X-linked hypophosphataemia (XLH).

Six Australian Stories.

KYOWA KIRIN

In February 2021 Kyowa Kirin Australia interviewed a group of X-linked hypophosphataemia (XLH) patients.

The interviews were aimed at enabling patients to share their personal experiences of living with XLH: how the condition has affected them physically, psychologically and emotionally as well as the impact it has had on their families.

XLH throws up many challenges: initial diagnosis, a lack of management options that address the underlying cause of the disease, patient compliance with distasteful medication, and ongoing monitoring and treatment of diverse symptoms as patients age.[1]

For patients, the challenges are compounded by the physical[1], emotional[2], and psychological[3] burden of a condition that very few healthcare professionals, and even fewer members of the public understand. Ignorance of the disease leads to issues such as delayed or incorrect diagnoses[1] and bullying.[4]

Given all of the difficulties faced by those affected by XLH the following stories are remarkable for the courage, resilience and hope that shines through.

Georgia

Being familiar with the genetics of X-linked hypophosphataemia (XLH), Royce and Angela knew that Royce's XLH would be passed on to any daughter they may have. Whilst Georgia's XLH diagnosis was initially confronting, they have faced it with enormous courage, determination, and unwavering care.

Like her father Royce, aunt Angie, and grandmother Sue, Georgia has X-linked hypophosphataemia (XLH). Her mother Angela says that prior to starting a family she and her husband Royce "spoke very openly and honestly, so I had a really great understanding of the condition and the family history before we decided to have kids."* Nevertheless, after falling pregnant she found it confronting to find out they were having a girl as she knew XLH would be passed on to any daughter fathered by Royce.

It was difficult for Angela to see Georgia start taking phosphate supplements at 3 months of age, saying "it seemed like she gagged on it." She was also concerned as to how Georgia's medication could be administered at kindergarten, not to mention all the paperwork required for workplace health and safety precautions every time the dosage was changed. She worried too about the possibility that Georgia might refuse to take the medication and was concerned that, as she got older, she might throw it away as Georgia's father did with his phosphate medication when he was at school. As well as phosphate supplements, Georgia was prescribed active vitamin D twice a day to help manage the condition.

The frequent medical appointments and assessments required to manage Georgia's condition were also difficult for Angela and Royce: "it's heartbreaking when you've got to pin your child down".

Angela is very conscious about the possible issues that Georgia might face as she grows older such as restricted growth, bowing of the legs and "how other kids would treat her." Indeed, XLH caused Georgia to be pigeon-toed and affected her gait. She would also fatigue very easily with Angela commenting: "That would turn into her being naughty" because being so little she couldn't express how exhausted she was. "From the beginning" she says, Georgia was "a really cautious child. She would avoid physical activity" like riding her bike.

Royce says that since becoming Georgia's father and through the influence of Angela, who he says is "such a good partner and such an amazing mum," his outlook on XLH has changed considerably. The effect that XLH has had on Georgia and the emotional impact it has had on his wife Angela has "certainly made me more aware of how the condition can be quite hard to deal with emotionally, physically, mentally and how there are a lot of hurdles to overcome with medications, appointments and any complications that could arise." He considers himself to have "gotten off really lightly" from XLH and is aware that Georgia may not "get off as lightly as I have."

Royce and Angela are not only concerned about the challenges that face Georgia while she is young but also those she may face as she ages. Their hope is, as with all families dealing with XLH, that advances in treatment therapies mean patients will soon be able to live lives free of the many burdens associated with the condition.

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Angela and Royce about their experience as parents of a child with XLH.
**All comments in inverted commas are verbatim quotes from either of Georgia's parents, Angela or Royce.*

Georgia's Journey

- **Diagnosis 2017**
- **Third generation of XLH inheritance**
- **Major challenges to parents**
- **First medication at three years old**
- **Looking to the future with hope**

"My daughter is magical. I wouldn't have it any other way."

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Naomi

Despite receiving standard treatment options available at the time, Naomi suffered from numerous effects of X-linked hypophosphataemia (XLH) from a very early age. Her dream is that new therapies will be developed that allow children to live normal lives free from the trauma she endured.

