

A Parent's Guide

A Guide to Living with ALD (Adrenoleukodystrophy)



Ken, Suzanne, Charlotte, Patrick, & Gavin

With proactive, comprehensive medical care the symptoms of ALD can be managed and give the individual the best quality of life possible.

aldnewbornscreening.org

Letter from an ALD Mom

You will have the constant support and guidance of ALD specialists and other ALD parents. You are not alone.

Dear Parent(s):

This welcome letter is written with much love from a mother who understands all too well how you are feeling in this moment. I have sat where you sit and felt the pain and devastation of having my son diagnosed with Adrenoleukodystrophy (ALD) through Newborn Screening (NBS).

I felt the anguish and fear wash over me, washing away all of my hopes and dreams for my child. It felt like the world was coming to an end. Please let my words comfort and assure you that this is not the end. In fact, it is the beginning. It is the beginning of a journey you will take to ensure the health of your precious child. Early diagnosis through NBS is the key. Knowledge is power.

Life with ALD can be a full, healthy, and normal one. While it will not always be easy, I can assure you that it is absolutely possible. With NBS for ALD being new, and ALD just beginning to be diagnosed in growing numbers, there was little information available to help new parents. This booklet is our way of sharing all that we have learned to help guide you on this journey. I know you are overwhelmed at the thought of doctors' appointments, blood work, and MRIs, which will be a big part of monitoring your child, but all of this is absolutely doable. You will have the constant support and guidance of ALD specialists and other ALD parents. You are not alone.

My story began in March of 2014 when we joyfully welcomed Patrick, our third child and second son. Through NBS, we learned that Patrick was identified as having ALD. Since this is genetic, our older children were immediately tested, and our four year old son, Gavin, was also diagnosed with ALD. While we were devastated, we quickly recognized the blessing and special gift in our precious baby. Thanks to NBS and this early diagnosis, we would have the opportunity to save both our boys.

Today I am the proud mother of boys who are energetic, fun loving, healthy and thriving both academically and athletically, and who will be able to realize their full potential in life. The doctors' appointments, blood work, and MRIs have become a part of life and even embraced by our boys who always seem to find the fun in everything, as children can often do. This will be your son. A diagnosis of ALD in no way takes away from how beautiful and precious your baby is and the joy he brings. Always keep your hopes and dreams for him intact because they will be realized. Have faith, and believe that your story, like mine, will be a positive one.

With love,
Suzanne Flynn

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What is Adrenoleukodystrophy (ALD)?

Adrenoleukodystrophy, or ALD, is a genetic disease that affects 1 in 17,000 people. It is an X-linked genetic disease, which means, it most severely affects boys and men.

Adrenoleukodystrophy, or ALD, is a genetic disease that affects 1 in 17,000 people. It is caused by mutations in ABCD1, a gene located on the X chromosome. X-linked diseases most severely affect boys and men. The result is an inability to breakdown very long chain fatty acids (VLCFAs). ALD involves multiple organs in the body, but most prominently affects the brain and spinal cord. The disease destroys myelin, the protective sheath that surrounds the brain's neurons. Without myelin, nerve cells that allow us to think and to control our muscles no longer function correctly. ALD knows no racial, ethnic, or geographic barriers.

There are different forms of ALD:

- (1) Asymptomatic – patients show no signs or symptoms
- (2) Adrenal Insufficiency – most patients will develop adrenal insufficiency over time
- (3) Cerebral ALD – affects the brain, most often in childhood, but can also occur in adolescence and adulthood
- (4) Adrenomyeloneuropathy (AMN) – begins in adulthood and affects mobility.

Unfortunately, there is no reliable way to predict how the disease will present.

What is myelin (white matter) and why is it so important in the nervous system?

Myelin constitutes the “white matter” of the brain. It consists of fatty acid molecules, and provides the protective covering of the nerve cells, similar to insulation surrounding an electric wire. Myelin is required for the rapid, precise transmission of information to and from neurons throughout the brain and spinal cord. Demyelination is the stripping away of the fatty coating (white matter) that keeps nerve pulses confined and maintains the integrity of nerve signals. This process inhibits the nerves ability to conduct properly, thereby causing neurological deficits. In childhood cerebral ALD, not only do cells undergo demyelination, but there is also an inflammatory response, all of which destroy the brain.

When myelin is damaged, communication is lost during transmission. This results in the loss of voluntary and involuntary functions in the body.

Currently there is no known treatment to reverse damaged myelin, although there are options to manage symptoms. Proactive, comprehensive medical care will allow families and caregivers to give the affected individual the best quality of life possible. Furthermore, through **ALD Newborn Screening**, affected children have the opportunity to benefit from lifesaving treatment, which can halt the disease (see Treatment Section).

What causes ALD? And why does the disease typically impact boys?

ALD is caused by mutations in ABCD1, a gene located on the X chromosome that codes for ALD Protein (ALDP). ALDP functions as a peroxisomal membrane transporter. The transporter is required for the normal turn over, or metabolism, of a special type of fatty acids in the brain and spinal cord. Without the transporter, the normal metabolism of fatty acids does not occur. Therefore, the brain and spinal cord undergo demyelination. Biochemically, individuals with ALD show very high levels of unbranched, saturated, very long chain fatty acids, particularly - the one that has 26 carbon chains called cerotic acid (26:0).

ABCD1 resides on the X chromosome. Boys inherit only one X chromosome, which is passed on from mom. Because boys only have one copy of the gene, when it is mutated, they become susceptible to ALD.

