


Living with XLH
(X-Linked Hypophosphataemia)

An Introduction for Canadian Patients, Caregivers, and Families

ultragenyx

WHAT IS XLH?

Hereditary, progressive & lifelong

XLH, or X-Linked Hypophosphataemia, is a **hereditary, progressive and lifelong disease** that affects both children and adults.[1] It can have serious consequences in the bones, muscles and teeth, and affects individuals differently, even within the same family.

Hereditary – XLH is an inherited disease, which means it runs in families. In some cases, XLH may occur *spontaneously* (no family history).

Progressive – New symptoms of XLH may appear at any age and can worsen over time.

Lifelong – Individuals with XLH will continue to experience symptoms throughout their lives.

Gabriella and her parents Carol and Sylvain
Living with XLH in Quebec

XLH used to be called by other terms, but sometimes they still get used:[2,3]

- X-linked hypophosphataemic rickets
- Hereditary hypophosphataemic rickets
- Familial hypophosphataemic rickets
- Vitamin D–resistant rickets (VDRR)
- Vitamin D–resistant osteomalacia
- X-linked vitamin D–resistant rickets
- Hypophosphataemic rickets
- Hypophosphataemic vitamin D– resistant rickets (HPDR)
- X-linked rickets (XLR)
- Genetic rickets
- Familial hypophosphataemia

XLH is a multifaceted disease – it affects a whole range of aspects of a person's life[4]

Whole body – XLH is often viewed as a bone disorder but XLH affects the entire body, not just the bones.

Whole life – XLH was once perceived as a childhood disease, however XLH symptoms not only persist but usually worsen throughout adulthood. In addition, new symptoms may arise.

Whole family – Families may have several members with XLH and the burden of XLH also affects the lives of family members not diagnosed with XLH as well as friends, peers, and colleagues.

***84%** of people living with XLH surveyed said **all areas of life were impacted** as XLH progressed[4]*

WHOLE BODY

XLH affects the entire body

With XLH, consistent low levels of phosphate affects the whole body, not just the bones. In addition to affecting bone formation, XLH can also impact:

- teeth
- muscle/nerve function
- ligament & tendon calcification
- hearing
- energy levels
- other cellular processes

Elliot
Living with XLH in Ontario

Large head size

Hearing loss

Dental abnormalities (dental abscesses)

Fatigue

Bone and joint pain

Short stature

Muscle weakness

Softening of the bones

Bowing of the arms and legs

Adapted from Linglart and Ruppe[1,2]

What causes the symptoms of XLH?[1,2,5]

People with XLH produce too much of a protein called fibroblast growth factor 23, or FGF23.

Kidneys play a role in keeping phosphate levels at the right level in our body. Too much FGF23 causes kidneys to lose phosphate through urine, leading to levels of phosphate in the blood that are too low. This is called hypophosphataemia.

Consistently low levels of phosphate causes bones to become weak and soft. Weak bones are an underlying cause of the symptoms of XLH.

XLH needs to be actively managed in both children and adults

Treatment for XLH aims to:

- Address growth issues
- Improve the mineralization of bones and teeth
- Correct leg abnormalities
- Improve physical function
- Reduce the pain, fatigue and stiffness of the bones, muscles and joints
- Correct skeletal abnormalities and fractures
- Improve bone and dental health

Everyone with XLH is unique

Proper management of XLH should be in response to the needs of each individual and may include[1-3]:

- Medications or dietary supplements
- Physical and occupational therapy
- Mental health support
- Pain management
- Dental care
- Hearing consultation
- Genetic counselling

WHOLE LIFE

XLH is lifelong and progressive[1,4]

The symptoms of XLH are progressive and the impact of the disease is lifelong. Childhood symptoms can worsen throughout adulthood and new symptoms can arise and also progress with time.

The XLH Network's fall 2017 survey of 186 people living with XLH, revealed:[4]

***84%** of people living with XLH said **worsening symptoms** have greatly affected additional areas of their lives over time[4]*

***59%** of people living with XLH said sports and recreational activities were important pursuits that were affected by XLH progression*

SYMPTOMS IN CHILDHOOD…	…OFTEN WORSEN IN ADULTHOOD[4]
☐ 29% of adult patients with XLH scored their childhood symptoms as severe	☐ 46% scored their adult symptoms as severe[4]
☐ 18% of children living with XLH reported chronic pain as having the greatest negative impact on their lives[4]	☐ 38% of adults reported chronic pain as having the greatest negative impact[4]

Alice and her parents Shari and Stephen
Living with XLH in Ontario

Gabriella
Living with XLH in Quebec

"When I'm older and looking back at my life, I hope to have left a positive mark on the world."