By the age of two Naomi's legs were bowed and she wasn't walking like other children her age. Her mother took her to numerous doctors who weren't able to diagnose her condition. It wasn't until an astute general practitioner suggested seeing a specialist in Brisbane that her X-linked hypophosphataemia (XLH) was finally diagnosed.

Once diagnosed, she was prescribed six phosphate tablets daily to supplement the phosphate lost through her kidneys due to the XLH. She describes the taste and associated side effects as "the most disgusting thing on the planet. It gives you diarrhoea and stomach cramps."*

Growing up Naomi's legs remained bowed and she was pigeon-toed. Although at school she was able to play handball and do other activities she "couldn't really participate in athletics or anything like that because I can't really run."

Despite having a group of supportive friends as a teen, Naomi found it difficult to "have a normal teenage relationship." XLH had retarded her growth and "one boy said to me, 'call me when you grow up and then we'll go out.'" At the time, she suffered some serious psychological turmoil when "trying to deal with the taunts and looking different."

At age 17 Naomi felt that she wasn't receiving appropriate medical support: "I aged out of the children's health system. I had a specialist that I didn't particularly know or get along with." At one point when her knees locked she couldn't move her legs and had to attend an emergency department. When she tried to tell the doctor that the locked knees were a consequence of her XLH he dismissed her explanation as "rubbish." In her 20's she had her first arthroscopy. Three more were to follow.

Problems with her teeth have also been a recurring issue in her adult years. Because of dental abscesses, she has now had most of her teeth removed and replaced by dentures.

Naomi has two sons, both of whom are also affected with XLH. Naomi took their diagnoses badly: "It was pretty awful actually. I cried, my husband cried. I blamed myself quite a lot." Reflecting further on being a mother with XLH she noted: "One of the cruellest things about this condition" she says, "is the genetic trauma, the generational nature of it." Because of this, Naomi and her husband have talked to their boys from an early age about the fact that any daughters they have will inherit XLH.

As an adult, Naomi has learned to accept life with XLH. It has taught her that "if you're happy with yourself and your family and the friend group that you have, you don't actually need anything else."

Naomi has lived with XLH for 48 years and is unaware of any new treatment options having become available in Australia in that time. Her dream is for a new XLH treatment that allows children to have a normal life and not have to face the emotional and physical traumas that she endured.

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Naomi about her experience as a patient with XLH.
** All comments in inverted commas are verbatim quotes from Naomi.*

Naomi's Journey

- **Delay in diagnosis of XLH**
- **High dosage of phosphate from an early age**
- **Bowed legs**
- **Challenges of parenting XLH affected children**

"if you're happy with yourself and your family and the friend group that you have, you don't actually need anything else."

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Sue

Sue's story is one of extraordinary resilience. It spans the recent history of XLH from the days when it was referred to as Vitamin D-resistant rickets through to the present when there is hope that her granddaughter, also affected by XLH, will live life as if there wasn't anything wrong at all.

Sue's first symptoms of X-linked hypophosphataemia (XLH) started at an early age with bowing of her legs. Attempts were made to straighten them by manipulation and plastering, which in Sue's words "achieved very little".* She was subsequently diagnosed with "vitamin D-resistant rickets" and started on vitamin D2, which was considered the best available treatment at the time.

At about age 10, Sue underwent a procedure known as an osteotomy, which involved surgically breaking the tibia and fibula bones of both legs to try to straighten them. Unfortunately, the osteotomy wasn't successful and Sue's legs re-bowed. Sue reflects: "so although I still think I had the best treatment available at the time, it's certainly not the best treatment now. The osteotomy was an attempt to cosmetically change the appearance of the lower part of the leg. It didn't do anything to correct the bowing in the femur."

During Sue's early primary school years she experienced multiple dental abscesses, which ultimately resulted in all her teeth having to be removed. Unfortunately, Sue's hardships weren't just physical. She remembers other children calling her 'bandy legs', having snow rubbed in her face, and having to call out "wait for me, wait for me" because fatigue made it difficult for her to keep up with other children while walking up a hill to school. Despite everything Sue's remarkable resilience and strength developed with the support she received from her mother and grandparents.

