XLHLink

X-linked hypophosphataemia (XLH) and families

What you need to know

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Who is this leaflet for?

This leaflet is intended for people who have just been diagnosed with X-linked hypophosphataemia (XLH) and their carers. After reading through the information here you should have a better understanding of the following topics:

What is XLH?

How does XLH affect me?

How is XLH inherited?

How will my family be affected?

What is family mapping?

What are the benefits of family mapping?

How do I make a family map?

What is XLH?

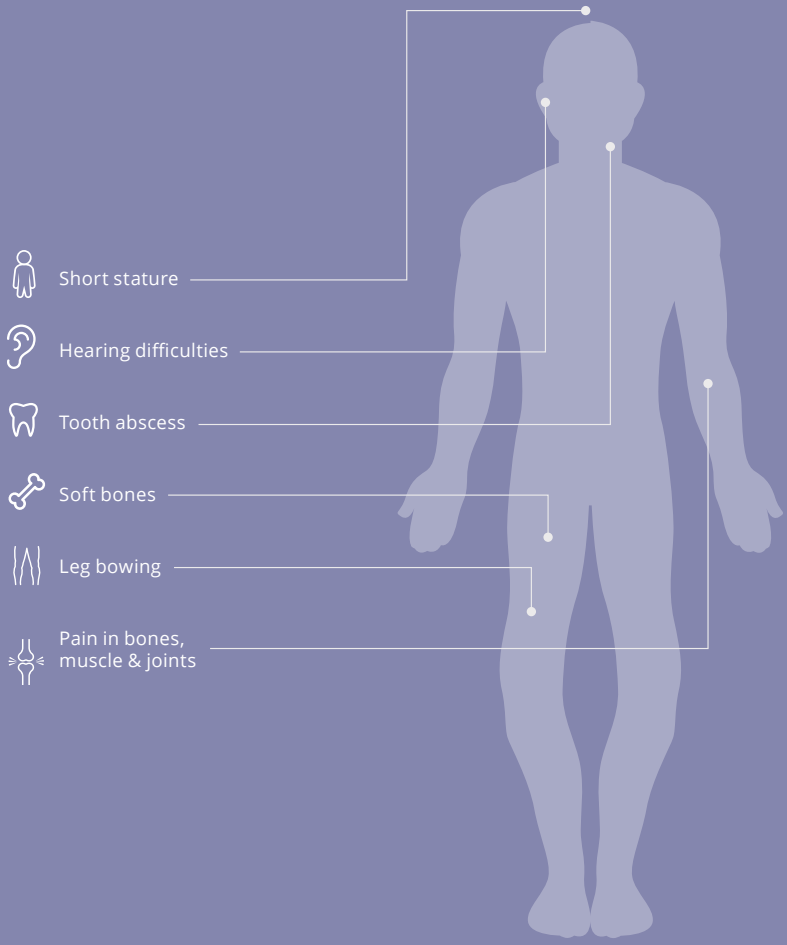
X-linked hypophosphataemia, or XLH, is an inherited bone disease caused by a gene mutation. Because of this mutation, the kidneys lose an excessive amount of phosphate into the urine.[1] Phosphate is important for building healthy bones, teeth and muscles.[2] Having low amounts of phosphate in the blood causes soft bones.[1,2]

XLH is a rare, lifelong condition that affects about 1 in 20,000 people, its symptoms vary in children and adults.[2]

How does XLH affect me?

With XLH, challenges often begin in childhood and continue or increase through adulthood.[2] Children may experience symptoms of rickets, such as limited growth, difficulty walking and bowed legs.[1,2]

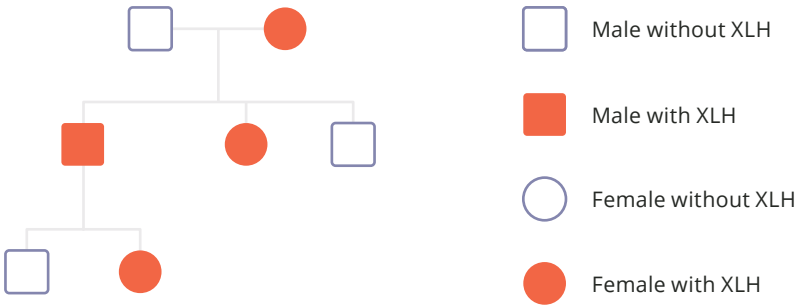
Some of the common symptoms in children and adults are[2]



How is XLH inherited?

