

## **Definition**

Hypophosphatasia (HPP) is an inherited metabolic (chemical) bone disease that results from low levels of an enzyme called alkaline phosphatase (ALP). Enzymes are proteins that act in the body's chemical reactions by breaking down other chemicals. ALP is normally present in large amounts in bone & in the liver. In HPP, abnormalities in the gene that makes ALP lead to production of inactive ALP. Subsequently, several chemical – including Phosphoethanolamine, phridoxal 5'-phosphate (a form of vitamin B6) and inorganic phosphophosphate- accumulate in the body and are found in large amounts in the blood and urine. It appears that the accumulation of inorganic pyrophosphate is the cause of the characteristic deficient calcification of bones in infants and children (rickets) and in adults (osteomalacia). Nevertheless, the severity of HPP is remarkably broad-ranging from patient-to-patient.

## **Symptoms & Diagnosis**

The most severely affected, fail to form a skeleton in the womb and are stillborn. The most mildly affected patients may show only low levels of ALP in the blood, yet never suffer bony problems. In general, patients are categorized as having "perinatal", "childhood", or "adult" HPP depending on the severity of the disease which in turn is reflected by the age at which bony manifestations are first detected. *Odontohypophosphatasia* refers to children and adults who have only dental, but not skeletal problems (premature loss of teeth). The x-ray changes are quite distinct to the trained eye. Similarly, the diagnosis of HPP is largely substantiated by measuring ALP in the

blood (a routine test) that is low in HPP. However, it is important that the doctors use appropriate age ranges for normal when interpreting an ALP level.

## **Prevalence**

It has been estimated that severe forms of HPP occur in approximately one per 100,000 live births. The more mild childhood and adult forms are probably somewhat more common. About one out of every 200 individuals in the United States may be a carrier for HPP.

Depending on the severity of the skeletal disease, there may be deformity of the limbs and chest. Pneumonia can result if chest distortion is severe. Recurrent fractures can occur. Teeth may be lost prematurely, have wide pulp (inside) chambers, and thereby be predisposed to cavities.

## **Inheritance Factors**

The severe perinatal and infantile forms of HPP are inherited as autosomal recessive conditions. The patient receives one defective gene from each parent. Some more mild (childhood or adult) HPP cases are also inherited this way. Other mild adult and odontohypophosphatasia cases seem to be inherited in an autosomal dominant pattern (the patient gets just one defective gene, not two, transmitted from one of his/her parents). In this form, mild HPP can occur from generation-to-generation. The perinatal form of HPP can often be detected during pregnancy by ALP gene mutation analysis. Individuals with HPP and parents of children with HPP are encouraged to seek

genetic counseling to explain the likelihood and severity of HPP recurring in their families.

## **Prognosis**

The outcome following a diagnosis of HPP is variable. In general, the earlier the diagnosis is made the more severe the skeletal manifestations. Cases detected in the womb or with severe deformity is made before six months of age, some infants have a downhill and fatal course, others survive and may even do well. When diagnosed during childhood, there can be presence or absence of skeletal deformity from underlying rickets, but premature loss of teeth (less than 5 years of age) is the most common manifestation. Adults may be troubled by recurrent fractures in their feet and painful, partial fractures in their thigh bones.

## **Treatment For Hypophosphatasia**

For many years, treatment has been generally directed toward preventing or correcting the symptoms or complications. Procedures such as rodding, especially in adults, can be helpful with painful partial fractures in their thigh bones. Expert dental care and physical therapy are recommended. Monitoring levels such as alkaline phosphatase, B6, and calcium (which are/can be outside the limits of normal in hypophosphatasia) should be undertaken and are dependent upon how the patient is being treated.

In October 2015, a new treatment was introduced in the form of the targeted enzyme replacement therapy Strensiq (asfotase alfa). Strensiq is a tissue-nonspecific alkaline phosphatase indicated for the treatment of perinatal, infantile, and juvenile-onset

hypophosphatasia (HPP), and works by replacing alkaline phosphatase. Since its approval, many of our families have chosen to begin this therapy. Careful consideration and consultation with a physician knowledgeable about this treatment, and the disorder hypophosphatasia itself, is recommended before starting this therapy. We have many resources available to patients and providers who are considering starting this drug to treat their hypophosphatasia. Please see the resources section below for general MAGIC information, and additional resources regarding hypophosphatasia and its treatment with Strensiq.

**Many resources are available for families and their physicians on MAGIC's website, [www.magicfoundation.org](http://www.magicfoundation.org), such as**

- Downloadable HPP brochure
- Patient information for drug Strensiq
- Physician information for drug Strensiq
- Member benefits or to join MAGIC
- HPP Facebook group for Parents
- HPP Facebook group for adults
- Physician referrals or to speak to someone about HPP

This brochure is for informational purposes only. Neither The MAGIC Foundation nor the contributing physician assumes any liability for its content. Consult your physician for diagnosis and treatment.

**Revised 2016**

## Contributing Authors:

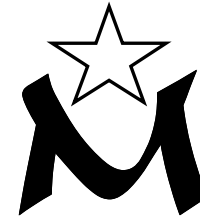
Michael P. Whyte, M.D.  
Medical Director  
Center for Metabolic Bone Disease  
and Molecular Research  
Shriners Hospital  
St. Louis, Missouri

The MAGIC Foundation is a national nonprofit organization created to provide support services for the families of children afflicted with a wide variety of chronic and/or critical disorders, syndromes and diseases that affect a child's growth. Some of the diagnoses are quite common while others are very rare.

## **MAGIC**

Continues and develops through membership fees, corporate sponsorship, private donations and fundraising.

# Hypophosphatasia



**The MAGIC Foundation®**  
*For Children's Growth*

---

Not an illusion or magical,  
But the caring for children  
and their families

\* \* \* \*

Dedicated to the growth  
and overall development  
Of children

---

4200 Cantera Dr.  
Suite 106  
Warrenville, IL 60555  
630-836-8200  
630-836-8181 fax  
800-3MAGIC3  
[www.magicfoundation.org](http://www.magicfoundation.org)