As she moved into adulthood, Sue recalled that "during what you would call a woman's reproductive years I was fairly symptom free. I mean, the deformity was obvious, but I don't recall getting any great aches or pains".

However, this changed during her post-menopausal years, when her XLH progressed and resulted in a stress fracture, joint pain associated with osteoarthritis, and hearing loss. She's also endured frequent muscle pain and agonising muscle cramps.

The increasing progression of Sue's XLH symptoms is making it more difficult for her to cope with some of the basic activities of daily living, such as vacuuming, and leads to her concern that she might eventually require a premature move into an aged care facility.

Sue's experience and understanding of XLH has increased markedly over the years. Her son Royce, daughter Angie, and granddaughter Georgia are all affected by XLH. Since the days when it was known as Vitamin D-resistant rickets she has seen significant improvements in diagnosis and management.

The ability to diagnose earlier has particularly benefited her son Royce whose treatment started "virtually at birth". Sue feels that her daughter Angie, whose treatment commenced at around 18 months of age, had a more challenging treatment journey. Even with the existing available treatments at the time, Angie still developed a 'wind swept deformity' of her legs in addition to experiencing complications with one of the prescribed vitamin D treatments which led to hearing and visual loss.

Regardless of all the challenges XLH has thrown at her, Sue remains remarkably positive, maintaining that through everything she has been fortunate. Her wish is that new treatments will allow younger XLH sufferers like her children and grandchild to live lives free from some of the difficulties she has endured as she has aged.

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Sue about her experience as a patient with XLH.
** All comments in inverted commas are verbatim quotes from Sue.*

Sue's Journey

- **Bone deformity**
- **Orthopaedic surgery at an early age**
- **Supportive mother and grandparents**
- **Daughter, son and granddaughter affected by XLH**
- **A beacon of hope and strength**

"I think of myself as being blessed."

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Royce

Royce has remained remarkably optimistic and strong despite the difficulties XLH has thrown at him. He is now focussed on supporting his wife Angela as they navigate through the challenges faced by their young daughter Georgia, who is also affected by XLH.

Royce's earliest memory of being treated for X-linked hypophosphataemia (XLH) was the phosphate supplement he had to drink five times every day. He recalls it being tolerable to begin with but 'torture' after being on it for several years. "We tried absolutely everything from mixing it with orange juice to chasing it down with a glass of Milo. But it was really hard to take at the end".*

In addition to the challenging taste and frequent dosing schedule, one of the side effects of the phosphate was "quite bad diarrhoea. It was really awkward and really hard to deal with".

Royce had to deal with numerous painful physical experiences as a result of XLH. He had multiple dental extractions and he also underwent several years of daily human growth hormone injections. However, he maintains that the experience of getting the growth hormone needle was much easier to deal with than drinking the phosphate.

When his specialist decided to stop phosphate therapy for Royce around age 15, he called it "a hallelujah moment. It was so, so good. And I had good steady bowel movements that I hadn't had for 15 years."

Despite being relatively symptom free, Royce had a sense of being "a bit different" when he was a child. He recalls it feeling a bit strange when he had to undress so that his specialist could check the straightness of his legs – "do all the kids do this?" he wondered.

Being teased by other children because of how XLH affected the way he walked and ran could have caused him much more distress, but he quickly learned to turn things around on his potential tormentors by pointing out that "people are different, most people have some sort of condition and mine was XLH."

Despite his experiences with XLH, Royce remains remarkably upbeat. He says, "I've gone on to have a really good life, a happy life. Physically it hasn't limited me too much, if at all. I didn't avoid much physical stuff myself. I didn't suffer from any bone pain".

Coming from a strong and supportive family unit, Royce always wanted to start his own family, but he was very "cautious and measured" when considering it. He discussed the issues of XLH inheritance in depth with his wife Angela, early in their relationship. Even with his own resilience and natural optimism, it was very confronting to see their daughter Georgia diagnosed with XLH. Seeing her subjected to numerous blood tests, medical examinations, and ongoing doctors' appointments required to manage the condition was "pretty hard" for him.

