA-Talk.html> and click on the "subscription request form.") An annual parent directory is published for active families. In addition, the LSA sponsors international conferences every two years to bring together families and professionals to exchange information and provide mutual support.



The LSA is a member organization of the Genetic Alliance and the National Organization for Rare Disorders. The LSA receives advice and assistance from its Medical and Scientific Advisory Board, a group of distinguished physicians and scientists who work closely with LSA leaders in areas relating to medical research and information. The LSA has awarded many research grants since 1988 and for a list of grants please go to the LSA website at [www.lowesyndrome.org](http://www.lowesyndrome.org). In addition, the LSA has formed a partnership with the Brain and Tissue Bank of the University of Maryland (See Research, Section V) and encourages its family members to register.

The LSA is primarily supported financially through gifts and donations from LSA members and friends. Occasionally, the LSA receives grants for special projects. LSA friends and members can also help in fundraising. If interested, please contact the LSA for more information. Any person or agency with an interest in Lowe syndrome is invited to join the LSA. The basic annual membership fee is \$15, although larger gifts are encouraged. Donations to the LSA are tax-deductible as charitable contributions, as allowed by law. Parents of affected individuals who cannot afford membership dues may join at no charge.

## **XII. PARENT RESOURCES**

### **BEHAVIOR MANAGEMENT**

Greene, Ross W., PhD (2001). *The Explosive Child: A New Approach for Understanding and Parenting Easily Frustrated, Chronically Inflexible Children* (2nd ed.). New York: HarperCollins.

Greenspan, Stanley I., MD, Chair (1995). *The Challenging Child: Understanding, Raising, and Enjoying the Five "Difficult" Types of Children*. Reading, MA: Addison-Wesley.

Kurcinka, Mary Sheedy (1992). *Raising Your Spirited Child: A Guide for Parents Whose Child is More Intense, Sensitive, Perceptive, Persistent, Energetic*. New York: HarperCollins.

### **EATING AND NUTRITION**

Ernsperger, Lori, PhD, and Tania Stegen-Hanson (2004). *Just Take a Bite: Easy, Effective Answers to Food Aversions and Eating Challenges!* Arlington, TX: Future Horizons.

### **LEARNING, SCHOOLS, AND SPECIAL EDUCATION**

*Individuals with Disabilities Education Improvement Act of 2004*, referred to as *IDEA 04* (Public Law 108-446).

<http://edworkforce.house.gov/issues/108th/education/idea/conferencereport/confrept.htm>

Silver, Larry B., MD (1998). *The Misunderstood Child: Understanding and Coping with Your Child's Learning Disabilities* (3rd ed.). New York: Three Rivers Press.

Smith, Sally L. (1995). *No Easy Answers: The Learning Disabled Child at Home and at School*. New York: Bantam.

### **ORAL-MOTOR DEVELOPMENT**

Frick, Sheila M., Ron Frick, Patricia Oetter, and Eileen W. Richter (1996). *Out of the Mouths of Babes: Discovering the Developmental Significance of the Mouth – a Book Especially for Parents and Other "Grown-ups."* Hugo, MN: PDP Press.

### **SENSORY DIET AND SENSORY-MOTOR ACTIVITIES**

Henry, Diana (1998). *Tool Chest for Teachers, Parents and Students: A Handbook to Facilitate Self-Regulation*. (Accompanies two videos: *Tools for Students: OT Activities for Classroom and Home*, and *Tools for Teachers: an Overview of School Based Occupational Therapy*.) Youngtown, AZ: Henry OT Services.

Henry, Diana and Tammy Wheeler (2001). *Tools for Parents: A Handbook to Bring Sensory Integration into the Home*. Youngtown, AZ: Henry OT Services.

Mauro, Terri. (2006). *THE EVERYTHING PARENT’S GUIDE TO SENSORY INTERGRATION DISORDER. Get the right diagnosis, understand treatments and advocate for your child.*

Williams, Mary Sue, and Sherry Shellenberger. *An Introduction to "How Does Your Engine Run?" The Alert Program for Self-Regulation* (1992), and *Take Five! Staying Alert at Home and School* (2002). Albuquerque: TherapyWorks.

