



HYPOPHOSPHATASIA

Understanding the Need

Case For Support



FINDING THE KEY TO HPP

The Current Landscape

Few genetic conditions have the life-altering impact of hypophosphatasia, also called HPP.

A rare and sometimes fatal metabolic bone disorder, HPP is in many respects a medical enigma. This inherited disorder occurs when a gene mutation causes the body to produce low levels of alkaline phosphatase (ALP), an enzyme essential to building healthy bones. Without it, bones become weak and soft, causing skeletal deformities, fractures, premature tooth loss, chronic pain and even death.

HPP is a rare disease with limited research funding, making finding a cure as elusive as the condition itself.

HPP can also affect the brain and other major organs. The condition has so many disparate symptoms and levels of acuity, in fact, that patients and physicians sometimes fail to connect them to the same disease. The result? HPP often goes undiagnosed – leaving patients no choice but to live with debilitating symptoms that worsen as the disease progresses.

HPP is also one of 7,000 rare diseases that receive limited research funding, making finding a cure as elusive as the condition itself.

Despite these challenges, there is some good news: in November 2015 the FDA approved the use of Strensiq – the first-ever enzyme-replacement therapy for pediatric HPP in the U.S. And while preliminary results appear promising, there is still much work to be done.

Meeting the Challenge

The Soft Bones Foundation is a non-profit organization devoted exclusively to finding the key to HPP. Formed in 2009, we are the first and only U.S. based advocacy group whose mission is to educate, empower and provide a community to people living with hypophosphatasia, their families and caregivers. We also promote clinical research through an annual grant. Under the leadership of founder Deborah Nettune Fowler, Soft Bones has raised awareness at home and around the world so that HPP receives the policy recognition and research funding it deserves.

FUNDING NEEDS

The Soft Bones Foundation is seeking philanthropic funding to support three vital initiatives that will expand the scope of our work. Funds will support patient advocacy, education and outreach, as well as clinical and basic research. We invite you to partner with us to improve the lives of people with HPP today while we work toward a cure.

