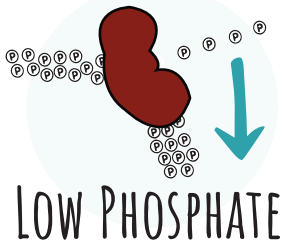
What is XLH?

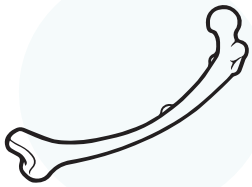
X-linked hypophosphatemia (XLH) is a hereditary, progressive, lifelong disorder.

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



Low Phosphate

Too much FGF23 causes kidneys to "waste" phosphate through urine, leading to low levels of phosphate in the the blood, called hypophosphatemia.

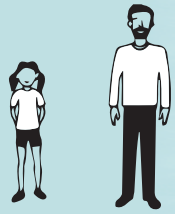


Chronic low phosphate causes bones to become weak and soft. Weak bones are the underlying cause of the symptoms of XLH.

XLH Symptoms

Symptoms vary from person to person and affect children and adults differently. The first and most noticeable signs are bowed legs or knock-knees, which first appear when a child begins to walk.[1]

XLH is rare, occurring in about **12,000 people** in the U.S.



~3,000 children

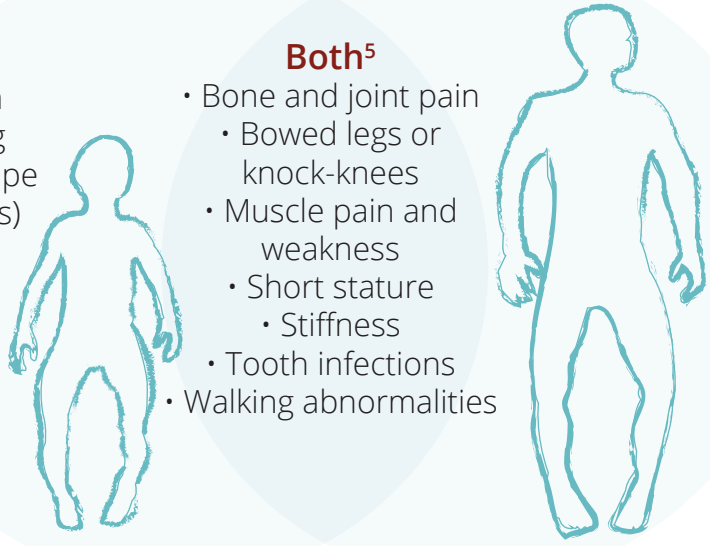
~9,000 adults

Child[1]

- Delayed growth
- Delayed walking
- Unusual head shape (craniosynostosis)
- Rickets

Both[5]

- Bone and joint pain
- Bowed legs or knock-knees
- Muscle pain and weakness
- Short stature
- Stiffness
- Tooth infections
- Walking abnormalities



Adult[4,5]

- Fatigue
- Hearing problems
- Hardening of tendons or ligaments
- Osteoarthritis
- Pseudofractures
- Fractures
- Spinal stenosis (narrowing of the spaces within the spine)

A Lifelong Condition

XLH is progressive and can impact physical function.

Skeletal deformities, pain, stiffness and fatigue can:[2]

- **Limit mobility**
- **Decrease range of motion**
- **Cause disability**

XLH is usually inherited, but

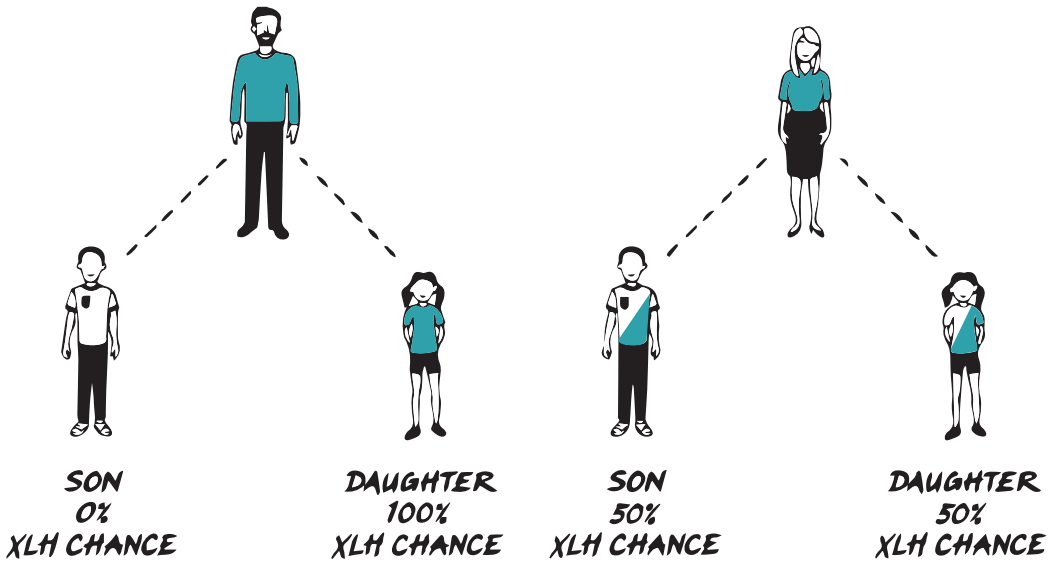
20% to 30%

of cases are spontaneous mutations.[6]

Who Gets XLH?

XLH is usually inherited. A mutation in the PHEX gene, which is carried on the X chromosome, is passed down from a parent to a child.

Because men have only one X-chromosome, a man with XLH will pass along the condition to **all** of his daughters, but to **none** of his sons. A woman with XLH has a **50%** chance of having a child with XLH because all children inherit one X-chromosome from their mother.



References

1.What is XLH? *The XLH Network Board of Directors.* ; August, 2017. Available at: https://xlhnetwork.org/what-is-xlh/. Accessed February 5, 2018.
2.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 97th Annual Meeting and Expo, San Diego, Calif., March 7, 2015. Abstract #PP29-3.
3.Hereditary hypophosphatemic rickets. ***Genetics Home Reference;*** January, 2018. Available at: https://ghr.nlm.nih.gov/condition/hereditary-hypophosphatemic-rickets. Accessed February 5, 2018.
4.Melinda S Sharkey, Karl Grunseich, Thomas O Carpenter. Contemporary Medical and Surgical Management of X-linked Hypophosphatemic Rickets. *The American Academy of Orthopaedic Surgeons.* July 2015; http://www.ncbi.nlm.nih.gov/pubmed/26040953.
5.Linglart A. Biosse-Duplan M. Briot K. et al. Therapetuic management of hypophosphatemic rickets from infancy to adulthood. Endocr Connect. 2014 March 1; 3(1):R13-R30.
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.

MRCP-KRN23-00262
February 2018