Yack, Ellen, Shirley Sutton, and Paula Aquilla (2002). *Building Bridges through Sensory Integration: OT for Children with Autism and other Pervasive Developmental Disorders* (2nd ed.). Las Vegas: Sensory Resources

### **SENSORY PROCESSING**

Heller, Sharon, PhD (2002). *Too Loud, Too Bright, Too Fast, Too Tight: What to Do If You Are Sensory Defensive in an Overstimulating World.* New York: HarperCollins

Kranowitz Stock, Carol MA and Lucy Jane Miller, PhD, OTR. *The Out-of-Sync Child: recognizing and Coping with Sensory Processing Disorder*

Smith, Karen A., PhD, and Karen R. Gouze, PhD (2004). *The Sensory-Sensitive Child: Practical Solutions for Out-of-Bounds Behavior.* New York: HarperCollins.

Wilbarger, Patricia, and Wilbarger, Julia Leigh (1991). *Sensory Defensiveness in Children Aged 2-12: An Intervention Guide for Parents and Other Caretakers.* Van Nuys, CA: Avanti Educational Programs.

### **SPECIAL NEEDS**

Baker, Bruce L. and Alan J. Brightman. *Steps to Independence: Teaching Everyday Skills to children with Special Needs.*

Freeman, John M. MD, Eileen P.G. Vining, MD. and Diana J. Pillas. *Seizures and Epilepsy in Childhood: A Guide for Parents.*

Greenspan, Stanley I., MD, Chair and Serena Wieder, with Robin Simons (1998). *The Child with Special Needs: Encouraging Intellectual and Emotional Growth.* Reading, MA: Perseus.

Klass, Perri, MD, and Eileen Costello, MD (2003). *Quirky Kids: Understanding and Helping Your Child Who Doesn't Fit In – When to Worry and When Not to Worry.* New York: Ballantine.

### **SPEECH, LANGUAGE, AND COMMUNICATION**

Agin, Marilyn C., MD, Lisa F. Geng, and Malcolm J. Nicholl (2003). *The Late Talker: What to Do if Your Child Isn't Talking Yet.* New York: St. Martin's.

Kashman, Nancy, and Janet Mora (2002). *The Sensory Connection: An OT and SLP. Team Approach*. Las Vegas: Sensory Resources.

Whitney, Rondalyn Varney (2002). *Bridging the Gap: Raising a Child with Nonverbal Learning Disorder*. New York: Perigee

## **VISION**

Brockett, Sally (Summer 1995). Vision therapy: A beneficial intervention for developmental disabilities. *New Developments*, 1(2). Bethesda, MD: Developmental Delay Resources (DDR).

Cirigliano, Suzette (August 2004). About vision problems.  
[www.Vision-Therapy.com](http://www.Vision-Therapy.com)

Cirigliano, Suzette (October 2004). Visual abilities, vision therapy, and the myths of 20/20 vision.  
[www.vision-therapy.com/drtoler/booklet.htm](http://www.vision-therapy.com/drtoler/booklet.htm)

Hickman, Lois, and Rebecca Hutchins, OD (2000). *Seeing Clearly: Fun Activities for Improving Visual Skills*. Las Vegas: Sensory Resources.

Kavner, Richard S., OD (1985). *Your Child's Vision: A Parent's Guide to Seeing, Growing, and Developing*. New York: Simon & Schuster.

Lane, Kenneth A., (1993). *Developing Your Child for Success: Easy to Follow Activities to Develop Children's Perceptual and Motor Skills and Prepare Them for Their Early School years*. Lewisville, TX: Learning Potentials.

## **WEBSITES FOR INFORMATION, EQUIPMENT AND MATERIALS**

ABILITATIONS [www.abilitations.com](http://www.abilitations.com) Therapist-selected rehabilitation products designed to improve the lives of children with differing abilities and specialized physical needs.

