HYPOPHOSPHATASIA (HPP)
THE CRITICAL ROLE OF DENTISTS IN IDENTIFYING HPP

What is HPP?
- HPP is an inherited metabolic disease with life-threatening systemic consequences that can strike at any age.\(^1,2\)
- Low alkaline phosphate (ALP) activity, resulting from loss-of-function mutations from the \(ALPL\) gene, is the cause of HPP.\(^2\)
  - Skeletal formation and tooth development are dependent upon tissue-nonspecific alkaline phosphatase (TNSALP).\(^3\)

What role do dentists play in identifying HPP?
- It often takes a patient seeing many specialists before one realizes that he/she has HPP. Any healthcare provider (HCP) can be the one to identify the disease. Dentists have often been the first to suspect that a patient has HPP.\(^4\)
- Misdiagnosis is common and often leads to treatment that can worsen an HPP patient’s condition.\(^5,6\)
- A dentist who suspects HPP should refer the patient to a pediatric endocrinologist or geneticist, who can confirm diagnosis and ensure proper management.

What signs should a dentist be on the lookout for?
- Premature tooth loss (usually fully rooted with root intact) due to lack of cementum formation on tooth roots that results in weakened attachment of tooth to bone.\(^7\)
  - Incisors most likely to be effected.\(^6\)
- Dental radiographs sometimes show enlarged pulp chambers and root canals that characterize the “shell teeth” of rickets.\(^7,8\)
- 99% of patients with HPP experience premature tooth loss before the age of 5.\(^9\)

Systemic Clinical Manifestations of HPP\(^2,3,10,:\)
- SKELETAL: Severe hypomineralization, craniosynostosis, rachitic chest, rickets, bowing, short stature, osteomalacia, bone pain, fractures, osteopenia
- MUSCULAR/RHEUMATOLOGIC: Delayed or missed motor milestones, weakness, chronic muscle or joint pain, waddling gait, difficulty walking
- RENAL: Nephrocalcinosis, renal failure
- RESPIRATORY: Pulmonary insufficiency, respiratory failure
- NEUROLOGIC: Vitamin \(B_6\)-responsive, seizures, increased intracranial pressure

References:

Learn more about HPP at www.Hypophosphatasia.com
How is a diagnosis for HPP made?

- Patients with HPP have low alkaline phosphatase (ALP) activity due to their body’s inability to properly encode the TNSALP enzyme.²,³
- Patients will often have high levels of serum vitamin B₆ (pyridoxal 5’-phosphate or PLP) and/or urinary phosphoethanolamine (PEA).³
- Low ALP activity can be easily determined by a commonly available blood test, however, results must be compared to age- and gender-adjusted ALP reference ranges, since ALP levels vary considerably over a lifetime.³

Why might a dentist be the first to identify an HPP patient?

- Premature tooth loss is a hallmark of HPP.
- In childhood HPP, dental changes may be the only clinical expression of the disorder.⁷
- Because patients see dentists regularly and receive dental radiographs, changes in dentition can lead to the diagnosis.

If you suspect HPP, inform the family and refer the patient to a pediatric endocrinologist or geneticist for appropriate follow-up as soon as possible.

**AGE- AND GENDER-ADJUSTED ALP REFERENCE RANGES (U/L)**

<table>
<thead>
<tr>
<th>Age</th>
<th>ALP activity (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 mo</td>
<td>60-320</td>
</tr>
<tr>
<td>1-3 mo</td>
<td>70-350</td>
</tr>
<tr>
<td>4-6 y</td>
<td>125-370</td>
</tr>
<tr>
<td>7-9 y</td>
<td>150-440</td>
</tr>
<tr>
<td>10-12 y (M)</td>
<td>150-530</td>
</tr>
<tr>
<td>10-12 y (F)</td>
<td>150-525</td>
</tr>
<tr>
<td>12-13 y (M)</td>
<td>150-550</td>
</tr>
<tr>
<td>12-13 y (F)</td>
<td>150-550</td>
</tr>
<tr>
<td>13-15 y (M)</td>
<td>150-530</td>
</tr>
<tr>
<td>14-15 y (F)</td>
<td>55-395</td>
</tr>
<tr>
<td>16-19 y (M)</td>
<td>60-315</td>
</tr>
<tr>
<td>16-19 y (F)</td>
<td>60-315</td>
</tr>
<tr>
<td>≥20 y</td>
<td>40-120</td>
</tr>
</tbody>
</table>


Note: Reference intervals vary somewhat by performing laboratory and testing methodology.