Learn more about X-linked hypophosphatemia (XLH)

Rachael and her son, Benjamin, and daughter, Brooke, have XLH.

This information is for educational purposes only and is not intended to provide medical advice. Your healthcare professional should always be your primary source of medical advice for any health, diagnosis or treatment practices.
What Is XLH?

XLH, or X-linked hypophosphatemia, is a hereditary, progressive and lifelong disease that can affect children and adults. It is a rare disorder, occurring in anywhere from 1 in 20,000 to 1 in 25,000 people.

People with XLH lose too much phosphorus through the urine causing low levels of phosphorus in the blood (called low serum phosphorus). This can have serious consequences in the bones, muscles, and teeth. Phosphate is a molecule that is made up of phosphorus and oxygen. The body needs phosphorus for cells to work properly and phosphorus also provides the body with energy.

Doctors may call XLH by many other names:

- Familial Hypophosphatemia
- Familial Hypophosphatemic Rickets
- Genetic Rickets
- Hereditary Hypophosphatemic Rickets
- Hypophosphatemic Rickets
- Hypophosphatemic Vitamin D-Resistant Rickets
- X-Linked Hypophosphatemic Rickets
- X-Linked Rickets
- X-Linked Vitamin D-Resistant Rickets
- Vitamin D-Resistant Osteomalacia
- Vitamin D-Resistant Rickets

Siblings Jason and Gina have XLH.
WHAT CAUSES XLH?

- In people with XLH, the body produces too much of a protein called fibroblast growth factor 23 (FGF23).\(^5\)
- FGF23 controls the amount of phosphorus that is present in the blood.\(^5\)
- Too much FGF23 causes the body to behave like a leaky bucket for phosphorus. Phosphorus is lost through the urine, called phosphate wasting.\(^3\)
- Phosphate wasting causes low levels of phosphorus in the blood, a condition called hypophosphatemia.\(^1\)
- Hypophosphatemia can make bones become weak and soft.
- Weak and soft bones are the underlying cause of the symptoms of XLH.

Phosphate wasting by the kidneys reduces the amount of phosphorus that is able to reach bones and teeth.
XLH is an inherited disease, which means parents pass down the disease to their children. The “X” in XLH stands for “X-linked” because the disease is due to a defect (mutation) in the X chromosome. Females have two X chromosomes and males have both an X and a Y chromosome.⁶

A father passes down his X chromosome to his daughters and his Y chromosome to his sons, which means all his daughters will have XLH. Mothers always pass down an X chromosome, which means their children have a 50% chance of inheriting the disease, regardless of their sex.

Children can be born with XLH, even if there is no family history of the disease. This is called a **spontaneous case** and it happens in about one third (20-30%) of cases. Once a person has XLH, they can pass it down to their children, following the x-linked inheritance pattern.
WHAT ARE THE SYMPTOMS OF XLH?

The symptoms of XLH vary from person to person and affect children and adults differently. They can appear at any age and can worsen or change over time.

XLH is typically diagnosed during childhood between 1 and 2 years of age, around the same time a child begins to walk and their legs start supporting weight. The first and most noticeable signs of XLH in children are bowed legs or knock-knees.

While some might think that XLH is only a childhood disease, adults with XLH continue to experience the effects of unresolved childhood symptoms.
If you think you or your child may have XLH, discuss your concerns with your doctor. An early and accurate diagnosis is important for improved symptom and disease management.8

Diagnosing XLH can be tricky because it is a rare disease or can be mistaken for other conditions such as nutritional rickets, and hypophosphatasia, another rare disease that affects bones and teeth. Doctors may also think that early symptoms are due to normal variations in the appearance of the legs. A diagnosis of XLH is typically based on clinical tests and biochemical findings, in combination with family history.1,4

- To take a family history, your doctor will ask you about other members of your immediate and extended family, and whether they have similar symptoms.
- If there is no family history, the appearance of bowed legs or knock-knees in a child may alert parents and doctors that more testing is needed.
- Blood tests, including those that measure the amount of phosphorus in the blood and urine, may be helpful. Your doctor may also take x-rays or order a confirmatory genetic test.