ACHIEVEMENT PRODUCTS FOR CHILDREN (800) 373-4699 [www.specialkidszone.com](http://www.specialkidszone.com)  
Products for home, school and clinic that help children achieve their best and make life more comfortable for children with sensory problems, as well as a great variety of sensory-motor products.

### **INDIVIDUAL FAMILY SERVICE PLAN (IFSP)**

An IFSP documents and guides the early intervention process for children with disabilities and their families. [www.education.com/reference/article/Ref\\_Individual\\_Family/](http://www.education.com/reference/article/Ref_Individual_Family/)

LOWE SYNDROME ASSOCIATION ([www.lowesyndrome.org](http://www.lowesyndrome.org))

OT IDEAS, INC. (877) 768-4332 [www.otideas.com](http://www.otideas.com) Tools for OTs and teachers for use in clinics and schools. Special items include children's scissors, tools, and toys to develop hand coordination and fine-motor and visual-motor skills.

POCKET FULL OF THERAPY, INC. (800) PFOT-124 [www.pfot.com](http://www.pfot.com) Therapeutic equipment and fun materials and toys for therapists, teachers, and parents to use to motivate children with special needs.

SENSORY COMFORT (888) 436-2622 [www.sensorycomfort.com](http://www.sensorycomfort.com) Sensory-friendly products to make life more comfortable for children and adults with sensory processing differences.

SENSORY RESOURCES ([www.SensoryResources.com](http://www.SensoryResources.com)) and Special Needs Project ([www.SpecialNeeds.com](http://www.SpecialNeeds.com)) offer extensive lists of books.

SPECIAL NEEDS PROJECT (800) 333-6867 [www.specialneeds.com](http://www.specialneeds.com) Resource for disability-related information, including books on SPD, autism, Asperger syndrome, and learning disabilities, with many translated into Spanish.

THERAPRO (800) 257-5376 [www.theraproducts.com](http://www.theraproducts.com) Therapeutic equipment and toys for sensory processing, including unique kits and oral-motor skills.

INFORMATION PROVIDED BY INDIVIDUAL WEBSITES SHOULD NOT BE TAKEN AS MEDICAL ADVICE. THE INFORMATION GATHERED HERE IS SO YOU CAN MAKE AN INFORMED DECISION IN PARTNERSHIP WITH YOUR MEDICAL PROFESSIONAL.

### XIII. GLOSSARY OF COMMON MEDICAL TERMS IN LOWE SYNDROME

**Acidosis.** A condition of acid-base imbalance characterized by a body pH level that is lower than normal.

**Amino acids.** A group of 20 different kinds of small molecules that link together in long chains to form proteins. Often referred to as the "building blocks" of proteins.

**Amniocentesis.** Prenatal diagnosis method using cells in the amniotic fluid for genetic or biochemical studies.

**Animal model.** A laboratory animal useful for medical research because it has specific characteristics that resemble a human disease or disorder. Scientists can create animal models, usually laboratory mice, by transferring new genes into them.

**Antiepileptic Drugs (AEDs).** Medications used to control seizures.

**Buphthalmos.** Abnormal enlargement of the eye caused by increased pressure (glaucoma).

**Carrier.** A person whose genetic make-up includes the gene for a specific condition but who does not have the condition.

**Cataract.** Clouding of the lens of the eye.

**Chromosome.** Structures in the nucleus of a cell which are sets of linear DNA on which the genes are arranged, carrying all the instructions for a species.

**Congenital.** Any trait or condition that exists from birth.

**Cornea.** The transparent part of the eyeball that covers the iris and pupil.

**Creatinine.** A waste product which can be measured in the blood to determine kidney function.

**Cryptorchidism.** Undescended testes at birth.

**CT scan.** (Sometimes referred to as CAT scan) Computed tomography, an X-ray technique that uses a computer to construct images of the body.