TRANSITIONS INTO ADULTHOOD[4]

The XLH Network has identified that as adolescents enter adulthood there is a need for transitional care from a pediatric care team to an adult care team. **There is an outdated perception that XLH is a childhood disorder,** and this can make the transition challenging. You may need to advocate for yourself during this transition.

Pediatric and adult specialists who may diagnose and treat XLH include:

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

Orthopaedists – doctors who specialize in treating bone conditions

Other members of your individualized care team may include:

General Practitioners – your family doctor or local clinic doctor

Rheumatologists – doctors who specialize in treating disorders involving inflammation

Endodontists – dental specialists who treat the soft tissue inside the tooth

Periodontists – dentists who specialize in gums and bones

Social workers – professionals that focus on social wellbeing

Physiotherapists – professionals that focus on physical wellbeing

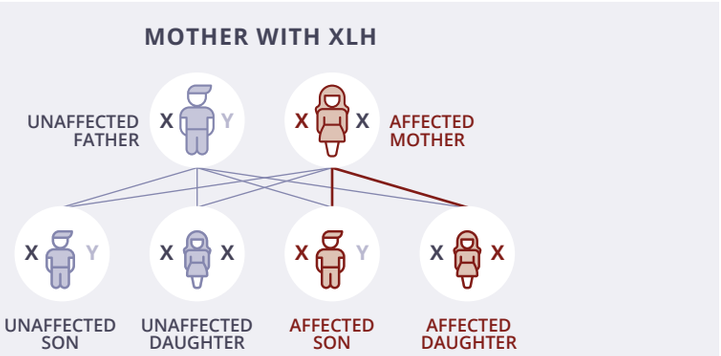
Mental health professionals – professionals that focus on mental wellbeing

WHOLE FAMILY

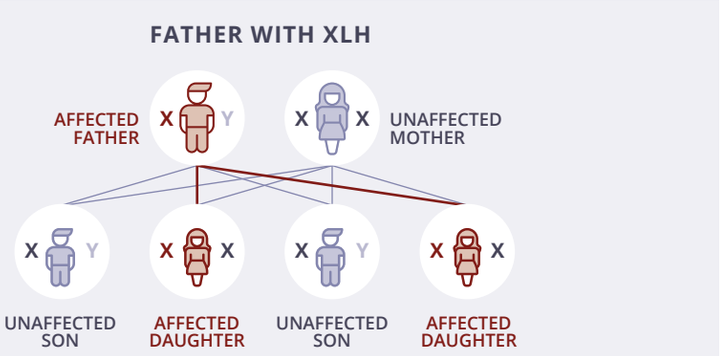
If you or a relative has XLH, there's a **significant possibility** that other relatives have it too

XLH is inherited disease that impacts children and adults. The "X" in XLH stands for X-linked, because the disease is due to a genetic change (a mutation) in the X chromosome that can be passed on to children of someone with this genetic change. Males have XY chromosomes, and females have XX chromosomes.[6]

XLH INHERITANCE PATTERN[2]



If a mother has XLH, each child has a **50% chance of inheriting XLH, regardless of sex.**



If a father has XLH, **all of his daughters and none of his sons will inherit XLH.**

About 1/3 of XLH cases are spontaneous, which means that there is no family history of XLH.[6]

Families living with XLH[4]

XLH can impact multiple members of a family, yet XLH can affect the lives of family members even if they themselves don't have it. The physical limitations associated with mobility issues, fatigue, and pain can impact families living with XLH. A person living with XLH may not be able to fully participate in family activities. This can add to the daily workload of family members providing care.

"We're up to 21 living family members that have gotten a genetic test confirming their XLH diagnosis."

– **Emily**, living with XLH

TAKE ACTION

Fill in your own family tree on the next page to see if any relatives might have XLH

How is XLH diagnosed?

A diagnosis of XLH is based on a combination of family history, symptoms and lab tests.[1,3]

Your doctor should take a family history by asking about family members and whether they have similar symptoms, or refer you to a genetic counselor.

XLH is often diagnosed during childhood, but many people are diagnosed later in life.

XLH is typically diagnosed during childhood, usually within 2 years of age.[2]

TAKE ACTION

Could other members of your family have XLH? You can help!