It is important that you find doctors who are knowledgeable about XLH and can identify and help manage the disease. Upon recognizing the symptoms, your doctor can refer you to the specialists who usually diagnose and treat patients with XLH.

- **Endocrinologists** - doctors who specialize in treating hormone conditions
- **Nephrologists** - doctors who specialize in treating kidney conditions
- **Medical geneticists** - doctors who specialize in treating genetic conditions
- **Orthopedic surgeons** – doctors who specialize in treating bone conditions

Elizabeth (right), her son Simon (middle) and mother Jean (left) manage XLH together.
WHAT CARE IS AVAILABLE FOR PEOPLE WITH XLH?

Finding the right team of doctors and healthcare providers that you are comfortable with can make a difference in your care. Your healthcare team can provide personalized care, support and disease education.

COMPREHENSIVE CARE\(^{1,3,4}\)

- **Medications** can be used to treat XLH. Speak with your doctor about what medications are available, and which ones might be right for you.

- **Physical and occupational therapy** may help reduce pain by improving joint stability, flexibility and muscle strength.

- **Pain management** can be important for people with XLH. Your doctor will be able to help you decide which pain management techniques are most suitable for the type of pain you have.

- **Dental care** is important because people with XLH often have unique challenges with their teeth, including spontaneous abscesses (infections) and gum disease. Tell your family dentist if you or your child has XLH.

- **Hearing consultation** may also be helpful, as some people with XLH may experience hearing issues, such as hearing loss or ringing in the ears. If you feel your hearing is being affected, talk to your healthcare team.

- **Genetic counseling** helps patients and families understand inheritance patterns and the risk of other family members having or getting XLH.

XLH is a lifelong disease. Children who have XLH will need to transition from pediatric to adult care as young adults. Parents and doctors can guide them by helping them understand their disease and encouraging them to take charge of their medical care.
SUPPORT AND ADVOCACY ORGANIZATIONS

You are not alone. Patient support and advocacy organizations provide useful information and resources for people and families living with XLH.

**The XLH Network, Inc.** is a US-based, nonprofit organization that has been serving the XLH patient community for more than 20 years. XLH Network members have access to a variety of tools that help them connect with each other, with clinicians, and with researchers.

[xlhnetwork.org](http://xlhnetwork.org)
[twitter.com/XLH_Network](http://twitter.com/XLH_Network)
[facebook.com/xlhnetwork/](http://facebook.com/xlhnetwork/)

**National Organization for Rare Disorders (NORD)** is an organization committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

[raredisease.org](http://raredisease.org)

**Global Genes** is a rare disease patient advocacy organization that works to build awareness, educate the global community, and provide connections and resources.

[globalgenes.org](http://globalgenes.org)

**NIH Genetic and Rare Diseases (GARD) Information Center** provides access to current, reliable, and easy to understand information about rare or genetic diseases.

[rarediseases.info.nih.gov](http://rarediseases.info.nih.gov)

**USEFUL WEBSITES**

**XLHLink.com** is an informational website for individuals, caregivers, and families living with XLH that offers education on diagnosis, symptoms and disease management techniques.

**UltraRareAdvocacy.com** is a place to find links to valuable resources and hear from individuals living with XLH and other rare diseases.

**REFERENCES**

7. Skrinar A, Marshall A, San Martin J, Dvorak-Ewell M. X-linked hypophosphatemia (XLH) impairs skeletal health outcomes and physical function in affected adults. Poster presented at: Endocrine Society’s 97th Annual Meeting and Expo; March 5-8, 2015; San Diego, CA.

© 2019 Ultragenyx Pharmaceutical Inc. All rights reserved.