**CVS (Chorionic Villus Sampling).** A prenatal test done at 9-10 weeks.

**Cysts.** Fluid-filled sacs.

**Dialysis.** A method for removing waste such as urea from the blood when the kidneys can no longer do the job. The two types of dialysis are: hemodialysis and peritoneal dialysis. In hemodialysis, the patient's blood is passed through a tube into a machine that filters out waste products. The cleansed blood is then returned to the body. In peritoneal dialysis, a special solution is run through a tube into the peritoneum, a thin tissue that lines the cavity of the abdomen. The body's waste products are removed through the tube.

**DNA (Deoxyribonucleic Acid).** The substance of heredity; the primary genetic material of all cells which tells the cells what to do and when to do it. DNA is the blueprint for all of the structures and functions of a living being.

**EEG (electroencephalography).** A neurological test that measures brain waves to evaluate seizure disorders.

**Enzyme.** A special type of protein that helps the body's chemistry work better and more quickly by speeding up a chemical reaction or causing a chemical change in another substance.

**Fanconi Syndrome.** A condition seen in several diseases (including Lowe syndrome) in which substances filtered by the kidney are excreted rather than reabsorbed due to abnormal tubules.

**Gene.** The fundamental unit of heredity. A gene is the position on a chromosome where a specific DNA sequence, or allele, resides in the cells and mitochondria. A gene contains the code

for a specific product such as an enzyme.

**Genetic Counselor.** A medical professional (not a physician) specializing in working with patients and families with genetically inherited conditions. Genetic counseling may include a discussion and analysis of a person's family tree and testing procedures.

**Geneticist.** A geneticist is a scientist and/or physician specializing in the study of genes and in the treatment of genetic disorders.

**Glaucoma.** An eye disease associated with increased pressure within the eye. Glaucoma can damage the optic nerve and cause impaired vision and blindness.

**Glomeruli.** Part of the kidney in which filtering takes place.

**Golgi Apparatus.** A specific part of the cell that is active in the modification and transport of proteins.

**G-Tube (Gastrostomy Tube).** A method to facilitate feeding in which a tube is surgically placed directly into the stomach, through the abdominal wall.

**Hernia.** The protrusion of part of an organ or tissue through an abnormal opening.

**Hypermobility.** Greater than normal range of movement of joints.

**Hypotonia.** Poor or low muscle tone, such as seen in "floppy babies."

**Inborn errors of metabolism.** Inherited diseases resulting from alterations in genes that code for enzymes.

**Keloid.** A thick scar resulting from excessive growth of fibrous tissue.

**Kidneys.** Two organs in the lower back that clean waste and poisons from the blood and pass them out of the body as urine. The kidneys are shaped like two large beans, and they act as the body's filter. They also control the level of some chemicals in the blood such as hydrogen, sodium, potassium, and phosphate.

**L-Carnitine.** A small molecule protein responsible for the transport of long chain fatty acids into mitochondria.

**Magnetic Resonance Imaging (MRI).** An imaging technique in which magnetic energy is used to examine tissues in the body, and the information is used by a computer to create an image.

**Metabolite.** Product of metabolism.

**Mutation.** A change (in the number, arrangement, or molecular sequence) in the sequence of DNA coding in a gene.

**Nephrocalcinosis.** Calcium deposits in kidney tissue.

**Nephrolithiasis.** Calcium deposits in the urine collecting system of the kidney (kidney stones).

**Nephrologist.** A medical doctor who sees and treats people with kidney diseases.

**Neurologist.** A medical doctor who sees and treats people who have problems of the nervous system, the brain, spinal cord and peripheral nerves.

**NG (Nasogastric) Tube.** A method to facilitate feeding in which a tube is placed through the mouth or nose into the stomach.

**NIH (National Institutes of Health).** A U.S. government-supported biomedical research center made up of 25 institutes and centers in Bethesda, Maryland. In recent years Lowe syndrome research has taken place in the National Human Genome Research Institute.

**Nystagmus.** Uncontrollable rhythmical oscillation of the eyes.

**OCRL.** Oculo-cerebro-renal syndrome of Lowe (Lowe syndrome)

**Ophthalmologist.** A physician who diagnoses and treats people with eye problems or diseases.

**Prenatal.** Before birth.

**Prenatal diagnosis.** Examining fetal cells taken from the amniotic fluid, the primitive placenta

(chorion), or the umbilical cord for biochemical, chromosomal, or gene alterations.