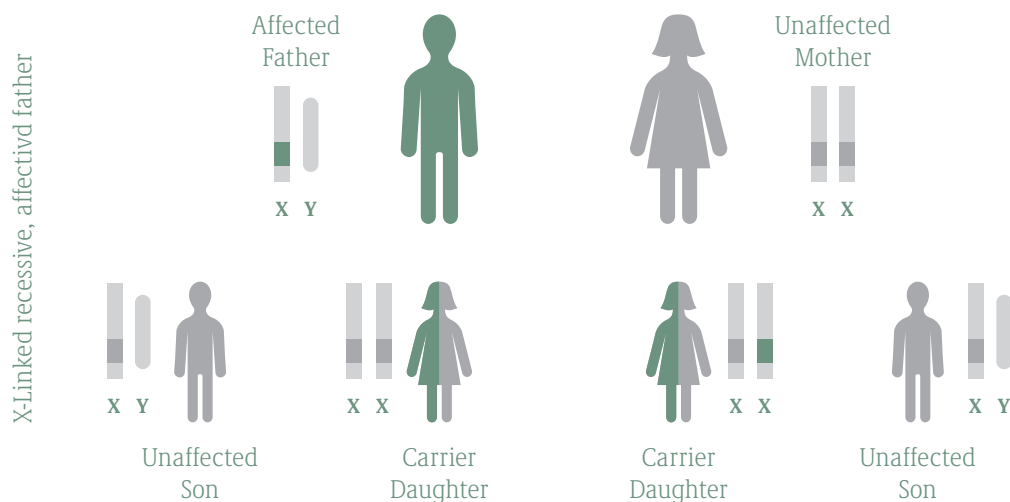
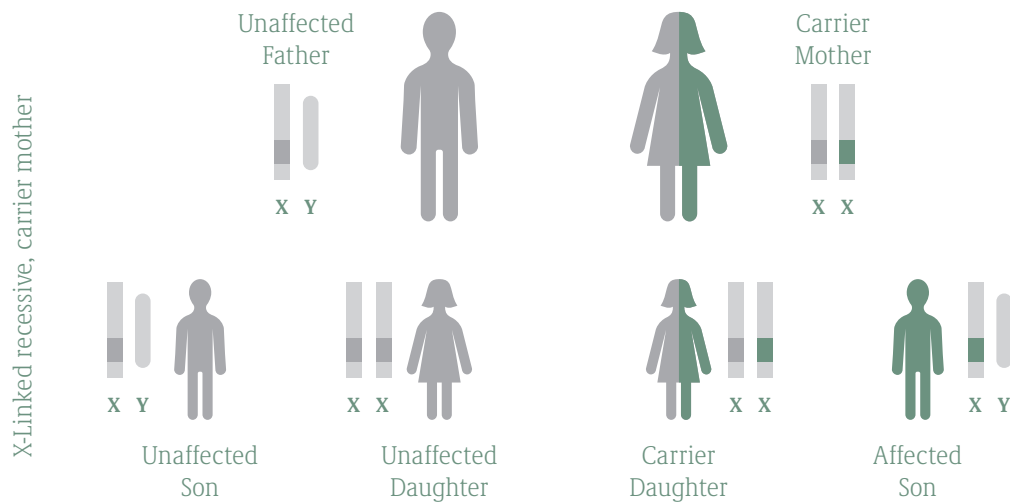
Girls inherit two X chromosomes, one from each parent. The functional copy inherited from dad usually protects female children from the disease. Females with the mutation are traditionally referred to as “carriers”, and can pass the abnormal X chromosome on to offspring. Importantly, the field is evolving, and we are now starting to find that some women experience neurological symptoms later in adulthood. It is possible – but very rare – for girls to inherit 2 copies of the mutation from both parents.



Jack

How do you get ALD?

ALD disease is a genetic, or inherited, disorder. If a mother is a carrier of ALD, there is a 50% chance of passing this on to her children. If a father is a carrier of ALD, he will pass this on to his daughters 100% of the time, but never to his sons.



Spontaneous, or de novo, mutations are another way a baby can inherit ALD. This means that the mother and father are not carriers of ALD, but the mutation of the gene causing ALD happens in utero. Spontaneous mutations arise randomly often during DNA replication.

With proactive, comprehensive medical care the symptoms of ALD can be managed and give the individual the best quality of life possible. Furthermore, through ALD newborn screening, affected children have the opportunity to benefit from lifesaving treatment.

Who else in my family needs to be tested for ALD?

If a mother has ALD, there is a 50% chance of each of her other children also having ALD. This is crucial if the child is male and they should be tested immediately. If there are other female children, they can be tested when they are of childbearing age. Extended family – sisters, brothers, aunts, uncles, nieces, and nephews of the affected parent should also be tested for ALD.

To determine if other children in the family are affected by or carriers of ALD disease, it is best to consult with your genetic counselor or your child's primary care physician.

You can also request a blood spot card from the Kennedy Krieger Institute. The requisition form may be downloaded at <http://genetics.kennedykrieger.org/forms/pero1.pdf>. Results are available within 7 to 10 days, unless there are special circumstances.

Contact information related to testing:

Kennedy Krieger Institute Genetics Laboratory - Peroxisomal Diseases Section
707 North Broadway
Baltimore, MD 21205 USA
Phone: +1.443.923.2760
Fax: +1.443.923.2755

How is ALD diagnosed?

ALD is diagnosed through a blood test, which analyzes the amount of very long chain fatty acids, which are elevated in ALD.

An MRI diagnoses cerebral ALD.

Although newborn screening for ALD is available in some states it is NOT a diagnostic test. Newborn screening can, however, lead to a proper and early diagnosis upon confirmatory testing.

ALD Newborn Screening is currently active in 16 states: New York, Connecticut, California, Minnesota, Pennsylvania, Washington, Tennessee, Florida, Nebraska, Illinois, Texas, Rhode Island, Vermont, Kentucky, Washington, D.C., Michigan, and Delaware. More states are slated to come on board in the coming year. If you currently live in a state which is not testing or have extended family living in a state that is not testing, please contact the Kennedy Krieger Laboratory, listed above, for a blood spot card.

How does ALD affect the individual?

ALD is a multisystem disease, but most prominently affects both the central and peripheral nervous systems, which are responsible for all of the body's voluntary and involuntary functions. Damage to the brain results in blindness, seizures and hyperactivity. Other effects include problems with speaking, listening, and understanding verbal instructions. Damage to the spinal cord results in the loss of the ability to walk and maintain normal breathing.

The most severely affected tissues outside of the nervous system are the adrenal cortex, and the Leydig cells in the testes. Damage to the adrenal cortex results in adrenal insufficiency or Addison's Disease. Damage to the testes results in infertility.

The rate of progression depends on what form of the disease the individual has.



Kelly & Jalen

Through ALD newborn screening, affected children have the opportunity to benefit from lifesaving treatment.

*Courtney, Katie
& Demitri*



What are the different forms of ALD?

ALD has different faces with some individuals presenting during childhood and others not until later in life during adult years.

Childhood Cerebral Demyelinating ALD

Childhood Cerebral ALD (CCALD) is the most devastating form of ALD, representing about 35% of all cases. It is characterized by an inflammatory process that destroys the myelin, causing relentless progressive deterioration. It generally occurs between the ages of four and ten years old. Normal, healthy boys suddenly begin to regress. At first, they may simply show minor behavioral problems, such as withdrawal or difficulty concentrating, vision problems, or start to have coordination issues. Gradually, as the disease spreads throughout the brain, their symptoms grow worse, including blindness, deafness, seizures, loss of muscle control, and progressive dementia. This relentless downward spiral leads to a vegetative state or death usually within 2-5 years of diagnosis.