DO ANY OF YOUR FAMILY MEMBERS HAVE ANY OF THESE SYMPTOMS?[1,2]

- Large head size
- Dental abnormalities (dental abscesses)
- Hearing loss
- Fatigue
- Bone and joint pain
- Short stature
- Bowing of the arms and legs
- Softening of the bones
- Muscle weakness

SHARE THIS WITH YOUR FAMILY MEMBERS AND TALK ABOUT YOUR DIAGNOSIS

TAKE ACTION

You and your family should ask your doctor about genetic testing and genetic counselling.

References: 1. Linglart A, Biosse-Duplan M, Briot K, et al. Therapeutic management of hypophosphatemic rickets from infancy to adulthood. *Endocr Connect.* 2014;3(1):R13-R30. **2.** Ruppe MD. X-linked hypophosphatemia. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews®* [Internet]. University of Washington, Seattle; 1993-2020. Published February 9, 2012. Updated April 13, 2017. https://www.ncbi.nlm.nih. gov/books/NBK83985/. **3.** Carpenter TO, Imel EA, Holm IA, Jan de Beur SM, Insogna KL. A clinician's guide to X-linked hypophosphatemia. *J Bone Miner Res.* 2011;26(7):1381-1388. **4.** Hamilton AA, et al. Whole Body, Whole Life, Whole Family: Patients' Perspectives on X-Linked Hypophosphatemia. *J Endoc Soc.* 2022;6:1–4. doi:10.1210/jendso/bvac086. **5.** Martin A, Quarles LD. Evidence for FGF23 involvement in a bone-kidney axis regulating bone mineralization and systemic phosphate and vitamin D homeostasis. *Adv Exp Med Biol.* 2012;728:65-83. **6.** Gaucher C, Walrant-Debray O, Nguyen TM, et al. PHEX analysis in 118 pedigrees reveals new genetic clues in hypophosphatemic rickets. *Hum Genet.* 2009;125(4):401-411.

