Real families affected by ALD have helped inspire this guide. Their photos will be featured throughout.

TODAY'S TO-DO LIST

- [x] get new bike helmets ~~for the family~~
- [ ] Book hotel for ALD conference
- [ ] schedule Alfie's 6-month MRI
- [ ] collect eggs from the chicken coop

ALD DOESN'T MEAN PUTTING LIFE ON HOLD

BUILDING AN ADRENOLEUKODYSTROPHY CARE TEAM AND CREATING A PLAN FOR YOUR FAMILY

Receiving an ***adrenoleukodystrophy (ALD)*** diagnosis may be overwhelming and confusing. Whether you've been on your ALD journey for a while or you're just beginning, **you can help take control of your child's ALD with a care team and a plan**.

This guide will provide you with information that may help you build an experienced ALD care team. Your care team can then help you create a plan that will help you and your family manage ALD. Although you may learn more about ALD from this guide, you should rely on your care team for professional medical advice. No matter where you are in your journey with ALD, your care team will be there to support you.

Beyond your care team, there is an entire ALD community, including parents, caregivers, and individuals living with ALD who help each other. These are the people who have helped inspire this guide by sharing their personal experiences. In turn, this community has received support from various advocacy organizations that work to provide resources and ongoing support to the ALD community. These organizations include ALD Connect, Alex TLC, Global Leukodystrophy Initiative, and World Leukodystrophy Alliance. They have also helped to inform this guide. To learn more, visit **NavigatingALD.com**.

Throughout this guide, there are words that may be new to you, which we have indicated in bold italic. You can find definitions of these words in the glossary on page 14.

bluebird bio wants to thank the incredible organizations who helped inform this guide. We could not have done it without every one of you.

Meet the Flynn family! Suzanne and Ken are parents to their daughter, Charlotte (12), and their sons, Gavin (10) and Patrick (5), who have ALD.

A CARE TEAM MEANS YOU'RE NOT ALONE

WHAT IS ALD?

Understanding the basics of ALD can be both empowering and helpful, especially when speaking with your team of healthcare providers.

ALD is a rare, *X-linked genetic disease* that occurs in about 1 in 21,000 males and about 1 in 17,000 newborns in the total population. Caused by an underlying ***genetic mutation*** in the ***ABCD1 gene***, ALD affects the body's ability to create the protein that helps in the process of breaking down ***very long–chain fatty acids (VLCFAs)***. A buildup of VLCFAs can cause adrenal problems and can potentially lead to brain damage. (ALD that progresses to affect the brain is referred to as cerebral ALD.)

Everyone's journey with ALD is unique. Some individuals may only experience one manifestation of ALD, whereas for others, these manifestations may change or overlap during their lifetime.

Since there is no way to predict the way that ALD will change over time, your ALD care plan can help you to be prepared.

There are a few main ways ALD can manifest:

- ***Asymptomatic***—ALD without signs or symptoms
- ***Adrenal insufficiency***—ALD that only results in adrenal symptoms
- ***Adrenomyeloneuropathy (AMN)***—ALD that commonly starts in adulthood and affects the spinal cord and nerves
- ***Cerebral ALD***—ALD that progresses to affect the brain

There are a few ways a child may be diagnosed with ALD:

- **Adrenal symptoms**
- **Newborn screening**
- **Family history**
- **Neurologic symptoms**

For those who were not diagnosed through ***newborn screening***, an endocrinologist or genetic counselor can confirm an ALD diagnosis by measuring VLCFA levels in blood plasma and testing for a mutation in the *ABCD1* gene.

ALD can also occur as a result of a spontaneous mutation. You may hear this form of ALD described as *de novo*.

WHAT IS CEREBRAL ALD?

Cerebral ALD is a progressive form of ALD that occurs in about 40% of boys with ALD. In cerebral ALD, the layer of myelin that protects nerves in the brain is broken down. If left undiagnosed or untreated, this can have severe effects. These effects can potentially include significant disabilities, such as an inability to speak or respond, blindness, or even death.

However, progression of cerebral ALD can be effectively stopped if it is detected early. **Working with your team to monitor for cerebral ALD will be a crucial component of your plan.**

> "The main reason I can come home and be a normal mother and enjoy my children and raise them without this ALD hanging over my head is because I know they've been seen by their ALD care team."

Suzanne Flynn

Mother of Charlotte, Gavin, and Patrick

BUILDING AN EXPERIENCED ALD CARE TEAM

In order to manage your child's health and to help monitor for potential progression to cerebral ALD, your family may choose to work with a select group of healthcare professionals (also referred to as a care team).

