

MONITORING XLH OVER TIME: WHAT TO EXPECT

XLH, or X-linked hypophosphatemia, is a **hereditary, progressive, and lifelong disease that can affect children and adults.**¹ Because XLH is a rare disorder, it may be difficult to find information about what to expect. This brochure includes information about **symptoms and how they may change over time, common tests, types of doctors you may encounter, and healthy living tips.**



Natascha, living
with XLH

This is not intended to provide medical advice, but rather as a guide to use when talking with your doctor about XLH. Your healthcare team should always be your source of medical advice.

LIVING WITH XLH

XLH symptoms:



Vary from person to person



Progress over time



Can be different in children
and adults

In XLH, the tests, symptoms to monitor, and kinds of doctors a person needs may change over time. People with XLH may also experience changes in their physical abilities and activity levels as they get older.



“Each day we have to do a lot of things, but I think XLH has made us stronger, better people.”

– Melissa, living with, and raising a son with, XLH

AGES 0-18

XLH SYMPTOMS: AGES 0-18

XLH can typically be 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.²

POSSIBLE SYMPTOMS:^{1,2}



- Bowing of the arms and legs
- Craniosynostosis (when the bones in the skull join together too early, causing an unusual head shape), and/or larger than usual head size
- Delayed walking and/or waddling gait
- Delayed growth
- Bone and joint pain
- Dental abscesses
- Rickets (the softening and weakening of bones)
- Short stature

TIPS:



Young children may not speak up about their pain levels and may want to participate fully in activities with friends despite their symptoms. They may also need help finding ways to explain or describe their pain. It's important to check in often and ask how they are feeling.

Talk regularly with teens about taking on some of their own care responsibilities, like writing out a medication schedule, making doctor appointments, and speaking with the doctor on their own. Check out the [XLH Transitions Toolkit](#) for more information to help young adults as they prepare to transition to adult healthcare.

AGES 19-35

Understanding the progression of XLH and how the symptoms may affect daily life can help you or your loved one better prepare for the future.

ADDITIONAL SYMPTOMS THAT MAY APPEAR:^{1,2,3,4}

- Bone and joint pain
- Early osteoarthritis of the spine, hip, and knees
- Joint pain and stiffness
- Muscle pain and weakness
- Osteomalacia (softening of the bones, which can lead to fractures)
- Waddling gait (walk)
- Wrists, ankles, or knees that appear larger than normal

TIPS:



Activity levels may begin to decrease as young adults grow into adults. Osteomalacia, the softening and weakening of bones, continues into adulthood. As a result, new symptoms may continue to appear or existing symptoms may worsen over time, which can limit the body's movements.

During this time, young adults will likely need to transition off their parents' health insurance. Learn health insurance basics at [Understanding Health Insurance](#).

“
As I got older and started having back pain and stiffness – and problems that you shouldn’t necessarily have in your early thirties – just knowing that there was a reason why was the best part of my diagnosis.”

– Emily, 34

AGES 35+

Older adults may need to pay special attention to mobility needs, new physical limitations, and minimizing risks of falls or fractures.

ADDITIONAL SYMPTOMS THAT MAY APPEAR:^{1,2,3,4}

- Bone and joint pain
- Enthesopathy (mineralization) of tendons and ligaments surrounding the ankles, knees, hips, and spine
- Fatigue
- Fractures
- Hearing loss
- Osteoarthritis (inflammation in the joints)
- Pseudofractures (a kind of fracture where the bone thickens at the site of an injury but is not completely broken)
- Spinal stenosis (narrowing of the spaces within the spine)

TIPS:



1

Calcium and Vitamin D are crucial components of good bone health. Calcium is the principal mineral that makes bones strong, and people need vitamin D to aid calcium absorption into the bones. Talk to your doctor about whether calcium or vitamin D supplements might be right for you, and about adding foods rich in these minerals to your daily diet.⁵

2

Weight-bearing exercises trigger a response that stimulates the bone cells to build more bone. Ask your medical care team whether weight bearing, muscle strengthening, balance, or posture exercises can help reduce your risk of fractures.⁶

3

Ask your doctor if you could benefit from an assessment of your home, work, and social environments to help identify fall risks and/or suggest possible adaptive equipment to address physical limitations. This may help you **minimize risk of fractures** and other injuries. Occupational therapists and/or physical therapists may be able to perform such assessments.⁷



Rhonda, 55



DID YOU KNOW

In one study of adults ages 45-60 with XLH, 100% of participants reported bone and joint pain that grew worse with activity, and 100% reported difficulty with walking long distances.⁷

COMMON TESTS FOR XLH

The frequency of these tests, and the ages at which they are performed, varies widely based on a person's symptoms, severity and progression of disease, medical history, medications being taken, and more. Always check with your or your child's doctor for specific recommendations.