Royce's positive outlook extends to Georgia's future; he anticipates that medical advances to treat the underlying cause of the condition will allow her to live her life to its full potential, free from the obstacles and difficulties that XLH forced him to contend with over the course of his own life.

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Royce about his experience as a patient with XLH.
** All comments in inverted commas are verbatim quotes from Royce.*

Royce's Journey

- Daily phosphate from the age of four
- Painful teeth extractions
- Supportive family
- Bone deformities
- Challenges of passing on a genetic condition (XLH)

"My experiences with pain and XLH is probably all to do with sitting in the dentist chair."

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Angie

In spite of the significant health challenges Angie has faced because of XLH, she feels "blessed" in a number of ways. These include relishing the joys of being an aunt and embracing the fact that she has a condition which makes her unique.

Like her mother and her brother, Angie is affected by X-linked hypophosphataemia (XLH). XLH can affect those with the condition differently (even those in the same family). As a case in point, when Angie compares herself to her brother she says, "I think I've got kind of the bigger double whammy of it."*

Unlike her brother, Angie suffered significant bone problems. She needed surgery for bone deformities, suffered frequent bone pain and cramps, and had significant limitations on her physical activity.

As she was growing up, XLH caused her to have "knock knees" which affected both her confidence and her ability to keep fit. To worsen matters, the children at her school teased her about the way she walked. Around the age of 13, she had surgical staples inserted in her bones to straighten her knees. The procedure itself also caused her significant difficulty: she recalls "to stand up, I'd have to put one knee in front of the other or I'd have to spread my legs slightly apart to keep my balance." The staples made her knees badly swollen and painful. Accidentally discovering hydrotherapy helped her to "learn to walk again".

Angie's doctor monitored her progress carefully and after ensuring her legs were growing in the correct way, the staples were removed. Angie says that their removal wasn't as painful as having them put in and that overall, she definitely feels the treatment was quite effective at straightening her legs. Despite that, any weight bearing activity has been "an absolute challenge" for her. She remembers at school that "jogging around the oval was tortuous." There were things she wanted to do but avoided such as dancing, gymnastics, and typical schoolyard activities like cartwheels.

XLH also affected her teeth and she underwent several rounds of orthodontic treatment to try to straighten them. Eventually however, XLH caused her teeth to loosen, necessitating their removal and the fitting of dentures.

She agrees with her mother and other patients that XLH sufferers develop a high pain threshold. Sometimes she will wake up in the middle of the night with leg cramps but feels that the pain is nothing like the pain she experienced when she had the knee surgery.

As a female with XLH, Angie has a 50:50 chance of passing it on to any of her children. Given her experience with the condition, she made the "huge" decision not to have children because she didn't want to pass it on and have them go through what she did.

She says the decision is a "blessing in disguise" because she enjoys helping to look after her brother's children but then gets her freedom after she's "done my job for the day being an aunt."

A keen philosopher, Angie also counts her blessings in other ways; "I've got a condition that no one really knows about. It makes me unique. I'm different and I'm glad I'm different."

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Angie about her experience as a patient with XLH.
** All comments in inverted commas are verbatim quotes from Angie.*

Angie's Journey

- **Daily phosphate from an early age**
- **Surgery to correct "knock knees"**
- **Childhood teasing**
- **Teeth replaced with dentures**
- **Decision not to risk passing on a genetic condition (XLH)**

"I've got a condition that no one sort of knows about. It makes me unique. I'm different and I'm glad I'm different."

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Jack & Mikey

For brothers Jack and Mikey, X-linked hypophosphataemia (XLH) has been character-defining. With constant support from their mother combined with their own unique strengths, they have faced considerable challenges from early ages. Still in their teens, they offer wise words of encouragement and hope to others with the condition.

Having a mother with XLH, Jack and Mikey were both tested early to see if they also had the condition. The tests confirmed that they did. Despite treatment with phosphate supplements and active vitamin D the boys went on to have multiple surgeries and suffer other effects of XLH.