Most people are born with XLH by inheriting an X chromosome with a mutated gene from one of their parents (this is why the disease is X-linked). In some rare cases, the XLH mutation happens spontaneously before birth, which means it isn't inherited from either parent.[3]

Because XLH is passed on through the X chromosome, mothers can pass it on to both sons and daughters, whereas affected fathers pass it on only to daughters.[1] This is due to the X-linked dominant inheritance pattern.[1]



X-linked dominant inheritance

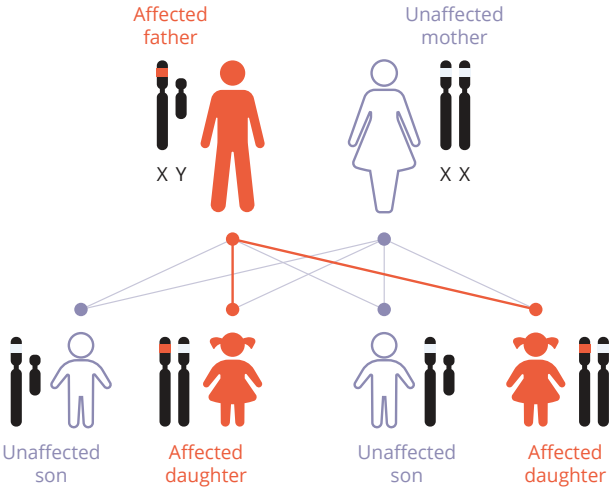
The X chromosome is one of the two sex chromosomes: women have two X chromosomes, while men have one X chromosome and one Y chromosome. XLH is inherited in an X-linked dominant pattern, so you only need one X chromosome with a mutated gene to have XLH.[1]

A man with XLH can only pass on the condition to his daughters. This is because his sons will all inherit his Y chromosome and won't receive the mutated gene on his X chromosome. His daughters must receive his X chromosome, so they are going to inherit the mutated gene.[1]

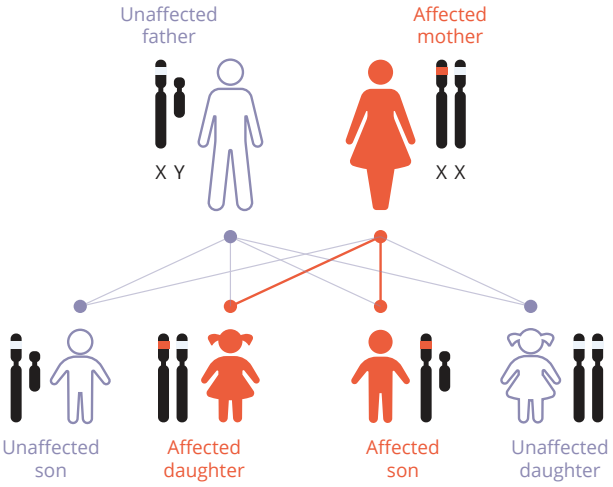
Women with the condition have a 50% chance of passing XLH on to all their children, regardless of sex, because they will pass on one of their

X chromosomes to all of their children, both male and female. If the inherited X chromosome has the gene mutation, then that child will have XLH too.[1]

XLH inheritance from an affected father



XLH inheritance from an affected mother



How will my family be affected?

Because XLH is a genetic condition, some of your relatives might also have it. They may or may not have symptoms.[2,4]

It is important to start conversations with family members soon after your XLH diagnosis. The process of family mapping can help identify other at-risk family members who would benefit from testing.[4–6]

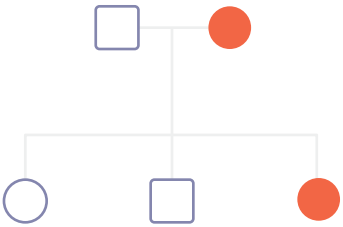
Diagnosing XLH as early as possible is essential to reduce the impact on those affected. Early interventions also help to reduce the impact on slow growth in children and improve symptoms like pain in adults.[3,7]

Mary has seen the importance of having open conversations about XLH first-hand. In her experience, this can help everyone who needs it get diagnosed:

"I think it's important to talk about XLH with the family because the more things are known about the disease, the sooner the diagnosis can be. Personally, I'd like to be there for anyone who might have XLH. My doctor said that newborns can be tested, but if you don't look, you won't know for a while if a child is affected."