BIOCHEMICAL TESTS TO CHECK LEVELS OF:⁸

- **Fasting serum phosphate:** a mineral the body uses to repair bones and teeth that keeps cells healthy. In adults, normal fasting serum phosphate levels generally range from 2.5 to 4.5 milligrams per deciliter of blood (mg/dL); normal ranges tend to be higher in children because they need more of this mineral to help their bones develop.^{9,10}
- **Alkaline phosphatase (ALP):** an enzyme found in several body tissues, mainly in the liver.¹¹ Normally, ALP ranges from 20-140 international units per liter (IU/L).¹² An increased ALP level is a common hallmark of XLH.
- **Calcium:** a mineral the body uses to maintain strong bones and teeth. In adults aged 40 years or older, normal calcium levels generally range from 9-10 mg/dL. In younger people the upper limit of normal may be as high as 10.7 mg/dL at age 15.¹³
- **Creatinine:** a chemical waste product made by muscle metabolism. Normal creatinine levels may range from 0.84-1.21 mg/dL, although this can vary from lab to lab, between men and women, and by age. Too much creatinine may indicate that the kidneys are not working properly.¹⁴
- **Parathyroid hormone (PTH):** regulates calcium and phosphorus levels in the blood, normally ranges from 10-55 picograms per milliliter (pg/mL).¹⁵
- **TmP/GFR:** an abbreviation for the maximum rate of renal tubular reabsorption of phosphate per glomerular filtration rate; measures phosphate reabsorption and can help doctors understand how much phosphate wasting is occurring. The normal range for TmP/GFR in adults is 2.5-4.2 mg/dL, though it is higher in children.¹⁶
- **Forms of vitamin D:** vitamin D regulates the amount of calcium and phosphate in the body (see Understanding Vitamin D, below). Normal vitamin D levels range from 20-40 nanograms per milliliter (ng/mL), though some experts recommend a level between 30-50 ng/mL.¹⁷

URINE TESTS TO CHECK LEVELS OF:

- Calcium
- Phosphate
- Creatinine



UNDERSTANDING VITAMIN D¹⁸

Two forms of vitamin D can be measured in the blood: **25-hydroxyvitamin D** and **1,25-dihydroxyvitamin D**. The 25-hydroxyvitamin D is the major form found in the blood and is an inactive precursor to the active hormone, 1,25-dihydroxyvitamin D.

- Vitamin **D₂** (ergocalciferol), comes from plants, while vitamin **D₃** (cholecalciferol), comes from animals
- The **D₂** form is found in fortified foods and in most vitamin preparations and supplements
- Vitamin **D₃** is the form produced in the body and is also used in some supplements
- Vitamin **D₂** and **D₃** are equally effective when they are converted by the liver and the kidney into the active form, 1,25-dihydroxyvitamin D

DURING YOUR YEARLY CLINICAL EXAM, YOUR PHYSICIAN IS LIKELY TO TEST THE FUNCTION OF MUSCLES AND BONES AS WELL AS:⁸

- **Yearly or twice-yearly blood pressure measurements**, with a more detailed work-up in the presence of persistently high blood pressure
- **Regular height** and growth assessments, plotting progress on both traditional and XLH-specific growth charts, as well as regular measurement of head size (see [Growth Curves in XLH](#))
- **Quality of life** questionnaires to assess how the person living with XLH is managing symptoms, as well as physical and emotional challenges of living with a rare disease
- **Spine examination** to look for curving of the spine

OTHER TESTS AND EXAMS THAT MAY BE ORDERED:⁸

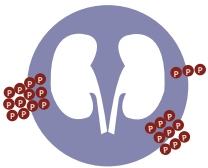
- **X-rays and other imaging tests (such as MRIs)** to have a baseline to measure against in future tests, to grade the level of rickets, and to look for bone abnormalities not otherwise visible
- **Hearing evaluation** to determine hearing difficulties
- **Dental exams** to look for abscesses; people with XLH may need twice yearly exams, and a full orthodontic evaluation around age 12
- **Neurological examination and/or MRI** of the brain to rule out craniosynostosis, especially in those experiencing persistent headache or vomiting, or exhibiting unusual head shape
- **Ultrasound of the heart** if there is persistent high blood pressure
- **Ultrasound of the kidneys**, depending on which medication the person is taking and whether there is evidence of nephrocalcinosis, or too much calcium in the kidneys

FAST FACTS: XLH IN THE BODY

It's important to have a basic understanding of the cause and common symptoms of XLH to understand how symptoms may progress over time and what doctors may do to monitor the disease.