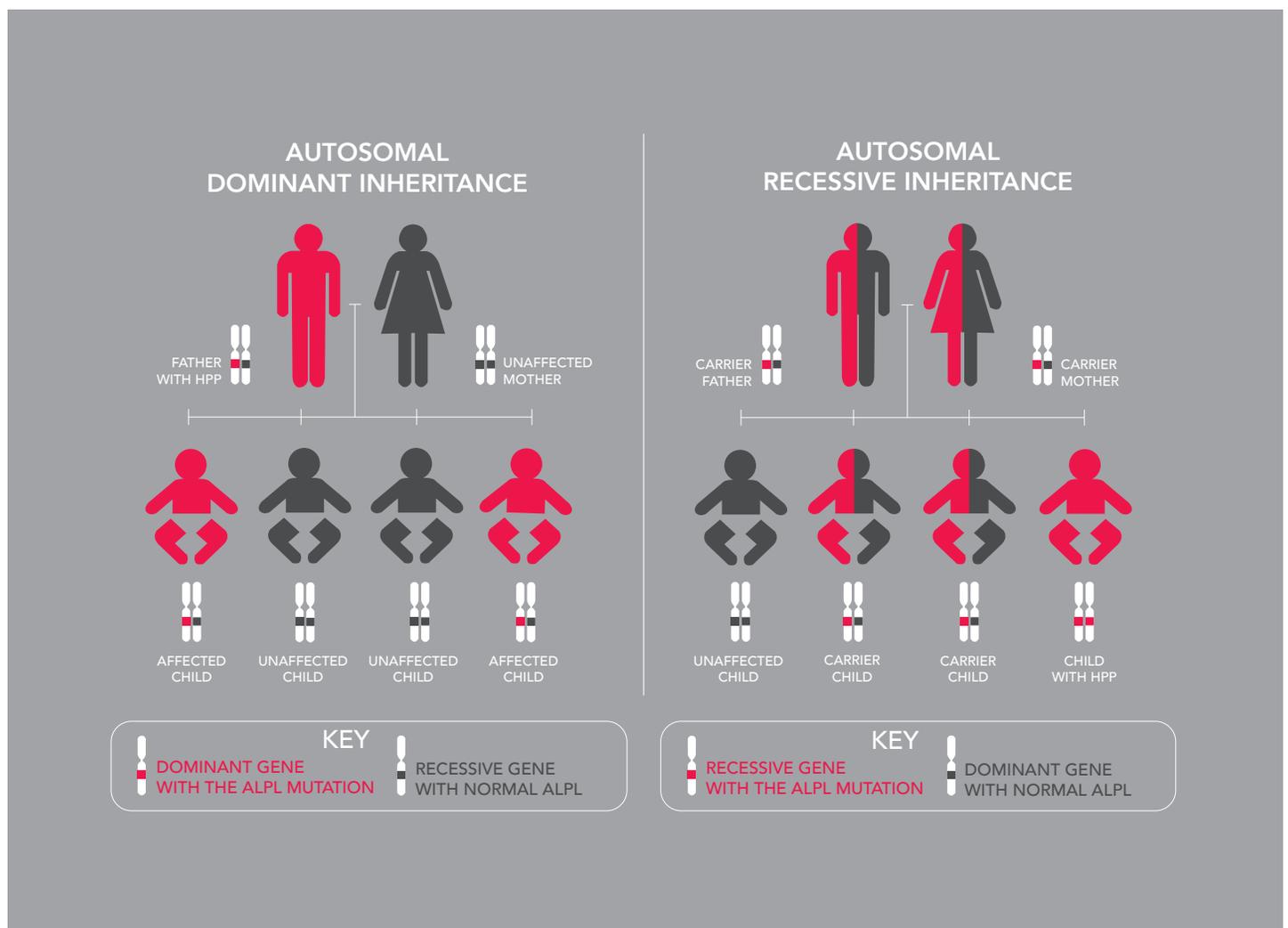
ABOUT HPP

Causes

People with HPP have trouble making the enzyme alkaline phosphatase, or ALP. A faulty gene (the TNSALP or ALPL gene) is to blame. Healthy bones are made strong and rigid when minerals, like calcium and phosphorus, are added to the bones through a process called mineralization. Without enough ALP, certain chemicals build up and prevent calcium and phosphorus

from binding together and depositing in the bones, leading the bones to be soft, curved and fragile and teeth to become loose or fall out prematurely.

The affected gene can be passed from generation to generation, but it is possible for people to carry the gene and not exhibit any symptoms. In the severe perinatal and infantile forms of HPP, one defective gene is inherited from each parent. Some milder childhood or adult HPP patients may develop it this way as well. Other mild adult cases seem to be inherited when there is only one defective gene from one parent. Genetic testing and counseling is strongly encouraged to determine the likelihood and severity of HPP recurring in families.



Conditions

HPP can present at any age. Typically, the earlier symptoms become apparent the more severe the condition. It is estimated that severe forms of HPP occur in approximately one of every 100,000 live births. The more mild childhood and adult forms are probably more common and one out of every 200 Americans may be a carrier for HPP. Ironically, a diagnosis is made through simple x-rays and blood tests – IF a physician is familiar with the disorder. Because it is rare, HPP often goes undiagnosed or is misdiagnosed for other conditions such as osteoarthritis in adults and rickets in children.

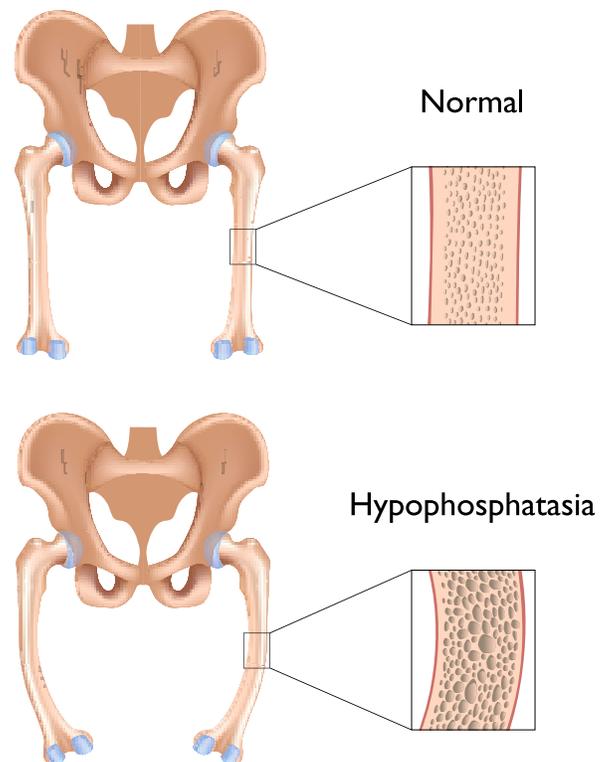
It is difficult to determine the true frequency of hypophosphatasia in the general population, but in the U.S. there are close to 300 diagnosed patients. It occurs with greatest frequency in the Mennonite population in Canada, and is relatively prevalent in Japan.