Adrenomyeloneuropathy

The majority of patients with ALD will experience the adult form of the disease known as Adrenomyeloneuropathy (AMN). It begins to affect men in their 20s and 30s, and progresses slowly. As people (men and women) with AMN age, more become affected. AMN affects the longest nerve fibers of the spinal cord. These fibers conduct signals from the brain to the legs and the bladder and back to the brain. Patients can experience some of the following symptoms:

► **Walking and balance problems**

These problems can begin as general leg weakness and stiffness and progress to walking difficulty. Some people have more problems with their balance. Leg weakness and balance problems can change the way a person walks. Mobility devices, such as canes, walkers, and wheelchairs may be needed over time.

► **Pain, numbness, or tingling in the legs**

► **Mild to moderate weakness of the arms/hands**

► **Urinary disturbances or incontinence and bowel urgency or incontinence**

► **Sexual dysfunction, or the inability to obtain or maintain an erection**

In approximately one third of these patients the brain also becomes involved. Men can undergo the same mental and physical deterioration as previously described in the boys with CCALD. The progress of the disease is slower, usually declining to a vegetative state and/or death in 5 years or longer.

Addison's Disease (Hypoadrenocorticism)

90% of boys and men with ALD/AMN have Addison's disease, a disorder of the adrenal gland; in about 10% of ALD cases, this is the only clinical sign of the disorder. The adrenal glands produce a variety of hormones that control levels of sugar, sodium, and potassium in the body, and help it respond to stress. In Addison's disease, the body produces insufficient levels of the adrenal hormone, which can be life threatening. Fortunately, this aspect of ALD is easily treated, simply by taking a steroid pill daily (and adjusting the dose in times of stress or illness).

Female ALD

Although women who carry the ALD gene mutation do not generally develop the brain disease itself, some display mild symptoms of the disorder. These symptoms usually develop after age 35, and primarily include progressive stiffness, weakness, or paralysis of the lower limbs, numbness, pain in the joints, and urinary problems.

► **Walking and balance problems**

These problems can begin as general leg weakness and stiffness and progress to walking difficulty. Some people have more problems with their balance. Leg weakness and balance problems can change the way a person walks. Mobility devices, such as canes, walkers, and wheelchairs may be needed over time.

► **Pain, numbness, or tingling in the legs**

► **Mild to moderate weakness of the arms/hands**

► **Incontinence**



*Anthony, Kelly,
Jalen & Kylar*

Monitoring

Neurology

Monitoring will consist of a multidisciplinary team consisting of your pediatrician, neurologist and endocrinologist. You may decide to see a dietitian as well. Following is a list of specialists and a description of how often and the tests they will be performing.

MRI Monitoring for CCALD

A neurologist is crucial in the care of your son. MRI of the brain is necessary in order to observe any changes to the brain, other than the blood test which confirms the VLCFA which confirms your child has an ALD Diagnosis, MRI will diagnose if a lesion is present and next steps in the treatment of preventing the progression of ALD. MRI is crucial in order to observe if ALD has been triggered. Before the onset of physical symptoms, a lesion can only be identified through MRI. It is extremely important to follow the approved guidelines for how often your son will have an MRI.

What is an MRI scan?

An MRI or Magnetic Resonance Imaging is a medical imaging technique used in radiology to form pictures of the brain. An MRI or Magnetic Resonance Imaging scanner is a machine that generates magnetic fields (the same magnetic field found on fridge magnets! But a lot stronger). The magnetic field “spins” water inside the body, and these spins generate the images of the brain. There is no radiation involved (unlike CAT or CT scans).

What is a contrast agent, GAD or gadolinium, and what does it have to do with ALD?

A contrast agent is a fluid that is injected into the patient’s IV during the MRI scan. For a short time, it is taken up by different parts of the body, and allows for greater differences to be seen on MRI scans, including inflammation.

Neurology

Role of Contrast Enhancement

If the contrast agent is also seen in a brain lesion (“contrast-enhancing”), it confirms the presence of an inflammatory Cerebral ALD. If the contrast agent is not seen in the lesion, it indicates that the lesion is inactive. This is very important in deciding to initiate life-saving therapies such as stem cell transplantation. Active, inflammatory Cerebral ALD requires urgent treatment.

Why does my son need multiple MRIs?

In ALD, if a lesion is seen on MRI, the patient is diagnosed with Cerebral ALD. Cerebral ALD occurs most often between the ages of 3 and 12 years old, this is why we need to actively monitor between these ages to make sure changes are not missed.

When and how often does your son need an MRI?

New guidelines have been published by a national work group of ALD experts. Surveillance Recommendations are summarized in the table here:

Table 1: MRI Surveillance Recommendations

Age	MRI Frequency	Contrast Administration Recommended?*
1 - 1.5 years old	Once	No
2 - 2.5 years old	Once	No
3 - 12 years old	Every 6 months	Yes, unless real time reading is available.
12+ years old	Yearly	Lesion Positive? Yes Lesion Negative? No
<i>*If, at any time a lesion appears, a repeat MRI with Contrast should be repeated 3 months later</i>		

Neurology

Surveillance Guidelines summarized in text form here:

- The 1st MRI Scan should be performed between 12-18 months old. This time period is variable, to allow the family some flexibility in setting up a schedule. Contrast is not needed at this time point as the likelihood of a brain lesion developing is lower in this age group.
 - The 2nd MRI Scan should be performed 12 months after the first scan. Contrast is not needed at this time point as the likelihood of a brain lesion developing is lower in this age group.
 - From the ages of 3 through 12 an MRI Scan should be performed every 6 months. Contrast should be administered (unless your child is at a center with 'real-time reading' capability[1]) as the likelihood of developing a brain lesion is highest in this age group.
 - From the age of 12 and up an MRI Scan should be performed annually. Contrast is not needed from this point onwards unless there is evidence of a lesion on a previous MRI.
 - If a lesion is apparent on MRI at any time, a repeat MRI should be performed with contrast within 3 months.
 - The MRI's should ALWAYS be reviewed by an ALD specialist.
(List of ALD specialists is listed at the end of this brochure)
-

[1] Real-time Reading

Some MRI centers have real-time reading capacities. A doctor with a specialization in radiology is present, will look at the scan while the patient is still in the machine, and will administer contrast only if a lesion is present. The purpose of real-time reading is to limit exposure to contrast and sedation time.