What is family mapping?

After your diagnosis, you may go through a process of family mapping with your healthcare professional. You may also hear this referred to as pedigree mapping or pedigree analysis. This is the process of drawing a family map or ‘tree’ and using special software to predict inheritance patterns of XLH. This can help identify which members of your family might be affected by XLH. Healthcare providers, like doctors and genetic counsellors, can help you trace XLH in your family.



Male without XLH

Male with XLH

Female without XLH

Female with XLH

What are the benefits of family mapping?[3,5]

Helps family members understand how the disease impacts the rest of the family, even if they do not have symptoms[2]

Helps identify at-risk family members. Early identification is key to help those affected and to keep the disease from progressing, especially when symptoms are less obvious[2]

If you are thinking about having a child, family mapping can help you understand if your children are at risk of having the disease before they are born

Many families have already seen the benefits of family mapping. Read Sofie's story and how it changed her and her family's relationship with XLH.

"The first person that we know had XLH in my family is my great-grandmother. My father, uncles and I have it. So does my younger cousin. In the beginning, my family didn't like talking about XLH. It seemed the topic was avoided. When we decided to do family mapping, it became more normalised. It is a normal thing for us now, and everyone now speaks about it. If anyone in my family feels like they need to ask or say something, they can."

How to make a family map

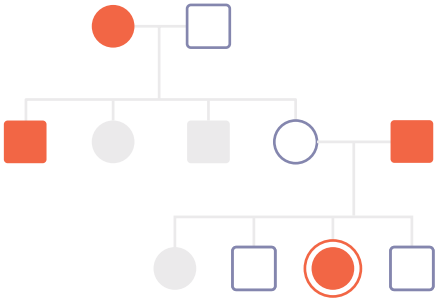
Even if only one person in your family has been diagnosed with XLH, a family map can still help you see other members who might benefit from testing.

You will likely work together with your doctor or a genetic counsellor to put together a family map. They can guide you on how to make it and help you identify who in your family might have had XLH.

Here are some of the things you might do in the process of making your family map:

- Speak to your family members and have a look through old photos. This could help you identify people in your family who might have been affected by XLH but weren't officially diagnosed
- Draw up a family tree of you and your relatives (including your immediate and extended family)
- Mark the people on the map who have been diagnosed with XLH. This might only be you
- Your doctor or genetic counsellor might use specialist software or other tools to predict who else in your family could be at-risk of having XLH
- Mark the people on the map who are at-risk of having XLH

XLH family map



Unaffected male

Undiagnosed, at-risk male

Diagnosed, affected male

Unaffected female

Undiagnosed, at-risk female

Diagnosed, affected female

Yourself

The next steps

Now that you know more about XLH, its inheritance and family mapping, you can start taking action. Managing a lifelong genetic condition like XLH will involve family members with or without the disease. It is important to have conversations early about how your condition could impact those around you. Having read this leaflet, hopefully you will feel more confident about your condition, discussing XLH and family mapping with your relatives.

Talk to your family about XLH

Talk to your family about your diagnosis. Explain the benefits of early identification, such as limiting the progression of the disease, and encourage them to investigate so that they know whether they are at risk of passing on the disease to their children.[5–6]

Talk to your doctor/nurse about family mapping

Talk to your doctor/nurse about the benefits of family mapping to support conversations with your family.[5–6]

Talk to your doctor/nurse to plan for the future

Talk to your doctor/nurse about what impact XLH may have in the future in terms of planning a family. Ask any questions you may have about the potential risks of passing on the mutated gene to help you plan for the future.[5–6]

References

1. MedlinePlus. Hereditary hypophosphatemic rickets. Available at: https://medlineplus.gov/genetics/condition/hereditary-hypophosphatemic-rickets/. Accessed October 2020.
2. National Organization for Rare Disorders. Rare Disease Database: Familial Hypophosphatemia. Available at: https://rarediseases.org/gard-rare-disease/12943/x-linked- hypophosphatemia/. Accessed June 2020.
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4. Haffner D, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia. Nat Rev Nephrol 2019;15: 435-455.
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6. Winger L. Living with genetic rickets. Arch Dis Child 2004;89:390-391.
7. Grosse SD, et al. What is the clinical utility of genetic testing? Genetics in Medicine. 2006;8(7):448-450.

Helpful resources

XLHLink.asia website
https://www.xlhlink.asia/

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