Clearly, HPP is a rare disease, but one with serious health risks and quality of life impact.

Complications

The first and most obvious symptoms are premature tooth loss and frequent bone fractures. HPP can affect other parts of the body as well. Some patients have an abnormally shaped head and suffer seizures or craniosynostosis (pressure on the brain); others develop kidney disease or failure from a buildup of calcium. Some experience muscle weakness and chronic pain, while others have underdeveloped lungs that make breathing difficult. Short stature, bowed legs and relentless bone pain are other disease traits.

One thing HPP patients have in common is the chronic and progressive course of the disease, which can severely limit basic functional ability – walking, jumping, standing, climbing and even lying down – and with it quality of life. In some cases, HPP can be fatal.



New Treatment, New Hope

As yet, there is no cure for hypophosphatasia and until recently no effective treatment. But in the summer of 2015, Strensiq™ (asfotase alfa) was approved for use in Japan, Canada and all 28 countries in the EU. Six months later it was approved for use in America. Developed by Alexion, a global pharmaceutical company specializing in rare diseases, Strensiq is indicated as an enzyme replacement therapy in pediatric HPP patients. It is currently being investigated as a therapy for adult HPP. The drug allows phosphate and calcium to bond and improve bone health. Strensiq has improved survival rates in perinatal/infantile-onset HPP (almost always fatal), and improved growth, mobility and gait in children with juvenile-onset HPP.

We recognize that this is a significant step forward in managing HPP, but Soft Bones is committed to do more.

WHO WE ARE

Soft Bones is built on three pillars:

- Advocacy and education
- Access to testing, treatment and resources
- Research aimed at treatment and finding a cure

Our mission is to provide accurate, up-to-the-minute information, education and support for people living with HPP. Deborah Nettune Fowler, whose son Cannon was diagnosed with HPP at 18 months old, established the first HPP advocacy organization in the U.S. in 2009. (Their story can be found at softbones.org).

Today Soft Bones is part of the Rare Bone Disease Advocacy Alliance, which allows us to lobby for increased federal spending to accelerate research and new therapies. We have conducted Congressional briefings and State House events to educate our leadership on the disease, and successfully worked with the Social Security Administration to allow HPP patients access to disability benefits. We also partner with HPP advocacy groups worldwide.

Our Patient Advisory Board provides invaluable experience about what it is like to live with HPP. Their job is to identify unmet needs within the HPP community and suggest ways in which Soft Bones can best meet them.

Our Scientific Advisory Board provides essential clinical expertise on educational material development and strategic guidance for research grants, among others. The board is chaired by Michael P. Whyte, M.D., Medical-Scientific Director at the Center for Metabolic Bone Disease and Molecular Research, Shriners Hospital for Children in St. Louis, MO.

FUNDING PRIORITIES

Advocacy and Outreach

International HPP Patient Registry **\$50,000**

Data collection is invaluable to the rare disease community. In 2015 Soft Bones partnered with the non-profit organization CoRDS (Coordination of Rare Diseases at Sanford Research) to create the first and only international HPP patient registry.

Our goal is to collect and stratify vital patient information - symptoms, specific gene mutation, blood panel results, treatment, functional ability, and so on. By recording statistics from as many patients as possible, clinicians will be able to improve care pathways, identify those eligible for a clinical trial, and analyze the effectiveness of an HPP intervention.