Prior to the MRI

1. Check in with your endocrinologist. Ask if your child will need stress dose steroids during the procedure.
2. "MRI Clearance": Many medical institutions require a physical exam by a pediatrician to "clear" the patient for an MRI. The physical exam is usually submitted to the office within 6 months of the MRI. It is also helpful to have your pediatrician review your child's routine metabolic labs (including kidney function: BUN and Creatinine) prior to the MRI.
3. "NPO prior to MRI": If your son requires sedation, expect that he will not be able to eat or drink prior to the MRI. The amount of time is usually 2-6 hours depending on the anesthesiologist's determination.

Neurology

Tips from Parents of Boys with ALD: What to do to make undergoing MRIs easier on you and your son

1. Practice wearing a play medical face mask at home with your son prior to the MRI so it is not foreign when it comes time for sedation. Making it a game beforehand will allow your child to be much more comfortable when it comes time to wear the mask in the hospital.
2. There are YouTube videos which replicates the noise of the MRI machine. Look under “MRI Sounds”. It would be useful to listen to this and make it a game with your child so they are not frightened by the noise.
3. Practice lying still at home prior to the MRI. Again, making it a game and practicing beforehand will make it familiar, and much easier for the boys to stay still during the actual MRI.
4. For younger children, it may be helpful to wake them up early on the day of the MRI and to keep them awake (no naps) such that they arrive sleepy to the scan. It will be easier to sedate the patients if needed, or allow them to sleep through the MRI.
5. If available at your local institution, utilize the “Child Life” staff. These are staff members specifically hired and trained to make the medical experience for pediatric patients easier and more fun.
6. Ask if your local institution can play music in the MRI scanner. Some facilities allow the parents to talk to their children through a microphone as well. Lastly, some facilities have movie goggles. They can play a movie for your son during the scan.

What to expect after the MRI

If your son required sedation, recovery time can range from 30 to 90 minutes. They will recover (i.e. slowly awaken from sleep) in the MRI suite in a bed under monitoring by a nurse. Each boy will wake up differently. While transitioning from sleep to fully awake, some patients can be disoriented or cry. This is transient, is usually not associated with pain, and patients do not remember this transition period.

Quick FAQs

Why does my son need MRI scans?

To routinely detect for cerebral disease, which is potentially life-threatening.

Is there radiation associated with MRI?

There is no radiation from MRI scans.

Will the child have to be sedated in the scanner?

Until the child can lie in the scanner for 20 minutes without moving, he will have to be sedated.

Are there risks from repeated MRI sedations?

Recent published data suggests that repeated exposure to anesthesia (sedations) does not have any adverse effect on IQ later in life. (<http://anesthesiology.pubs.asahq.org/article.aspx?articleid=2679328>)

Are there risks associated with gadolinium (the contrast agent)?

In healthy people, there are no known adverse events associated with receiving gadolinium. In patients with pre-existing Kidney Disease/Renal Failure, there is a known risk of developing nephrogenic systemic sclerosis. (More information from the FDA here: <https://www.fda.gov/Drugs/DrugSafety/ucm589213.htm>)

What happens if he has a lesion?

A repeat MRI should be repeated in 3 months with contrast.

What happens if I miss or forget an MRI appointment or forget to do a scan?

You should schedule a scan as soon as possible, following the timeline in the MRI guidelines.

What is the most important thing I can do for a child with ALD as a family member?

Make a personal schedule of your doctor appointments and MRI scan dates.

1. Schedule appointments with your providers ahead of time. In some cities there may be a longer time (months) needed to schedule an appointment, try to do this in advance.
2. Ask your neurologist to reach out to an ALD expert to discuss your son's case and MRI scans.

Endocrinology

Endocrinologists

Are doctors who specialize in glands and the hormones they make. They deal with metabolism, or all the biochemical processes that make your body work, including how your body changes food into energy and how it grows.

Adrenal Insufficiency in Adrenoleukodystrophy

Males with adrenoleukodystrophy (ALD) are at high risk for primary adrenal insufficiency. The largest studies suggest roughly 80 to 86% of males with ALD will develop adrenal insufficiency in their lifetime, with the majority developing adrenal insufficiency during childhood. Because of newborn screening, adrenal insufficiency can be detected before a child has significant symptoms and treated with standard therapies.

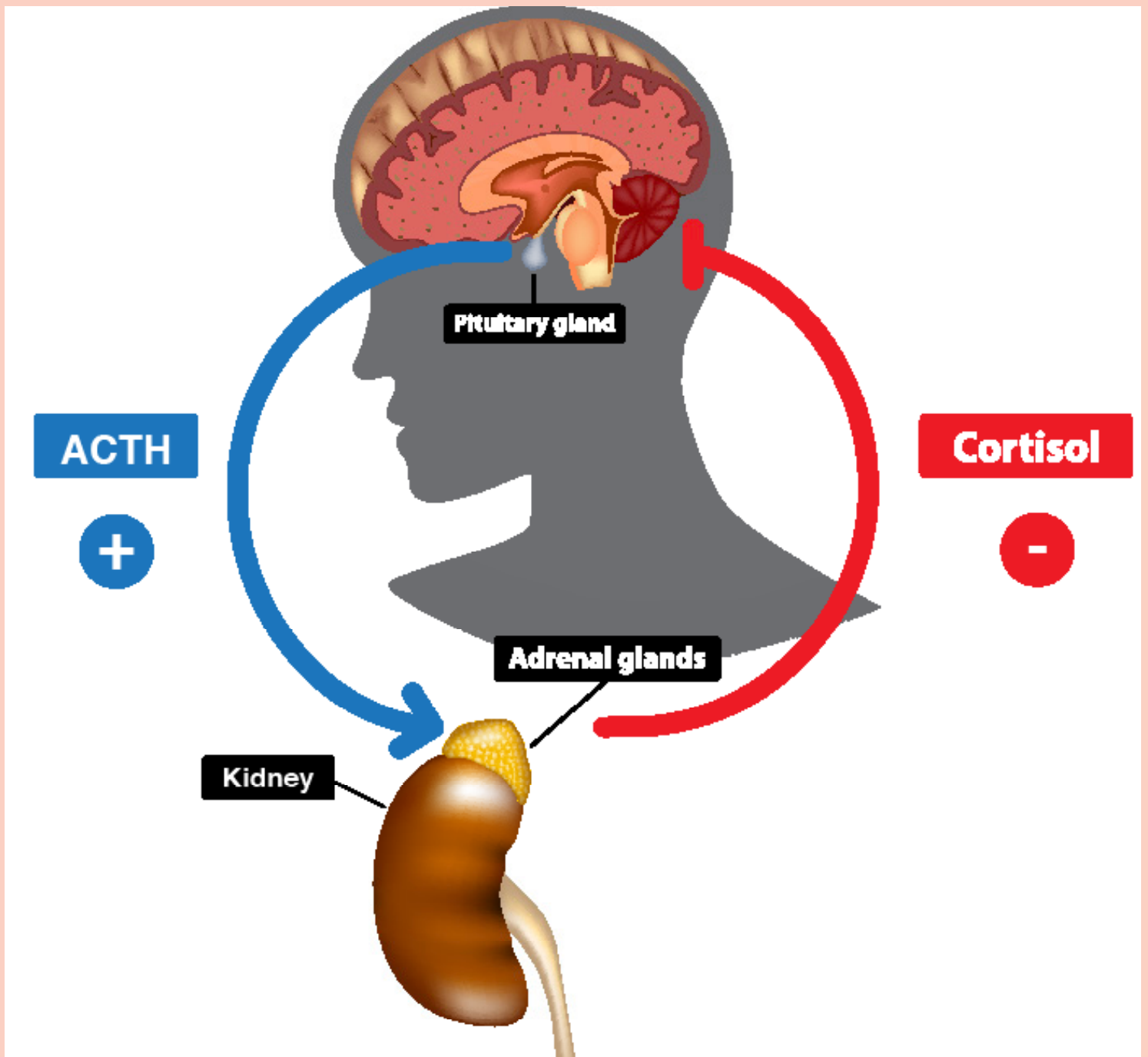
What do the adrenal glands usually do and how does ALD affect the adrenal glands?