At age 5, Jack had bilateral osteotomies to his lower leg bones, and, in the same operation, steel rods were inserted into those bones to provide stability. He remembers at the time the surgery being "quite scary".*

At age 7, Jack underwent further operations to insert 8-plates on both knees to help guide the growth of his legs. The plates were removed when he was 8 but unfortunately, he had to undergo the procedure again at age 10 before having this second lot removed at age 12.

Mikey also had surgery on his legs but apart from slight pain he remembers very little about his operation. He does, however, remember the difficult challenge of having to learn to walk all over again.

Because of his short stature, Jack received growth hormone therapy and though it significantly increased his height, he feels that his rapid growth caused his right femur to curve. At age 16, he underwent a 3rd 8-plate surgery on his right knee in an attempt to rectify this issue but unfortunately the procedure was unsuccessful. "I kind of feel like I have a bit of a limp because the curve in the upper part of my right leg has shortened that leg a bit." At the time of this interview, Jack was preparing for more surgery where the 8-plates will be removed from his knee and he will undergo a femoral osteotomy in an attempt to correct the problem.

Jack has also had to endure oral surgeries, but despite everything he is very grateful for the support received from his XLH specialists, saying "it's really good to know they are trying to know more about the condition to help us further."

Running has been challenging for both boys. For Mikey it is quite difficult and causes knee pain after about 50 meters. Jack can sprint for a "couple of hundred metres…then I start to feel it, my shins hurt a bit."

Both boys strongly dislike the taste of the phosphate supplement they've had to take. Mikey says "phosphate… disgusting…we don't like the smell, the taste is terrible."

Because XLH has restricted their growth, both boys have been frequently bullied. Jack however has used it to develop resilience, saying "I'm kind of immune to it now."

Now 18 years old, Jack is nervous about transitioning out of paediatric care and wonders if his new specialist will know enough about XLH and whether they will support him as much as his existing specialist does. He also worries a little about the thought of leaving home and having to handle his own medical affairs. Despite this, he remains positive and looks forward to the challenges self-management will bring.

Both have inspiring words for others who have XLH. Mikey hopes that in the future "I would like to see people with XLH to not let it get in their way – to act as if they don't have it." Jack urges people with XLH to "stand tall. XLH is quite impactful in your life but you've just got to make the most of your life. Try to find people who can support you and eventually things will work out for you."

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Disclaimer: This article was written by a medical writer based on an unpaid interview with Jack and Mikey about their experience as patients with XLH.
**All comments in inverted commas are verbatim quotes from Jack or Mikey*

Jack & Mikey's Journey

- Orthopaedic surgeries at an early age
- Supportive mother
- Daily phosphate
- Survivors of bullying
- Hope for the future

"Stand tall. XLH is quite impactful in your life but you've just got to make the most of your life. Try to find people who can support you and eventually things will work out for you."

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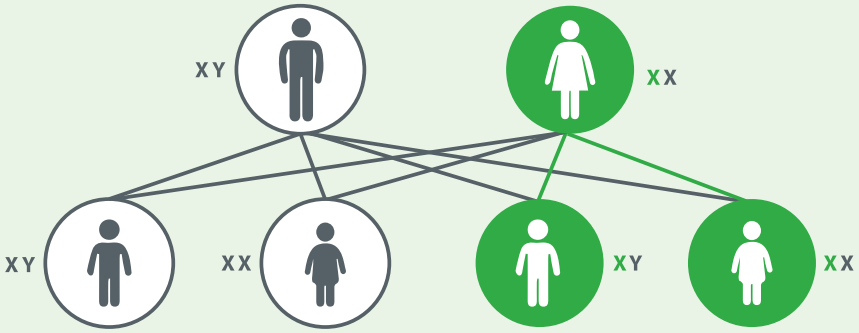
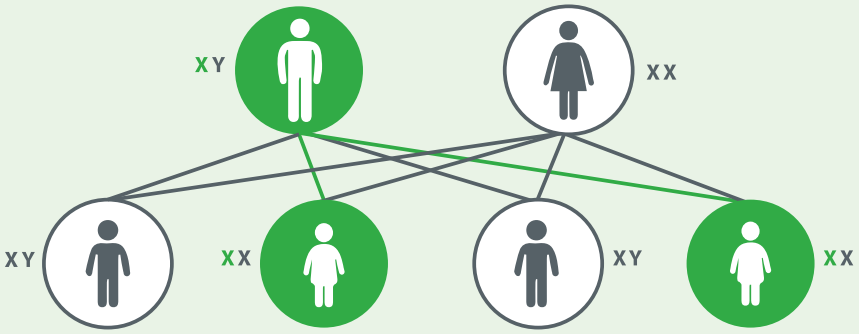
X-linked hypophosphataemia genetic inheritance patterns[5]