The way that your care team comes together may vary. You may have one physician who is an ***ALD specialist*** that helps you build out the rest of your team, or you may create your own team by finding the following pediatric specialists:

- ***Endocrinologist***—specializes in hormonal and metabolic issues
  – Manages adrenal symptoms of ALD
- ***Neurologist***—specializes in diseases of the brain and nervous system
  – Monitors for potential progression to cerebral ALD
- ***Transplant specialist***—specializes in bone marrow and stem cell transplants
  – If needed, treats cerebral ALD
- ***Geneticist or genetic counselor***—specializes in genetics
  – Helps identify and diagnose family members who may have ALD

Your child's pediatrician, nurse, nutritionist, social worker, and other healthcare professionals may be part of your team as well. This extended care team may provide what is referred to as ***palliative care***. This team may help to connect you to resources and further education when needed. As you are building out your team, you may want to confirm that all specialists are covered by your insurance.

REMEMBER: Finding a team that works for you and your family may take time. The patient advocacy community can help you locate an ALD specialist. Find support from organizations such as: ALD Connect, Alex TLC, Global Leukodystrophy Initiative, or World Leukodystrophy Alliance.*

*This list is meant as a starting point. You may find additional resources in your search for support.

Meet the Rowell family! Anna is the mother to her daughter, Annie (8), and her son, Alfie (12), who has ALD.

YOUR ALD CARE TEAM IS THERE TO SUPPORT YOU

Once you have a team in place, you can partner with them to build a care plan that works for you and your family.

MANAGING ADRENAL ASPECTS OF ALD WITH YOUR ENDOCRINOLOGIST

80% of males with ALD will develop adrenal insufficiency. Often, these adrenal symptoms are the first signs of the disease. These symptoms may include fatigue, loss of appetite, skin darkening, and belly pain. Regular visits to your endocrinologist will allow them to help monitor, assess, and treat these adrenal symptoms.

Treatment for adrenal insufficiency may include steroids or other medications. Managing the adrenal aspects of ALD is an important part of your child's care because adrenal insufficiency can lead to ***adrenal crisis*** (a medical emergency) if left untreated.

Initial symptoms of ALD mimic other diseases, like Addison's disease (a form of adrenal insufficiency), and can often go unnoticed or be misdiagnosed.

"It's just getting up in the morning and knowing you have a support network behind you is amazing. *And I could not do it without them.*"

Anna Rowell

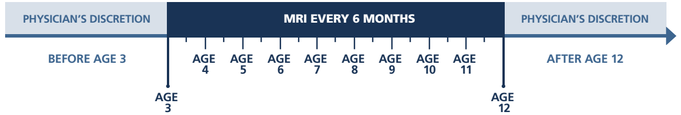
Mother of Alfie and Annie

MONITORING ALD WITH YOUR NEUROLOGIST OR ALD SPECIALIST

ALD progresses differently in every child. And although about 40% of boys will develop cerebral ALD, medical guidelines suggest that all boys with ALD should be monitored for progression through regularly scheduled ***magnetic resonance imaging (MRI)***. MRI provides the earliest opportunity to detect cerebral ALD before any symptoms appear. Detecting cerebral ALD early can have lifesaving results.

Cognitive deficits and behavioral problems that mimic the symptoms of *ADHD* may also indicate progression to cerebral ALD.

These visits can start when your child is a newborn (or later, depending on when they are diagnosed) and continue through adolescence. Your MRI schedule might look like this:



You can work with your care team to come up with a plan that works for you and your family. There are specialists in reading MRIs for patients with ALD, such as neurologists or neuro-radiologists, who will compare a new MRI to a previous MRI. These specialists may be a part of your team, or your team may send your scans to these specialists.

Waiting for the results of your child's MRI can be stressful. Setting expectations about when you will receive results from your care team can help you plan accordingly.

DISCUSSING POTENTIAL TREATMENT OPTIONS WITH A TRANSPLANT SPECIALIST

Remember, about 40% of boys diagnosed with ALD will develop cerebral ALD. You may want to discuss appropriate treatment options with a transplant specialist so that you are prepared if your child develops cerebral ALD in the future. This will help you take action quickly.

If your child's disease does progress to cerebral ALD, you will want to meet with a transplant specialist as soon as possible. Treatment for cerebral ALD at early stages is associated with better results. Your transplant specialist will help you to determine the appropriate treatment for your child.

Early diagnosis and treatment of cerebral ALD can have lifesaving outcomes.

TALKING TO YOUR FAMILY ABOUT ALD WITH THE HELP OF A GENETICIST OR GENETIC COUNSELOR

Because ALD is a genetic disease, you may want to meet with a geneticist or genetic counselor to determine if ALD has been passed down to your child or if it occurred spontaneously (***de novo***).

If genetic testing reveals that ALD does run in your family, your geneticist may recommend that certain members of your immediate and extended family be tested.

Conversations about diagnosing ALD and genetic testing can vary because every family is unique. However, testing is critical because it can lead to diagnosis of ALD before symptoms occur. This can also help your family develop their own care plan if needed.

> An advocacy organization has been there for us since the beginning. They have massively supported me, and Alfie has met some lovely friends through it as well.”