**Prognosis.** Telling a person now what is likely to happen in the future because of having a disease.

**Reflux (Gastroesophageal Reflux or GER).** A condition in which the sphincter muscle at the top of the stomach does not stay shut, allowing food or liquids to come back up the esophagus.

**Renal.** A term that means having something to do with the kidneys.

**Rickets.** Soft bones.

**Scoliosis.** Curvature of the spine.

**Seizures.** Disturbances of brain function, manifested as episodic impairment or loss of consciousness, abnormal often jerky movement, or sensory disturbances. Caused by disturbances in the electrical activity of the brain.

**SGOT.** A liver enzyme; lab values are frequently high in Lowe syndrome even in the absence of liver disease.

**Strabismus.** Crossed eyes.

**Syndrome.** A collection of many symptoms and signs associated with a single disease.

**Tubule.** Part of the kidney in which reabsorption takes place.

#### XIV. MEDICAL AND SCIENTIFIC REFERENCES

**Following is a list of papers published on Lowe Syndrome:**

Attree O, Olivos IM, Okabe I, Bafley LC, Nelson DL, Lewis RA, McInnes RR, Nussbaum RL (1992): *The Lowe's oculocerebrorenal syndrome gene encodes a protein highly homologous to inositol polyphosphate-5-phosphatase*. Nature 358:239-242.

Attree O, Olivos IM, Okabe I, Bailey LC, Nelson DL, Lewis RA, McInnes RR, Nussbaum RL. (1992) *The Lowe's oculocerebrorenal syndrome gene encodes a protein highly homologous to inositol polyphosphate-5-phosphatase*. Nature. 16;358(6383):239-42.

Bernard DJ, Nussbaum RL. (2010) *X-inactivation analysis of embryonic lethality in Ocr1 wt/-; Inpp5b-/- mice*. Mamm Genome. 21(3-4):186-94.

Chamas LR, Bemardini I, Rader D, Hoeg J, Gahl WA (1991): *Clinical and laboratory findings in the oculocerebrorenal syndrome of Lowe, with special reference to growth and renal function*. New England Journal of Medicine 324:1318-1325.

Chamas LR, Gahl WA (1991): *The oculocerebrorenal syndrome of Lowe*. Advances in Pediatrics 38:75-107.

Charnas LR, Nussbaum RL (1994): *Lowe syndrome (The Oculocerebrorenal syndrome of Lowe)*. Chapter 123 in the Metabolic and Molecular Basis of Inherited Disease. (Scriver CR, Beaudet AL, Sly WS, Valle DS, eds.) McGraw-Hill, New York 1994.

Coon BG, Mukherjee D, Hanna CB, Riese DJ 2nd, Lowe M, Aguilar RC. (2009) *Lowe syndrome patient fibroblasts display Ocr1-specific cell migration defects that cannot be rescued by the homologous Inpp5b phosphatase*. Hum Mol Genet. 1;18(23):4478-91.

Cui S, Guerriero CJ, Szalinski CM, Kinlough CL, Hughey RP, Weisz OA. (2010) *OCRL1 function in renal epithelial membrane traffic*. Am J Physiol Renal Physiol. 298(2):F335-45.

De Matteis MA, D'Angelo G. (2007) *The role of the phosphoinositides at the Golgi complex*. Biochem Soc Symp. 2007;(74):107-16

Dressman MA, Olivos-Glander IM, Nussbaum RL, Suchy SF (2000): *Ocr1, a PtdIns(4,5)P<sub>2</sub> 5-phosphatase, is localized to the trans-golgi network of fibroblasts and epithelial cells*. Journal of Histochemistry & Cytochemistry 48:179-189.

Erb BC, Velázquez H, Gisser M, Shugrue CA, Reilly RF (1997): *cDNA cloning and localization of OCRL-1 in rabbit kidney*. American Journal of Physiology 273 (Renal Physiology 42):F790-F795.