The adrenal glands sit on top of the kidneys and are under the control of the pituitary gland, which makes ACTH. The adrenal cortex is responsible for making several classes of hormones, including mineralocorticoids (which regulate salt balance in the body), glucocorticoids (which help maintain blood pressure and blood sugar levels during stress) and androgens (which promote the development of secondary sexual characteristics, including pubic hair). In ALD, the elevated very long-chain fatty acids preferentially accumulate in the adrenal cortex and disrupt the production of glucocorticoids (usually measured as cortisol), androgens and less often mineralocorticoids.

What are the signs and symptoms of adrenal insufficiency?

The signs and symptoms of adrenal insufficiency tend to be subtle and challenging to identify. The goal is to detect the adrenal insufficiency before the patient develops symptoms (see screening recommendations below), but caregivers should be aware of common signs and symptoms and alert the child's medical provider if signs or symptoms develop. The table below lists common signs and symptoms of primary adrenal insufficiency. Acute symptoms of adrenal insufficiency crisis frequently occur at times of significant stress, including infection or trauma.

Chronic Signs & Symptoms of Adrenal Insufficiency	Acute Signs & Symptoms of Adrenal Insufficiency Crisis
Hyperpigmentation (commonly seen in the genitals, nipples, palms and soles, gums, posterior helix of the ear and scars)	Vomiting/Nausea/Abdominal Pain
Fatigue	Low Blood Pressure (Hypotension)
Poor Appetite	Low Blood Sugar (Hypoglycemia)
Weight Loss or Lack of Weight Gain	Dehydration
Intermittent Abdominal Pain/Nausea	Dizziness/Loss of Consciousness
Loss/Lack of Pubic Hair and Underarm Hair	Change in Mental Status/Delirium
Salt-Craving (occurs with mineralocorticoid deficiency)	



Endocrinology

How should males with ALD be monitored for development of adrenal insufficiency?

The Pediatric Endocrine Society helped establish guidance for screening in order to detect adrenal insufficiency early in males with ALD [Regelmann MO, et al. Adrenoleukodystrophy: Guidance for Adrenal Surveillance in Males Identified by Newborn Screen. J Clin Endocrinol Metab. 2018;103(11):4324-4331]. Because ALD has only recently been added to newborn screening, and there is no known way to predict exactly when adrenal insufficiency will develop in boys with ALD, the recommendations are to start screening shortly after diagnosis is confirmed and to monitor every 3-4 months for the first two years of life and then every 4-6 months thereafter. Screening typically involves measuring cortisol (the glucocorticoid made by the adrenal gland) and ACTH (the hormone that stimulates the production of cortisol). Sometimes the endocrinologist will also recommend a cosyntropin (synthetic ACTH) stimulation test to help better understand the adrenal glands' ability to respond to stress. Plasma renin activity and electrolytes are the screening tests for mineralocorticoid deficiency. Because mineralocorticoid deficiency is less frequent in ALD, screening is typically recommended every 6 months during infancy and every 6-12 months or sooner if symptoms of salt-craving are noted in older children.

The reported incidence of adrenal insufficiency in females with ALD is less than 1% and routine monitoring for adrenal dysfunction is not recommended (but if a female has signs or symptoms of adrenal insufficiency, she should be checked).

How is adrenal insufficiency diagnosed?

Adrenal insufficiency is typically diagnosed when the cortisol is low and the ACTH is elevated. There is significant debate in the pediatric endocrine community regarding the exact cutoff values for cortisol and ACTH to define adrenal insufficiency. The reason for debate is there are poor normal reference range data in young children and during the first two years of life, the normal secretion of ACTH and cortisol is still developing, so relatively low cortisol levels or ACTH values just slightly above the established adult reference ranges may be normal for a child. An expert in pediatric endocrinology should be consulted to help interpret test results and confirm the diagnosis. The diagnosis of adrenal insufficiency is made based on a combination of laboratory tests, as well as an assessment for signs and symptoms of adrenal insufficiency. In cases of borderline test results, it may be reasonable to consider treating with hydrocortisone during times of stress but to hold off on starting daily treatment (see discussion of treatment below).

Once adrenal insufficiency is diagnosed, what should be expected?

The standard treatment for adrenal insufficiency is steroid replacement. In most growing children, hydrocortisone is the preferred medication to replace cortisol. Hydrocortisone is usually taken by mouth three times per day. During times of stress (fever, illness, trauma, anesthesia), the dose of hydrocortisone needs to be increased to mimic the normal rise in cortisol during stress in order to maintain normal blood pressure and blood sugar. If a child is experiencing severe stress and is unable to take hydrocortisone by mouth, hydrocortisone is administered as an injection, either into the muscle or through an IV. Caregivers are trained to give the intramuscular hydrocortisone once a child has been diagnosed with adrenal insufficiency. The pediatric endocrinologist will also provide you with emergency care instructions for home and school/daycare. Hydrocortisone is generally a safe medication when prescribed to replace the cortisol the adrenal glands should be making. Hydrocortisone is initially dosed based on the child's weight and height and then adjustments to the dose are made based on follow up assessments of growth, symptoms and additional laboratory tests. Once on replacement hydrocortisone therapy, your child should have routine follow up with a pediatric endocrinologist, typically every 3-6 months. If mineralocorticoid deficiency develops, the treatment is fludrocortisone (a mineralocorticoid), typically once daily, as well as salt replacement, as necessary.