FIRST GENERATION

GRANDPARENT — XLH Symptoms? Y N — Genetic Test? Y N

GRANDPARENT — XLH Symptoms? Y N — Genetic Test? Y N

GRANDPARENT — XLH Symptoms? Y N — Genetic Test? Y N

GRANDPARENT — XLH Symptoms? Y N — Genetic Test? Y N

SECOND GENERATION

AUNT / UNCLE — XLH Symptoms? Y N — Genetic Test? Y N

AUNT / UNCLE — XLH Symptoms? Y N — Genetic Test? Y N

PARENT — XLH Symptoms? Y N — Genetic Test? Y N

PARENT — XLH Symptoms? Y N — Genetic Test? Y N

AUNT / UNCLE — XLH Symptoms? Y N — Genetic Test? Y N

AUNT / UNCLE — XLH Symptoms? Y N — Genetic Test? Y N

YOUR GENERATION

COUSIN — XLH Symptoms? Y N — Genetic Test? Y N

COUSIN — XLH Symptoms? Y N — Genetic Test? Y N

SIBLING — XLH Symptoms? Y N — Genetic Test? Y N

YOU — XLH Symptoms? Y N — Genetic Test? Y N

SIBLING — XLH Symptoms? Y N — Genetic Test? Y N

COUSIN — XLH Symptoms? Y N — Genetic Test? Y N

COUSIN — XLH Symptoms? Y N — Genetic Test? Y N

NEXT GENERATION

NIECE / NEPHEW — XLH Symptoms? Y N — Genetic Test? Y N

NIECE / NEPHEW — XLH Symptoms? Y N — Genetic Test? Y N

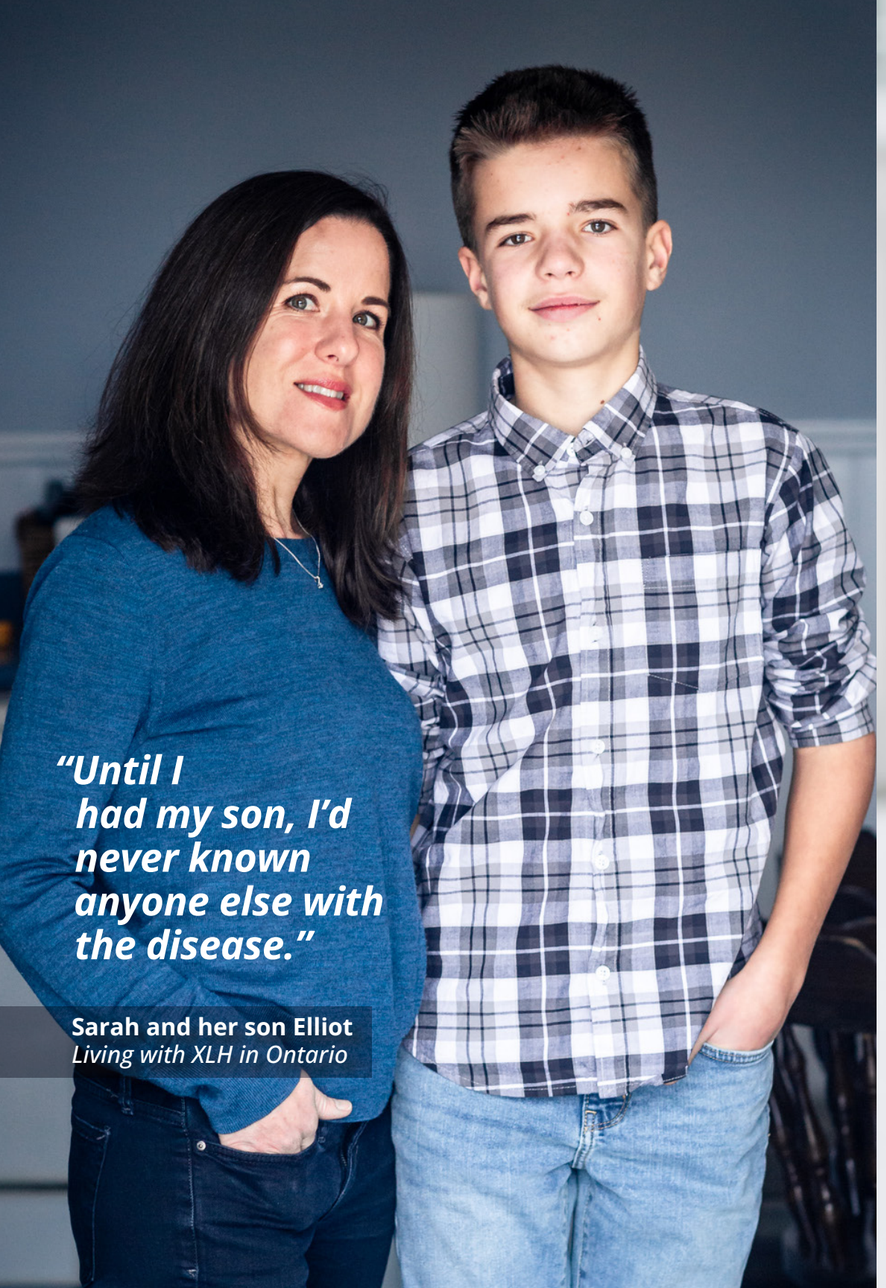
CHILD — XLH Symptoms? Y N — Genetic Test? Y N

CHILD — XLH Symptoms? Y N — Genetic Test? Y N

CHILD — XLH Symptoms? Y N — Genetic Test? Y N

NIECE / NEPHEW — XLH Symptoms? Y N — Genetic Test? Y N

NIECE / NEPHEW — XLH Symptoms? Y N — Genetic Test? Y N



“Until I had my son, I’d never known anyone else with the disease.”

Sarah and her son Elliot
Living with XLH in Ontario

“I want him to know that he’s different but that there’s nothing wrong with that.”

Shawna and her son Douglas
Living with XLH in British Columbia

YOUR NEXT STEPS WITH XLH

Know your family history

Take notes, discuss them at your appointment and ask how you can help your family. Fill out the family tree in this brochure to see if other family members also might have XLH, and encourage them to talk to their doctor. A proper diagnosis of XLH is the first step to proper management.

Ask your doctor about genetic testing

If you or a relative has XLH, there's a good chance that other relatives have it too. As a hereditary disease, XLH impacts children and adults. Without management, it can lead to serious, painful, debilitating and permanent symptoms in adulthood.

Advocate for your health

Take an active role and speak up when you have concerns and look for answers when issues arise.

Connect with other families living with XLH

Take an active role and speak up when you have concerns and look for answers when issues arise.

Rare diseases like XLH can be very isolating, and we feel very fortunate to have finally met so many other individuals and families with XLH through the Canadian XLH Network. Being part of this Network has given us an entire community of support, information and friendship.

– **Lynda Dumont and Spencer Christiansen**

Canadian XLH Network

https://canadianxlhnetwork.org/

XLHLink
Bringing people and ideas together

Learn more at: XLHlink.ca

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

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