- In people with XLH, the body produces too much of a protein called fibroblast growth factor 23 (FGF23).² FGF23 controls the amount of phosphorus in the blood.¹⁹



- 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 weak and soft. Weak and soft bones are the underlying cause of the symptoms of XLH.

THE XLH CARE TEAM

People with XLH can be seen by a multidisciplinary care team – several healthcare providers with different specialties – who are informed of the care provided by the other team members. Read on for information about types of healthcare providers you may see at some point. You may not need to see all these specialists. The kinds of providers you see will be based on things like your age, symptoms, and stage of disease progression.⁸



“It was difficult for me to find a new doctor. Don’t be afraid to advocate for yourself and ask for help with finding the correct resources because they’re out there, and it is possible to continue receiving the correct care for XLH.”

– Ashley, 26



Check in with your doctor regularly and tell them about all your symptoms or new issues and they can help you understand which specialists can help as health concerns may arise.

- **Audiologists** – treat hearing, balance, tinnitus, and other auditory disorders. Audiologists help people with these disorders better communicate and connect with the world around them.



- **Dentists** – diagnose and treat problems with teeth, gums, and related parts of the mouth. They provide advice and instruction on taking care of the teeth and gums.

- **Dieticians** – experts in food and nutrition.
- **Endocrinologists** – specialize in the diagnosis and treatment of hormone-related diseases and conditions.
- **Genetic counselors** – certified healthcare workers with experience in medical genetics and counseling. Referrals include those with questions about family planning and prenatal diagnosis.
- **Geneticists** – doctors who specialize in genetics.
- **Nephrologists** – specialize in treating diseases of the kidney and are knowledgeable about how kidney disease or dysfunction can affect other parts of the body.
- **Neurologists** – specialize in disorders of the brain and nervous system. Referrals include people with unusual head shapes or findings on MRI.
- **Occupational therapists** – treat injured, ill, or disabled people through the therapeutic use of everyday activities. They help people develop, recover, improve, or maintain the skills needed for daily living and working.



- **Ophthalmologists** – specialize in eye and vision care.
- **Orthodontists** – specialize in dental and facial irregularities.
- **Orthopedic surgeons** – specialize in disorders of the bones, joints, ligaments, tendons, and muscles. Referrals include those who have lower limb discrepancies. If surgery is necessary, your doctor may refer to you an orthopedic surgeon with experience in metabolic bone disease.
- **Otolaryngologists (ENTs)** – specialize in both medicine and surgery focused on the head, neck, ears, nose, and throat. They can help treat hearing loss as well.
- **Pain management specialists** – specialize in evaluating, diagnosing, and treating all types of pain; dedicated to relieving pain symptoms.
- **Physical therapists** – movement experts who work with patients who have injuries, disabilities, or other health concerns. Be sure to tell your physical therapist about your personal limits.



- **Podiatrists** – specialize in conditions of the foot, ankle, and related structures of the leg.
- **Psychologists** – specialize in helping people learn to cope more effectively with life issues and mental health problems.
- **Radiologists** – conduct medical imaging procedures or tests such as X-rays, computed tomography (CT) scans, magnetic resonance imaging (MRI), ultrasounds, and more.
- **Rheumatologists** – specialize in musculoskeletal disease and systemic autoimmune conditions that affect the joints, muscles, and bones.
- **Social workers** – provide psychosocial support to patients and families and help individuals reach their personal goals while living with issues such as depression, anxiety, and substance use disorders.



XLH SELF ADVOCACY

Having a rare disorder is challenging. It can be isolating and frustrating because you may need to constantly educate others, even doctors, on your condition. It's important for people with XLH and other rare diseases to develop a support network and to learn to advocate for what they need. Some tips that may help:

Be well-prepared for doctor visits, with questions and concerns written down in advance:

- [Communicating with Healthcare Providers](#)
- [Doctor Discussion Guide for Children](#)
- [Doctor Discussion Guide for Adults](#)

Help family, friends, colleagues, and others understand what XLH is as well as what you need to be comfortable in different situations:

- [Share your Rare Journey](#)
- [Life with XLH: Tips for Caregivers and Families](#)

Allen, living with XLH.



Build a support network and communicate with others who live with or understand rare disease. You may find support groups on social media and can also connect with others through these organizations:

- **The XLH Network, Inc.** is a US-based, nonprofit organization that has been serving the XLH patient community for more than 20 years. **xlhnetwork.org**
- **Canadian XLH Network** is a nonprofit organization serving the XLH community in Canada. **facebook.com/canadianxlhnetwork**
- **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. **rarediseases.org**
- **Global Genes** is an advocacy organization whose mission is to connect, empower, and inspire the rare disease community. **globalgenes.org**

“I definitely would have been better off had I learned at a younger age to advocate for myself and find doctors and professionals that could help me.”

– Natascha, 32



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