

# HYPOPHOSPHATASIA (HPP)

## HPP OVERVIEW

Hypophosphatasia, or HPP, is an inherited, progressive, ultra-rare metabolic disease in which patients experience devastating effects on multiple systems of the body, and face debilitating or life-threatening complications.<sup>1,2</sup> It is characterized by defective bone mineralization that can lead to deformity of bones and other skeletal abnormalities, as well as systemic complications such as profound muscle weakness, seizure, and respiratory failure leading to premature death.<sup>1-3</sup>

HPP can affect males and females of all ages and can have devastating outcomes at any stage of life.<sup>1</sup> Many patients with HPP have weak or soft bones, leading to frequent fractures, as well as skeletal deformities.<sup>1-3</sup> These abnormalities can impede growth in children and can continue to impair a person's ability to engage in routine daily activities such as walking, running, jumping, standing, and climbing stairs.<sup>4,5</sup>

Infants and young children, in particular, may experience severe symptoms of HPP such as seizures and respiratory failure.<sup>1</sup> Historically, infants who experienced their first symptom of HPP within the first six months of life had a very high mortality rate—73% at five years.<sup>6</sup>

## CAUSES

HPP is inherited, resulting from a defect (mutation) in the gene that makes an enzyme known as tissue non-specific alkaline phosphatase (TNSALP).<sup>1,7</sup> The result is low levels of alkaline phosphatase (ALP) activity.<sup>1,7,8</sup> When ALP is functioning normally, it allows two key minerals—calcium and phosphate—to bind together to form healthy, mineralized bones.<sup>7,9</sup> In patients with HPP, however, ALP activity is low, leading to improper mineralization of bone-building calcium and phosphate.<sup>10</sup> Instead, calcium and phosphate can build up in other places throughout the body, causing damage to bones and organs.<sup>10</sup>

## CONSEQUENCES

The signs and symptoms of HPP can vary from patient to patient, and can include problems in the bones, brain, muscles, joints, lungs, teeth, and kidneys.<sup>1,8</sup> Because of the progressive nature of the

disease, new symptoms can appear at any age and symptoms can worsen over time, causing significant disability.<sup>1</sup> Effects of HPP on different parts of the body could include:

### Bones

- Weak or brittle bones<sup>3,11</sup>
- HPP-related rickets<sup>1</sup>
- Frequent fractures, especially in the thigh bones, feet, and toes.<sup>1</sup> A patient-reported survey of 117 adults with HPP showed an average of nearly 12 fractures in a lifetime<sup>5</sup>
- Fractures that don't heal properly<sup>1,12</sup>
- Bowed legs<sup>1</sup>
- Bone pain that won't go away<sup>1</sup>
- Reliance on an assistive device such as crutches, a walker, or a wheelchair<sup>1</sup>

### Muscles and Joints

- Muscle weakness<sup>1</sup>
- Arthritis (in adults and children)<sup>1</sup>
- Pseudogout caused by deposits of calcium in the joints<sup>1</sup>
- Waddling gait<sup>1</sup>

### Ribs and Lungs

- Rachitic chest, a condition in which bones in the rib cage may not grow or develop (form) properly; this can lead to underdeveloped lungs, especially in children.<sup>13</sup> Historically, more than 80% of infant HPP patients with respiratory compromise died<sup>6</sup>
- Severe breathing complications that require an assistive breathing device, especially in children<sup>15</sup>
- Pneumonia<sup>6</sup>

### Brain

- Craniosynostosis, a condition in which the bony plate of the skull closes early, causing an abnormally shaped head and potentially causing increased pressure on the brain and swelling of the optic nerve<sup>11</sup>
- Seizures (especially in young children) that can be life-threatening. Historically, 100% of infant patients who experienced Vitamin B6-responsive seizures died<sup>1,14</sup>

### Kidneys

- A buildup of calcium in the kidneys (nephrocalcinosis) that may lead to decreased kidney function<sup>1</sup>

### Teeth

- Early tooth loss (before the age of 5)<sup>1</sup>
- Tooth loss in which the tooth and its entire root fall out painlessly<sup>9,11</sup>
- Gum disease<sup>15</sup>

## DIAGNOSIS AND MANAGEMENT

Since HPP shares symptoms with other, more common diseases, diagnostic delays and misdiagnoses are common.<sup>1,16</sup> However, getting a diagnosis for HPP can be straightforward through a combination of full clinical assessment and a simple blood test for low ALP.<sup>1,15</sup> It is critical to get an accurate diagnosis as early as possible to ensure that appropriate care is provided.<sup>1,15</sup>

**For more information on HPP, visit [hypophosphatasia.com](http://hypophosphatasia.com).**

## References

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