Erdmann KS, Mao Y, McCrea HJ, Zoncu R, Lee S, Paradise S, Modregger J, Biemesderfer D, Toomre D, De Camilli P. (2007) *A role of the Lowe syndrome protein OCRL in early steps of the endocytic pathway.* Dev Cell. 13(3):377-90.

Fivush BA, Racusen LC, Christenson MJ, Olson JL (1992): *Acute tubular necrosis associated with Lowe=s syndrome: possible role of rhabdomyolysis.* American Journal of Kidney Diseases 20:396-399.

Gaary EA, Rawnsley E, Marin-Padilla JM, Morse CL, Crow HC (1993): *In Utero detection of fetal cataracts.* American Institute of Ultrasound in Medicine 4:234-236.

Harrison M, Odell EW, Sheehy EC (1999): *Dental findings in Lowe syndrome.* Pediatric Dentistry 21:425-428.

Hayashi Y, Hanioka K, Kanomata N, Imai Y, Itoh H (1995): *Clinicopathologic and molecular-pathologic approaches to Lowe=s syndrome.* Pediatric Pathology and Laboratory Medicine 15:389-402.

Huttner IG, Strahl T, Osawa M, King DS, Ames JB, Thorner J. (2003) *Molecular interactions of yeast frequenin (Frq1) with the phosphatidylinositol 4-kinase isoform, Pik1.* J Biol Chem. 14;278(7):4862-74.

Jacobs D., Knight C., and Dolinsky Z., (2010): *Report on the Lowe Syndrome Comprehensive Survey - 2008.* Dallas, Texas: Lowe Syndrome Association.

Kenworthy L, Park T, Charnas LR (1993): *Cognitive and behavioral profile of the oculocerebrorenal syndrome of Lowe.* American Journal of Medical Genetics 46:297-303.

Kenworthy L., Charnas L (1995): *Evidence for a discrete behavioral phenotype in the oculocerebrorenal syndrome of Lowe.* American Journal of Medical Genetics 59:283-290.

Lahr TF, Record RD, Hoover DK, Hughes CL, Blazer-Yost BL. (2000) *Characterization of the ion transport responses to ADH in the MDCK-C7 cell line.* Pflugers Arch. 439(5):610-7.

Leahey A-M, Charnas LR, Nussbaum RL (1993): *Nonsense mutations in the OCRL-1 gene in patients with the oculocerebrorenal syndrome of Lowe.* Human Molecular Genetics 2:461-463.

Lewis R (1993): *Family planning: what do we do now?* On the Bearm, newsletter of the Lowe Syndrome Association 12/3:7-9.

Lewis RA, Nussbaum RL, Brewer ED. *Lowe Syndrome.* In: Pagon RA, Bird TC, Dolan CR, Stephens K, editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-.2001 Jul 24 [updated 2008 Mar 12].

Lichter-Konecki U, Farber LW, Cronin JS, Suchy SF, Nussbaum RL. (2006) *The effect of missense mutations in the RhoGAP-homology domain on ocr1 function*. Molecular Genetics and Metabolism 89(1-2):121-8.

Lin T, Lewis RA, Nussbaum RL (1999): *Molecular confirmation of carriers for Lowe syndrome*. Ophthalmology 106:119-122.

Lin T, Orrison BM, Leahey A-M, Suchy SF, Bernard DJ, Lewis RA, Nussbaum RL (1997): *Spectrum of mutations in the OCRL1 gene in the Lowe oculocerebrorenal syndrome*. American Journal of Human Genetics 60:1384-1388.

Lin T, Orrison BM, Suchy SF, Lewis RA, Nussbaum RL (1998): *Mutations are not uniformly distributed throughout the OCRL1 gene in Lowe syndrome patients*. Molecular Genetics and Metabolism 64:58-61.