Anna Rowell

Mother of Alfie and Annie

MANAGING ALD IS POSSIBLE WITH AN ALD CARE TEAM AND A PLAN

Again, how your care team comes together may vary. You may get help from a physician or reach out to other families to find out how they built their team. Here’s what your plan may look like:

- ☑ Find an ALD specialist who can help you build your care team
- ☑ Manage adrenal aspects with your endocrinologist
- ☑ Monitor for cerebral ALD with your neurologist or ALD specialist
- ☑ If needed, discuss treatment options for cerebral ALD with a transplant specialist
- ☑ Speak with a geneticist or genetic counselor about whether they recommend that certain members of your immediate and extended family be tested

A COMMUNITY OF SUPPORT

In addition to your care team and plan, there is an entire ALD community that understands what you’re going through. Although their experiences may be different from yours, they understand what it’s like to live with ALD. You can connect with them through online groups that share advice and encouragement. Advocacy communities and organizations such as ALD connect, Alex TLC, Global Leukodystrophy Initiative, and World Leukodystrophy Alliance can provide you with additional information and resources.* To learn more, visit **NavigatingALD.com**.

No matter where you are in your journey with ALD, you have people whom you can lean on for support. This greater community can help you keep to your plan, allowing you to enjoy life with your family and loved ones.

*This list is meant as a starting point. You may find additional resources in your search for support.

GLOSSARY

ABCD1 gene: a gene that encodes a protein that helps the body break down VLCFAs

ADHD: attention-deficit/hyperactivity disorder (ADHD) is a common mental disorder affecting children and many adults; symptoms include inattention (not being able to stay focused), hyperactivity (moving excessively) and impulsivity (acting without thought)

Adrenal crisis: a medical emergency with low blood pressure, marked by severe abdominal symptoms and laboratory abnormalities that require immediate treatment

Adrenal insufficiency: a medical condition in which the adrenal glands aren't producing enough of the hormones that are needed to regulate and balance the body

Adrenoleukodystrophy (ALD): a rare, X-linked disease caused by an underlying mutation in the *ABCD1* gene

Adrenomyeloneuropathy (AMN): a progressive nervous system disorder that typically affects adults

ALD specialist: someone who specializes in monitoring ALD. If your ALD specialist is not local, they may be able to view your child's MRI remotely

Asymptomatic: when an individual exhibits no symptoms associated with a particular condition

Cerebral ALD: the most severe form of ALD, occurring in about 40% of boys. It is characterized by a progressive neurologic decline, which can result in loss of cognition, vision, hearing, motor function, and eventually life

De novo: occurring from a spontaneous mutation

Endocrinologist: a physician who specializes in hormonal and metabolic issues

Genetic mutation: a permanent alteration in the DNA sequence of a gene

Geneticist or genetic counselor: an expert who specializes in genetics

Magnetic resonance imaging (MRI): a noninvasive 3-dimensional imaging process used to detect the progression of a disease or condition

Neurologist: a physician who specializes in diagnosing and treating diseases of the brain and nervous system

Neuro-radiologist: a doctor who interprets x-rays and magnetic resonance images (MRI) of the brain, spine and spinal cord, face and neck, and peripheral nerves to help diagnosis and treat disorders affecting these areas

Newborn screening: a test that screens newborn babies for certain genetic conditions

Palliative care: a type of supportive care for someone with an ongoing illness, regardless of stage or prognosis

Very long–chain fatty acids (VLCFAs): a specific type of fatty acid in the body

X-linked genetic disease: a genetic condition most commonly passed from a mother to her son. Males are likely to experience more severe forms of these diseases than females because they only have one X chromosome

References: 1. Bezman L, Moser AB, Raymond GV, et al. Adrenoleukodystrophy: incidence, new mutation rate, and results of extended family screening. *Ann Neurol.* 2001;49(4):512-517. **2.** Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2016;101(2):364-389. **3.** Engelen M, Kemp S, Poll-The B-T. X-linked adrenoleukodystrophy: pathogenesis and treatment. *Curr Neurol Neurosci Rep.* 2014;14(10):486. **4.** Engelen M, Kemp S, de Visser M, et al. X-linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow-up and management. *Orphanet J Rare Dis.* 2012;7:51. **5.** Moser HW, Mahmood A, Raymond GV. X-linked adrenoleukodystrophy. *Nat Clin Pract Neurol.* 2007;3(3):140-151. **6.** Raymond GV, Aubourg P, Paker A, et al. Survival and functional outcomes in boys with cerebral adrenoleukodystrophy with and without hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2019;25(3):538-548.

"I want my children to love themselves. I want them to embrace themselves just the way they are."

Suzanne Flynn

Mother of Charlotte, Gavin, and Patrick

For more information about building your care team and plan, visit **NavigatingALD.com**.

A *heartfelt* thanks to the Flynn and Rowell families for sharing their stories and helping us to create this guide. We hope their experiences help you and your family as you navigate your own lives with ALD.

bluebirdbio®

ALD-US-00035 11/2019