Lifestyle, Diet & Exercise

Eating healthy is important to overall well being. Generally, there are no diet restrictions. The general recommendation is to follow the American Heart Association Diet or the Mediterranean Diet. Please consult with your primary care physician for any specific questions pertaining to your child.



Download this helpful guide by visiting:

www.heart.org

Physical Activity

There is evidence that significant head injury may initiate cerebral disease. Appropriate equipment and supervision is needed and parents should take all precautions, make sure to use the appropriate safety equipment when participating in football, boxing, soccer or sports where head injury may be a factor.

Parents should be diligent in having their boys wear helmets when riding a bicycle, skiing, etc

It is recommended that your child avoid participating in sports that are known to cause significant head injury and to always wear protective headgear when enjoying sports and activities.

<https://www.ncbi.nlm.nih.gov/m/pubmed/19945717/>



Ethan

Lorenzo's Oil

The 1992 movie "Lorenzo's Oil" based on the true story of the Odone family and their quest to find a cure for their son, Lorenzo, who was diagnosed with ALD at the age of 6. Augusto Odone, Lorenzo's father, developed an oil to treat Adrenoleukodystrophy. The oil is still considered experimental and may have some benefit in normalizing the VLCFA (Very Long Chain Fatty Acids), which may prevent the childhood cerebral form of ALD. Lorenzo's Oil is not helpful for boys that are symptomatic. While it may offer some preventative effect against cerebral disease, this has not been clearly demonstrated. If it is to be used, it is best used on boys between the ages of 2-10 who are asymptomatic and only under a physician's supervision.

For more information:

Adrenoleukodystrophy: Biochemistry and management

The efficacy of Lorenzo's Oil

Newborn Screening and Expanded Access: What does this mean for Lorenzo's Oil?

Dr. Gerald Raymond, professor of Genetic Medicine and Neurology at Johns Hopkin, Baltimore, MD has created an educational webinar on adrenoleukodystrophy and Lorenzo's Oil for professionals.

Please go to: <https://www.nutricialearningcenter.com/en/metabolics/webinar/ald-and-lorenzos-oil-an-update/>

Lorenzo's Oil may be purchased for individual importation through WEP Clinical:

Yasmin Khera
Outreach Manager
951 Aviation Pkwy Suite 200
Morrisville, NC 27560

Mobile: 1 919 454 6467
Office: 1 919 694 5088
Fax: 1 919 822 1701
Email: ykhera@wepclinical.com

Please visit us at wepclinical.com for further information.

Reproductive Options

Preimplantation Genetic Testing (PGT)

Preimplantation Genetic Testing (PGT) is a procedure used to identify genetic defects within embryos (an egg fertilized with a sperm) before they implant in the uterus and develop into a pregnancy. This serves to prevent certain genetic diseases or disorders from being passed on to the child. The embryos used in PGT are created during the process of in vitro fertilization (IVF).

In Vitro Fertilization is an assisted reproductive technology, commonly referred to as IVF. IVF is the process of extracting eggs, retrieving a sperm sample and then combining an egg and a sperm outside of the body in a laboratory dish in order to create an embryo.

1. After the egg is fertilized, the embryo divides into many cells over the following 3 to 6 days.
2. On day 5 or day 6 of development, the embryo usually reaches the blastocyst stage. At this stage, the embryo usually contains approximated 100-120 cells. With PGT, approximately 4-8 cells are removed (commonly referred to as a biopsy) from the outer layer of cells. After this cell collection, the embryos are safely frozen until the results of the biopsy can be determined.
3. The DNA of the cells from the biopsy is then evaluated to determine if the inheritance of a problematic gene or condition is present in the embryo. This process usually takes 1-2 weeks.
4. Once PGT has identified an embryo(s) free of genetic problems, the embryo(s) will be placed in the uterus (an embryo transfer). Approximately 2 weeks later, a pregnancy test will determine whether the embryo implanted and is continuing to develop into a pregnancy in the body.
5. Any additional embryos that are free of genetic problems are kept frozen for possible later use while embryos with the problematic gene(s) are discarded.

From starting the egg retrieval process to the final results of PGT generally takes 4 weeks. This does not include the time it may take to undergo initial testing, preparation and consultation with a fertility specialist. If PGT is necessary to test for a known genetic mutation, for example in ABCD1, additional time is often necessary to create the specific test (probe) necessary to identify the mutation in the embryo. It is important to keep this in mind if you plan to pursue IVF with PGT so that you know what to expect!

Cost \$15,000 - \$30,000 per cycle

54% Delivery Rate (pregnancy rates with genetically normal embryos are approximately 65%-70%)

Many insurance plans cover IVF and PGT or some portion of the process, but many do not.

Reproductive Options

Amniocentesis and CVS:

If you are pregnant and did not undergo IVF/PGT, there are two options for diagnostic genetic testing. These are chorionic villus sampling (CVS) and amniocentesis. A diagnostic genetic test tells you (with as much certainty as possible) whether the baby actually has a specific genetic disorder.

Amniocentesis is a procedure in which a thin needle is used to withdraw a small amount of amniotic fluid. Amniotic fluid, which is the fluid that surrounds the baby inside the uterus, contains fetal cells and various proteins. This test is typically performed between 15 to 20 weeks of pregnancy, but can be done up until you give birth. There is a small risk of miscarriage (0.11%) with amniocentesis. Other risks include leakage of amniotic fluid or slight bleeding however these stop on their own in most cases.

Chorionic villus sampling (CVS) is a procedure where a sample of tissue is removed from the placenta. It is often thought of as a placental biopsy. The sample can be taken through the cervix (transcervical) or the abdominal wall (transabdominal). While a CVS and amniocentesis can give you the same information, the main advantage of CVS is that it is performed earlier, typically between 10 to 13 weeks of pregnancy. The risk of miscarriage may be slightly higher with CVS (0.22%)

Testing for specific genetic conditions, such as ALD, can be performed on the sample obtained by CVS or amniocentesis. A number of other types of testing may also be performed. Result times vary by lab and by what tests are performed but typically range from 1-3 weeks. Your doctor and/or genetic counselor can provide guidance on your choices and options and select the tests that are best for you.

