

## Insights

# For Those Born With Rare Diseases, Early Diagnosis Can Save Lives



*Lyra Cole*

Just three days after their daughter, Lyra, was born, Amber Cole and her husband realized that something was wrong. Lyra had lost an abnormal amount of weight and couldn't gain it back; and frighteningly, whenever they lifted her legs to change her diaper she would scream in pain.

"Every time we changed her, her scream broke our hearts," says Amber.

Amber and her husband immediately went to see Lyra's pediatrician, who assured them that Lyra was acting like other stubborn babies who didn't want to stretch. The Coles went home, but after six weeks things only seemed to be getting worse. Lyra still showed signs of pain, was struggling to gain weight and experienced severe projectile vomiting. The Cole's pediatrician suspected she might have pyloric stenosis, a disorder that would help explain the vomiting, and

referred the Coles for testing at their local hospital. When the tests came back, they showed something else entirely:

Lyra's ultrasound revealed excessive calcium deposits in her kidneys and her bones were so demineralized that they didn't show up on her x-ray—it looked as if they were just not there. There also appeared to be large gaps in her spine, her ribs were curved inwards, and her hip bones appeared jagged, which explained the pain Lyra felt when her legs were lifted.

Lyra and her parents spent four days in the hospital and, after additional genetic testing, Lyra was diagnosed with Hypophosphatasia (HPP), a rare and [potentially life-threatening disorder](#) that can begin prenatally and adversely affects teeth and bone development. While the severity of HPP varies, with some cases only affecting dental development, children born with more severe forms of HPP have [soft or weakened bones](#) that can cause skeletal deformities, fractures, pain and, in the most severe cases, death. It is estimated that severe forms of HPP occur in [one out of every 100,000 live births](#).

“The day she was diagnosed was the scariest part,” says Amber. “When they came in, they told us that it was a potentially fatal disease and we thought we were going to lose our daughter. But we haven't—she's still here, our little miracle baby, and she's doing amazingly.”

Once diagnosed, Lyra was started on a course of treatment that has proven incredibly effective. “Watching her develop as she should has been absolutely astounding,” says Amber. “When first diagnosed, they said she might need leg braces, but she doesn't—she can crawl, stand and is even trying to walk now. It's incredible. To go from how she was before diagnosed to how scary that initial diagnosis was to how hopeful we are today is just mind boggling.”

### **A need to raise awareness and improve diagnosis**

Lyra's remarkable progress was made possible because she was diagnosed early and able to start treatment. But for many people born with HPP, this isn't the case—this is a reality that the Coles know too well. After taking Lyra's family history, Lyra's endocrinologist recognized that Amber and her family had experienced similar symptoms and suggested they too have further testing. They then learned that Amber had been living with the same form of HPP as Lyra, and Amber's sister and three of her sister's children were also living with a less severe but still painful form of HPP.

Treatment for HPP includes regular injections, which can be painful. After Amber was diagnosed, she started doing her injections with Lyra so her daughter would know that was not alone:

“I want her to know how strong she is and to know I’m here for her, so we do our shots together,” says Amber. “I am a mom, and this is what moms do—we have to be strong for our kids, especially when we have incredibly special ones.”

“It took Lyra getting tested to find out what was going on,” says Amber. “No one has heard of this—Lyra’s endocrinologist said this was the first case she had seen in 30 years. So, if you have symptoms that you don’t know are symptoms of hypophosphatasia, you can go your entire life, and no one knows to test you. If my husband and I hadn’t had Lyra, we would have gone our whole lives thinking pain was normal.”

Even with Lyra’s early diagnosis, the rarity of her disease has made it difficult for her family: there is still so much unknown. No one can tell them when Lyra will hit her developmental milestones because every person with HPP develops differently. Amber and her family are committed to raising awareness about HPP, so that more people can benefit from early diagnosis and there’s increased momentum toward improvement treatment.

“The more people who know about it, the more people who will get diagnosed and have answers to their problems,” says Amber. “And, the more people diagnosed, the more research that goes into it, so maybe one day, we’ll have a cure or an even better treatment to begin with.”

## **Learn more about Hypophosphatasia (HPP)**

### **A Tool for Diagnosis**

Since normal alkaline phosphatase (ALP) activity varies based on age and sex, pediatric health professionals must refer to age- and sex-adjusted ALP reference ranges to ensure an accurate interpretation of [ALP levels](#). The CALIPER study has published readily accessible information for over 100 laboratory reference ranges in pediatric patients based on an extensive survey of almost [10,000 healthy children](#).

You can access that information here: <http://www.sickkids.ca/caliperproject/>

While there are clear signs of HPP in children—including poor weight gain, missed motor milestones, premature tooth loss, slowly-healing or recurrent fractures, and muscle weakness—HPP can be difficult to diagnose because many symptoms overlap with more common diseases, such as rickets. However, because HPP is caused by reduced ALP (alkaline phosphatase) enzyme activity, pediatricians can diagnose HPP based on both clinical symptoms and low ALP enzyme activity detected on routine bloodwork.

When signs and symptoms of hypomineralized bone are seen in pediatric patients, it's important to consider HPP and promptly evaluate ALP levels according to age- and sex-adjusted ranges. We're sharing this information to help more individuals like Lyra receive a timely diagnosis, so their families are connected with appropriate interventions and resources as early as possible.

### **Relevant articles and resources**

- Interested in learning more about NICHQ's approach to improving health outcomes for children born with rare diseases? Read [this article](#) from NICHQ president and CEO.
- Are you a family affected by HPP? <https://www.softbones.org/> provides resources and support.