Loovers HM, Kortholt A, de Groote H, Whitty L, Nussbaum RL, van Haastert PJ. (2007) *Regulation of phagocytosis in Dictyostelium by the inositol 5-phosphatase OCRL homolog Dd5P4*. Traffic. 8(5):618-28.

Mao Y, Balkin DM, Zoncu R, Erdmann KS, Tomasini L, Hu F, Jin MM, Hodsdon ME, De Camilli P (2009) *A PH domain within OCRL bridges clathrin-mediated membrane trafficking to phosphoinositide metabolism*. EMBO J. 28:1831-1842.

McSpadden K, Dolinsky Z, Schroerlucke K (1991): *Report on the Lowe's syndrome comprehensive survey*. West Lafayette IN: Lowe Syndrome Association.

Nussbaum RL, Orrison BM, Jänne PA, Charnas L, Chinault AC (1997): *Physical mapping and genomic structure of the Lowe syndrome gene OCRL1*. Human Genetics 99:145-150.

Olivos-Glander IM, Janne PA, Nussbaum RL (1995): *The Oculocerebrorenal syndrome gene product is a 105-kD protein localized to the Golgi Complex*. American Journal of Human Genetics 57:817-823.

Reilly DS, Lewis RA, Ledbetter DH, Nussbaum RL. (1988) *Tightly linked flanking markers for the Lowe oculocerebrorenal syndrome, with application to carrier assessment*. American Journal of Human Genetics 42(5):748-55.

Reilly DS, Lewis RA, Nussbaum RL. (1990) *Genetic and physical mapping of Xq24-q26 markers flanking the Lowe oculocerebrorenal syndrome*. Genomics. 8(1):62-70.

Satre V, Monnier N, Berthoin F, Ayuso C, Joannard A, Jouk P, Lopez-Pajares I, Megabarne A, Philippe HJ, Plauchu H, Torres ML, Lunardi J (1999): *Characterization of a germline mosaicism in families with Lowe syndrome, and identification of seven novel mutations in the OCRL1-gene*. American Journal of Human Genetics 65:68-76.

Schuske K, Beg AA, Jorgensen EM. (2004) *The GABA nervous system in C. elegans*. Trends Neurosci. 27(7):407-14.

Silver, DN, Lewis RA, Nussbaum RL (1987): *Mapping the Lowe oculocerebrorenal syndrome to Xq24-q26 by use of restriction fragment length polymorphism*. Journal of Clinical Investigation 79:282-285.

Suchy SF, Cronin JC, Nussbaum RL. (2009) *Abnormal bradykinin signalling in fibroblasts deficient in the PIP(2) 5-phosphatase, ocr11*. J Inherit Metab Dis. 32(2):280-8.

Suchy SF, Lin T, Horwitz JA, O'Brien WE, Nussbaum RL (1998): *First report of prenatal biochemical diagnosis of Lowe syndrome*. Prenatal Diagnosis 18:1117-1121.

Suchy SF, Nussbaum RL. (2002) *The deficiency of PIP2 5-phosphatase in Lowe syndrome affects actin polymerization*. Am J Hum Genet. 71(6):1420-7.

Suchy SF, Olivos-Glander IM, Nussbaum RL (1995): *Lowe syndrome, a deficiency of a phosphatidylinositol 4,5-bisphosphate 5-phosphatase in the Golgi apparatus*. Human Molecular Genetics 4(12):2245-2250.

Swan LE, Tomasini L, Pirruccello M, Lunardi J, De Camilli P. (2010) *Two closely related endocytic proteins that share a common OCRL-binding motif with APPL1*. Proc Natl Acad Sci U S A. 23;107(8):3511-6.

Thorner JW (2001) Greasing the wheels of secretory transport. Nature Cell Biol. 3: E196-E198.

Zhang X, Hartz PA, Philip E, Racusen LC, Majerus PW (1998): *Cell lines from kidney proximal tubules of a patient with Lowe syndrome lack OCRL inositol polyphosphate 5-phosphatase and accumulate phosphatidylinositol 4,5-bisphosphate*. Journal of Biological Chemistry 273:1574-1582.



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