Adoption:

Adoption can be another option for families, if you have had a baby diagnosed through ALD newborn screening or are a confirmed carrier and would like to add to your family.

There are many different ways to move forward with this choice, such as fostering a child, open adoption, closed adoption and international adoption. For the purpose of this guide we have not gone into depth, but here are some resources which can help if this is something your family would like to pursue.

www.adoption.org

<https://www.parents.com/parenting/adoption/>

Is there a treatment for ALD?

It is treatable.

Through ALD Newborn Screening, affected children have the opportunity to benefit from lifesaving treatment. While treatment through a cord blood/stem cell transplant can slow the progression of the disease, it is not considered a cure. Unfortunately, myelin that has already been damaged cannot be repaired by this treatment. This is why it is important for ALD disease to be detected as early as possible before symptoms begin, ideally through each state including ALD in their newborn screening program.

Adrenal Insufficiency or Addison's Disease

90% of boys with ALD will also have adrenal insufficiency or Addison's disease, which occurs when the adrenal glands do not produce enough of certain hormones. The adrenal glands are located just above the kidneys. Adrenal hormones, such as cortisol and aldosterone, play key roles in the functioning of the human body, such as regulating blood pressure; metabolism, the way the body uses digested food for energy; and the body's response to stress.

While ALD usually does not present before the age of 3, Adrenal insufficiency can present within the first year of life and therefore it is extremely important to test blood ACTH and cortisol levels. Adrenal insufficiency can be treated easily by replacing or substituting the hormones the adrenal glands are not making with daily steroids. The dose of each medication is adjusted to meet the needs of the patient.

Problems can occur in people with adrenal insufficiency, who have an illness, suffer an injury, or are undergoing surgery or sedation for a medical test. To prevent an adrenal crisis, which can lead to death, the dosage is increased to allow the body to handle the additional stress. People with adrenal insufficiency should always carry identification stating their condition, "adrenal insufficiency," in case of an emergency, as well as the supplies necessary to administer an emergency corticosteroid injection.

Bone Marrow Transplantation

Once a boy is diagnosed with cerebral ALD, it is crucial to undergo prompt evaluation in order to evaluate eligibility for a bone marrow transplant. It is crucial for a boy to undergo bone marrow transplantation at the earliest signs of the disease. A "Loes Score" is a system used to distinguish how far advanced their ALD is and if they are eligible for transplant. A "Loes Score" of less than 9, and closer to 1, has shown to have the most optimal results when considering bone marrow transplantation. For a cord blood transplant, stem cells come from umbilical cords that are donated and stored after live, healthy births of unaffected donors. To learn more about donating your baby's umbilical cord, please visit the Carolina Cord Blood Bank.

For AMN

For men with adrenomyeloneuropathy methods of care consist of rehabilitation therapy, symptomatic medications for pain and stiffness, creating a diet and exercise regimen for ideal health. There are also clinical trials for developing medications that may be useful.

Is there a treatment for ALD?

For Women Carriers

Diet and exercise have shown to help women with ALD.

Gene Therapy

Bluebird Bio, a company located in Boston, MA has conducted a clinical trial for ALD gene therapy. 17 boys with ALD have been treated with gene therapy with promising results. The first results have been published and the gene therapy treatment is very promising to be the next, safer method of treatment for ALD. Gene Therapy for ALD has yet to go through FDA approval. Gene Therapy would be the preferred method of treatment for ALD (once FDA approved) as there is no need to find a donor match in the bone marrow registry. Due to using the boys' own cells there is no chance of rejection, as there may be with bone marrow transplantation.

For more information:

Bluebird Bio

info@bluebirdbio.com

<https://www.bluebirdbio.com/patients-families/gene-therapy/>

<http://www.nejm.org/doi/full/10.1056/NEJMoa1700554>



Ethan

Clinical Trials/ Drugs in Development

There are clinical trials dedicated to different stages/forms of adrenoleukodystrophy to get the most updated list of current clinical trials go to:

www.clinicaltrials.gov

Key Word: adrenoleukodystrophy



Aidan

ALD Experts

CALIFORNIA

Lucille Packard Children's Hospital at Stanford

725 Welch Rd.
Palo Alto, CA 94304
Neurology:
Keith Van Haren, MD
650-723-0993
Maura Ruzhnikov, MD
650-723-0993
Endocrinology:
Sejal Shah, MD
650-721-1811

University of California Davis

3160 Folsom Boulevard
Sacramento, CA 95816
Neurology:
William Benko, MD
916-734-3588

ILLINOIS

Lurie Children's Hospital of Chicago

225 E. Chicago Ave
Chicago, IL 60612
Neurology:
Jennifer Rubin, MD
312-227-6120
Endocrinology:
Donald Zimmerman, MD
800-543-7362

MARYLAND

Johns Hopkins Medicine

707 N Broadway
Baltimore, MD 21205
Neurology:
Gerald Raymond, MD
443-923-9200

Kennedy Krieger Institute

707 N Broadway, 500V
Baltimore, MD 21205
Neurology:
S. Ali Fatemi, MD, MBA
443-923-2772

MASSACHUSETTS

Massachusetts General Hospital

165 Cambridge St.
Suite 820
Boston, MA 02114
Neurology:
Florian Eichler, MD
617-724-6510

MINNESOTA

University of Minnesota

Masonic Children's Hospital

420 Delaware St. SE
Minneapolis, MN 55454
Bone Marrow Transplant:
Paul Orchard, MD
612-365-1000
Troy Lund, MD
612-625-4185

NEW YORK

Weill Cornell Medicine-Memorial Sloan Kettering Kids

525 E 68th St, Box 91
New York, NY 10065
Neurology:
Eric J Mallack, MD, MBE
212-746-3278

Memorial Sloan Kettering Kids

1275 York Ave
New York, NY 10065
Bone Marrow Transplant:
Jaap-Jan Boelens, MD, PhD
212-639-3641

Children's Hospital at Montefiore

3415 Bainbridge Ave
Bronx, NY 10467
718-741-2450
Endocrinology:
Molly Regelman, MD
718-741-2450

NORTH CAROLINA

Duke Department of Pediatrics

2400 Pratt Street,
DUMC Box 102501
Durham, NC 27710
Neurology:
Joanne Kurtzberg, MD
919-668-1100

PENNSYLVANIA

Children's Hospital of Philadelphia

3401 Civic Center Blvd.
Philadelphia, PA 19104
Neurology:
Amy Waldman, MD
215-590-1000
Adeline Vanderver, MD
215-590-1000
Laura Adang, MD
215-590-1000
Endocrinology:
Jeffrey Roizen, MD, PhD, FAAP
215-590-1000