Mother with XLH



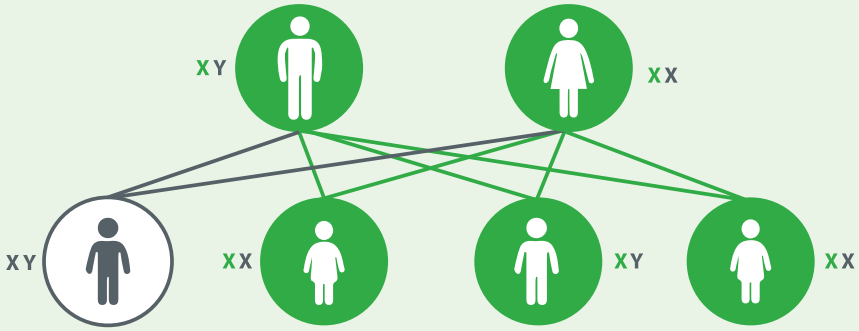
When a mother has XLH and the father is unaffected, 50% of all children are at risk

Father with XLH



When a father has XLH and the mother is unaffected, all daughters but none of their sons will inherit XLH

Mother and Father with XLH



When both mother and father have XLH, all daughters and 50% of their sons will have XLH

Glossary of terms

Arthroscopy
An arthroscopy is a minimally invasive surgical procedure to diagnose and/or treat injuries and other issues of a joint. It is often used to remove damaged or diseased bone.

Bowed legs
Bowed legs refer to legs that curve outward at the knees while the ankles are close or in contact.

Eight-plate surgery
Eight-plate (or 8-plate) surgery is used in children with abnormal bowing or knock knees. A small metal figure eight shaped device called an 8-plate is inserted across the knee growth plates. This procedure temporarily slows the bone growth at the site while the rest of the knee continues to grow and gradually straightens the knee.

Femur
The femur or thigh bone is the longest and strongest bone in the human body.

Fibula
The fibula is the smaller of the two bones of the lower leg. It is commonly called the calf bone and is located on the outside of the leg.

Human growth hormone
Human growth hormone is produced by the pituitary gland and stimulates growth in children and adolescents. It is also produced synthetically and can be used to stimulate growth in those with short stature.

Hydrotherapy
Hydrotherapy refers to using water as therapy. Examples include wading in a swimming pool and sitting in a warm bath.

Hypophosphataemia
A disorder in which there is an excessive loss of phosphate through the urine. Low phosphate levels can result in skeletal deformities, dental issues and muscle abnormalities.

Knock knees
Knock knees refers to an abnormal curve of the legs causing the knees to touch or nearly touch while the feet are apart.

Osteotomy
Bone surgery performed to correct problems such as bowed or bent legs. The procedure may involve removing a wedge of bone from the tibia and fibula and/or femur and rotating the bone into correct alignment. The bone is fixed into position using screws, pins, plates or a combination of all three. With bowed or knock knees the surgery often needs to be performed on both legs in a procedure known as a bilateral osteotomy.

Phosphate supplementation therapy
Phosphate supplementation therapy aims to increase the amount of phosphate in the body. This can be achieved by taking up to 6 oral doses of phosphate salts per day. Dosage varies based on a patient's age and weight.

Tibia
The tibia is the larger of two bones that make up the lower leg. It is commonly called the shin bone.

Wind swept deformity
A condition in which both legs may look as though a strong wind has swept both legs to one side of the body.

X-linked
'X-linked' refers to a condition, such as XLH, that is caused by a mutation that occurs only on the X chromosome. The X chromosome is one of the two sex chromosomes that humans have. Females have two X chromosomes. Males have an X and a Y chromosome.

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