Creating awareness of the registry is paramount, especially to encourage international participation. Funding will be used to promote the registry via social media and on the Soft Bones website, which will incur SEO fees. Funding will also be used to support staff time to maintain the sites.

Annual Meetings **\$35,000 annually**

Patient-Family Meetings – Soft Bones holds an annual meeting for HPP patients and families to gather together to learn what's trending in the disease and to share information and support.

We've increased the number of participants every year – especially our international patients. We hope to build on that success, as this is our most important community-building initiative. But not every family can afford to attend. Grant funding will be used to cover travel and hotel expenses for patients and families in financial need.

Medical Conferences – Soft Bones also has a presence at medical conferences – including the Endocrine Society's annual conference and the American Society for Bone and Mineral Research Meeting - in an effort to build physician-researcher awareness and to create a pipeline to the medical community.

We encourage HPP patients to attend these conferences through our "Advocacy in Action" program. Our goal is to empower patients to advocate for themselves and others directly with medical professionals to strengthen their voice and campaign for advances in research and treatment options. We provide formal communication/presentation skills training for participating patient advocates.

Funding will provide travel grants for 40 families in financial need to attend the Patient-Family annual meeting. Includes travel/hotel/meals. Funding will also cover a physician/patient dinner at the medical conference and travel grants for eligible patients.

Research Fund

\$100,000

Research is at the heart of all medical advances. That's why we actively raise funds to provide grants to further innovative studies by new and established investigators. Our goal is to support meaningful clinical and basic research that will contribute to the overall body of scientific evidence for HPP as we work toward a cure.

Faculty members at a private research center or university, as well as senior post-doctoral trainees or research associates are eligible to participate. To date, we have awarded three \$25,000 seed grants through the Maher Family Grant. 2015's grant recipient was Brian L. Foster, PhD, of The Ohio State University in Columbus, OH, for his scientific approach to understanding how

therapies for this rare disease might prevent and repair HPP-associated skeletal and dental problems

We are seeking private funding to increase our annual research grant award to \$100,000. Our goal is to attract top researchers and accelerate new therapies. At the same time, we will continue to lobby Congress and the National Institutes of Health to put federal dollars toward large-scale research studies.

Patient Emergency Fund **\$25,000**

The Children's Hospital of Philadelphia (CHOP) operates an international support program that brings at-risk pediatric patients to the United States for diagnosis and treatment for a range of medical conditions, including HPP. Because not all associated costs are covered by CHOP, Soft Bones has created a Patient Emergency Fund to offset the balance. This fund also covers unforeseen expenses for HPP children living in need in the United States.



LIVING WITH HPP

Sue's Story

Doctors knew something was wrong seconds after her birth. Her mother said she looked like a rag doll with no strength at all. She couldn't even grasp her mother's finger. Her head was enlarged and she had short bowed limbs. Doctors were baffled. After weeks of testing at Chicago's Children Memorial Hospital, she was diagnosed with HPP. The doctors told her parents there was no cure for this rare disease, and that she probably wouldn't make it through infancy and definitely wouldn't live past three years. Now at 56 years old, Susan Krug is thriving, despite fighting a constant battle with HPP. This is her story.

When she turned three, Sue had her first rodding surgery, which changed her life. She was able to walk around her house with crutches, and even went months without fracturing. Because Sue was now a toddler, her doctors began to question the initial HPP diagnosis, diagnosing her instead with osteogenesis imperfecta

(another genetic bone disorder). She lived with this diagnosis until 2009, when genetic testing confirmed HPP. Sue has since been receiving enzyme replacement therapy.

After 29 separate rodding surgeries, Sue remains positive: "Will I ever walk around a huge shopping center with just crutches? I doubt it. Will I never have a fracture again? Probably not; in fact I will be getting a new rod in my right tibia sometime this year. Will I have days and weeks without pain? No. I have HPP and Strensiq is only a supplement for my body; it's not a cure, it's a treatment. But I love this treatment. So I don't get down because this month, this week, this day I have pain. This is a slow and steady journey, so I keep smiling and enjoy the little things."