UTAH

Primary Children's Hospital/University of Utah

81 Mario Capecchi Dr
Salt Lake City, UT 84113
Neurology:
Josh Bonkowsky, MD, PhD
801-585-2457

ALD ORGANIZATIONS



Aidan Jack Seeger Foundation
70 North 15th St.,
Brooklyn, NY 11222
www.aidanjackseegerfoundation.org



Fight ALD
PO Box 3318,
Vista, CA 92085
www.fightald.org



ALD Connect
35 Village Rd, Suite 100,
Middleton, MA 01949
www.aldconnect.org



The Stop ALD Foundation
500 Jefferson St., Suite 2000,
Houston, TX 77002-7371
www.stopald.org



Brian's Hope
31 Beechwood Rd.
Branford, CT 06405
www.brianshope.org



ULF
224 North Second St., Suite 2,
DeKalb, IL 60115
www.ulf.org

Thank You

Thank you Aidan for being my inspiration for helping me to continue to help others with the disease that took you from us too soon.



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This content was inspired, designed, and created by the families of the ALD community and the dedicated clinicians and members of newborn screening laboratories across the country. All photos used in this brochure are actual ALD families. Bluebird Bio has not had any direct or indirect input into the content supplied.

Edited by Elisa Seeger and Eric Mallack, MD

Dr. Hugo Moser



This brochure would not be complete without honoring Dr. Hugo Moser who dedicated his life to leukodystrophies and through his research was instrumental in creating the test for ALD Newborn Screening. Dr. Moser was the president of the Kennedy Krieger Institute and his legacy continues at the Moser Center for Leukodystrophies. His wife, Ann Moser continues to work on ALD Newborn Screening and helping to have the test implemented not only throughout the country, but worldwide. The ALD community is grateful for the perseverance of the Mosers to improving the lives of boys with ALD.

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Hong Brereton, MS, RD¹, Marie Burlette², Michele Caggana³, Lani Culley⁴, Kerri Denies⁵, Florian Eichler, MD⁶, Ali Fatemi, MD⁷, Suzanne Flynn⁸, Kim Hart⁹, Elise Holmes¹⁰, Amanda Ingram¹¹, Jean Kelley¹², Julie Luedtke¹³, Eric Mallack, MD¹⁴, Adrienne Manning², Jamie Matteson¹⁵, Miranda McAuliffe¹⁶, Kelly Miettunen¹⁷, Joseph Orsini³, Kathleen O'Sullivan-Fortin¹⁸, Gerald Raymond, MD¹⁹, Armin Razavi, MD, FACOG¹⁴, Emily Reeves²⁰, Molly Regelmann, MD²¹, Elisa Seeger²², Janis Sherwood²³, Joshua Stewart, MD FACOG¹⁴, Kelly Strenges²⁴, Bela Turk, MD⁷, Keith Van Haren, MD²⁵, Beth Vogel³, Kelly Waterman²², Justin Whit²⁶, Brad Zakes²⁷, Nancy Zakes²⁷

- | | |
|--|---|
| 1. Johns Hopkins Institute for Clinical & Translational Research | 15. California Department of Public Health, Richmond, CA |
| 2. Connecticut Department of Public Health | 16. Parent Advocate, New York, NY |
| 3. New York State Department of Public Health, Albany, NY | 17. University of Minnesota Masonic Children's Hospital, Minneapolis, MN |
| 4. Washington Department of Public Health, Seattle, WA | 18. ALD Connect, Boston, MA |
| 5. Parent Advocate, California | 19. Johns Hopkins Institute for Clinical & Translational Research |
| 6. Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA | 20. Florida Department of Health Tallahassee, FL |
| 7. The Hugo W. Moser Research Institute, The Kennedy Krieger Institute, Baltimore, MD | 21. Department of Endocrinology, Children's Hospital at Montefiore, Bronx, NY |
| 8. Parent Advocate, New York, NY | 22. Aidan Jack Seeger Foundation, Brooklyn, NY |
| 9. Utah Department of Public Health, Salt Lake City, UT | 23. Fight ALD, San Diego, CA |
| 10. Minnesota Department of Health, Minneapolis, MN | 24. Parent Advocate, FL |
| 11. Tennessee Department of Health, Nashville, TN | 25. Department of Neurology, Stanford Children's Health Palo Alto, CA |
| 12. Brian's Hope, CT | 26. Pennsylvania Department of Health, Harrisburg, PA |
| 13. Nebraska Department of Public Health Omaha, NE | 27. Ethan Zakes Foundation, Seattle, WA |
| 14. Division of Child Neurology, Weill Cornell Medical Center, New York, NY | |

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THINGS TO REMEMBER

Primary Care Physician:

Neurologist:

Endocrinologist:

Medications:

Appointment Schedule:

Notes:



Aidan

Together We Can: Life with ALD

The diagnosis of ALD can be overwhelming. Remember you can have a normal life after the diagnosis. Managing your life with this diagnosis is doable. Know that your life goes beyond the doctor's office and there are many support systems to help you navigate this disease.

You may want to keep a journal to describe how you are feeling each day and keep a record of anything that seems out of the ordinary.

Please make sure to seek support and reach out to family, friends or others affected by ALD if you feel alone. I know from experience most have never heard of this disease. It may be good to join a facebook group and seek others going through the same things as you are. You are not alone and can connect with others when you need someone to talk to.

Make sure to take care of your mental health. You can't help your loved one if you are not taking care of yourself first. There are feelings of anger, confusion, sadness, etc. Please make sure to reach out to a psychiatrist or a support group if you need to. Take care of your body and your mental health at the same time. Seeing a therapist, eating healthy, exercising is important to keep your overall life in a good place and keeping positive about working through this diagnosis.

–Elisa Seeger

*Miranda, Jack &
Justin*



A woman with long brown hair, wearing a white long-sleeved button-down shirt and white pants, is smiling and holding the hands of a baby. The baby is wearing a white button-down shirt and striped shorts, and is standing on a sandy beach. The ocean and a sunset sky are in the background.

Kerri & Gregory

A young boy is smiling at the camera. He is wearing a dark blue hoodie with a white graphic on the front and a blue beanie with a white pom-pom. He is standing in front of a colorful mural that features a car and various figures. Other people are visible in the background.

Aidan

For more information visit:
aldnewbornscreening.org