UNDERSTANDING X-LINKED HYPOPHOSPHATEMIA (XLH)

X-Linked Hypophosphatemia (XLH) is a rare and life-long genetic bone disease that affects 1 in 20,000 people. XLH is usually diagnosed in childhood but some symptoms are too mild and unnoticeable until adulthood. An early and accurate diagnosis is key to managing XLH.

WHAT TO LOOK FOR

OTHER NAMES FOR XLH

Hypophosphatemic rickets
X-linked rickets
Vitamin-D resistant rickets
Phosphate diabetes

CHILDHOOD

Symptoms of XLH often first appear in early childhood, but because phosphorus is important for normal growth and development, children with XLH may grow slowly and not grow very tall.

- Short stature
- Bone and muscle pain
- Tooth problems or abnormal tooth development
- Deformities in the legs (bow or knock-knee)
- Rickets (soft weak bones)

ADULTHOOD

Some symptoms are so mild they are not noticed until adulthood.

- Joint and muscle pain
- Muscle weakness
- Chronic fractures
- Stiff ligaments and tendons
- Abnormal patterns of walking
- Impaired mobility from enthesopathy (disorder in tendons and ligaments)
- Hearing loss

*Symptoms of XLH vary from person to person.

Bone pain, tender joints, or undiagnosed fractures found on X-rays are often the first signs of XLH. Over time, short stature may develop in adults. Other signs are chronic fractures, tooth and bone pain, as well as calcium in the tendons.

WHAT YOU NEED TO KNOW

Phosphorus is a mineral found in bones and is responsible for building and repairing bones and teeth, making muscle contract, supplying the cells with energy and essential for normal growth and development. The PHEX gene is responsible for regulating phosphates in the body. When there is a mutation on the X chromosome from the PHEX gene it stops the kidneys from processing phosphorus correctly.

HORMONES AND XLH

The hormone Fibroblast Growth Factor 23 or FGF 23 is made in bone cells and controls how much phosphate and vitamin D the body absorbs. Whatever the body doesn't need flows out through urine. If too much phosphate leaves the body, it can lead to abnormally low phosphate levels.

(Phosphate Wasting = Hypophosphatemia)

Low levels of phosphate can lead to poor bone health, bone pain, short stature.

XLH AND GENETICS

XLH is most often passed on through families by the X chromosome. If a child inherits a PHEX mutation on the X chromosome, fathers can pass it to their daughters and mothers have a 50 percent chance of passing it down to any child.

There is about a 20-30 percent chance of a person developing XLH without a family history.

DIAGNOSIS AND TREATMENT
A MULTIDISPLINARY APPROACH

Early and accurate diagnosis is key to managing XLH. A healthcare team experienced in managing XLH can provide personalized care and support. During an appointment, a specialist may analyze blood and urine samples to measure phosphate levels and complete x-rays to evaluate the condition of the bones. A specialist may also use genetic testing and ask about family health history.

Burosumab is an antibody that fights against FGF23 hormone and is the only FDA approved specific therapy to treat XLH in adults and children at least 6 months old.

Other treatments will depend on symptoms and severity, these may include:

- Phosphate supplements combined with high dose vitamin D (calcitriol)
- Surgery to help lower limb bowing
- Growth Hormone (for children)
- Dental Procedures

TALKING TO YOUR HEALTH CARE TEAM

The goal of treatment is to increase the level of phosphate to allow the body to develop and function normally. If you or a loved one may have XLH, it's important to play an active role during your doctor's appointment.

Other strategies to treat and manage symptoms:

- **Physical therapy** to support and prevent further bone and joint paint. Exercises such as yoga can help relieve symptoms.
- **Good oral hygiene** to prevent tooth pain and infections.
- **Annual x-rays** to monitor bones, joints and calcium levels.
- For children, **school support** is needed. Try to have an open discussion with school counselors, staff, and teachers to educate them about XLH and its challenges.
- For adults, **genetic counseling** or emotional support may be needed. Try to cultivate positive relationships with family, friends, and other people who may be able to offer support.

Visit endocrine.org for more information.

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