Could it be HPP?

For some difficult-to-diagnose patients, symptoms may appear perplexing on their own. However, making the connection could lead to a diagnosis of hypophosphatasia (HPP).1

If you have adolescent or adult patients like this, review the following questions about potential symptoms and experiences. Select the relevant factors for more details to help determine whether you should consider a diagnosis of HPP.
Q.1 Patient Symptoms

Have your patients reported experiencing any of the following? (Select all that apply)

- Bone/muscle pain
- Limited mobility
- Interruption of daily activities
Joint, bone, or muscle pain, muscle weakness, fractures, and chronic fatigue are symptoms you may commonly see. In one patient survey, a majority of adult HPP patients reported bone (82%), joint (73%), and muscle pain (53%). Bone pain was severe enough to limit daily activities in 76% of patients.

Patients may be taking pain medication to cope.

Issues with mobility, impaired coordination, or poorly healing fractures that appear in young patients (under 50 years of age) may also add to the perplexing nature of HPP cases.

Patients may be using assistive devices, such as canes.

Most HPP patients have difficulty with critical daily activities, including lifting objects (56%), walking (78%), and ascending or descending stairs (74% and 81% respectively).

The burden of disease can be high, with physical symptoms that interrupt their personal and professional lives.

They may have to make modifications to manage certain activities they were once able to do.
Exploring your patients’ history may provide additional clues to help you make a proper diagnosis. Have they had, or do they have, any of the following?

(Select all that apply)

- Poor dentition or dental symptoms, including premature tooth loss occurring before the age of 5
- Lack of response to common treatments for other conditions (possible misdiagnoses)
- Growth and developmental delays or complications
- Personal or family history of unusual fracturing
Q.2 Patient History

Exploring your patients’ history may provide additional clues to help you make a proper diagnosis.¹ Have they had, or do they have, any of the following? (Select all that apply)

- **Poor dentition or dental symptoms, including premature tooth loss occurring before the age of 5**
  
  Pediatric patients may present with dental symptoms which can go unnoticed or be thought of as normal for growing children. Be sure to ask about premature primary tooth loss with the root intact, as this may be a key sign of underlying disease.¹

- **Lack of response to common treatments for other conditions (possible misdiagnoses)**
  
  While a diagnosis of fibromyalgia or osteoporosis may seem to fit the profile for some of these patients, if they aren't responding to common treatments for these conditions, this may be a sign to look for another diagnosis. As the symptoms of HPP are similar to those of other diseases, it may be mistaken for other skeletal, rheumatologic, and metabolic diseases.¹

- **Growth and developmental delays or complications**
  
  HPP patients may experience childhood developmental motor delays. They may report developmental issues including short stature, missing motor milestones, failing to thrive or falling behind when compared to their peers, and persistent musculoskeletal pain resembling growing pains.¹

- **Personal or family history of unusual fracturing**
  
  HPP patients may experience frequent or nonhealing fractures, and they may have family members with multiple nontraumatic fractures as well.¹ According to two patient surveys, patients with HPP experience approximately 13 fractures on average during their lifetime.³
Look for a value on a complete metabolic panel (CMP). For each patient you’re considering, which one of the following groups applies?

- **Adult**
- **Pediatric (under 18)**
For pediatric patients with perplexing symptoms, look for low levels of alkaline phosphatase enzyme activity. It’s important to remember that *age- and sex-adjusted alkaline phosphatase intervals must be used* to determine the low threshold. 

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**Patient Labs**

Look for a standard value on a complete metabolic panel (CMP). For each patient you’re considering, which one of the following groups applies?

- **Adult**
- **Pediatric (under 18)**

For pediatric patients with perplexing symptoms, look for low levels of alkaline phosphatase enzyme activity. It’s important to remember that *age- and sex-adjusted alkaline phosphatase intervals must be used* to determine the low threshold.
In adult patients with perplexing symptoms, look for alkaline phosphatase enzyme activity values that are $<40\text{ U/L}$.\(^*\)

*Limitations: An alk phos level of below 40 U/L is not conclusive for diagnosis of HPP. Patient should be evaluated for other symptoms of HPP and differential diagnoses should be ruled out. Check with your lab for their appropriate age- and sex-adjusted reference range.
Connecting perplexing symptoms to low alkaline phosphatase may lead to an HPP diagnosis.¹

This standard value on a CMP could be the crucial diagnostic factor you need for solving those puzzling cases. Looking for low alkaline phosphatase (alk phos) may help you correctly identify hypophosphatasia as the cause of your patient's perplexing symptoms.¹⁴⁵
Alkaline phosphatase plays an important role in bone mineralization and development.\(^1\)

Reduced levels of this enzyme activity disrupt bone mineralization, making it difficult to build strong, healthy bone. This disruption of the bone growth process may result in the life-limiting symptoms your patients experience.

In HPP, a patient’s alk phos values will be persistently low throughout their entire life.\(^1\)

It’s important to remember that age- and sex-adjusted alkaline phosphatase intervals must be used to determine the low threshold.\(^4,5\)

Check with your lab for their appropriate age- and sex-adjusted reference range.

<table>
<thead>
<tr>
<th>Age</th>
<th>Normal Alkaline Phosphatase</th>
<th>Low Alkaline Phosphatase in Females and Males &lt;18 years</th>
<th>Low Alkaline Phosphatase in Adults</th>
</tr>
</thead>
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<tr>
<td>0-14 days</td>
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<td>134</td>
<td>369</td>
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<td>156</td>
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<tr>
<td>Adults*</td>
<td>460</td>
<td>518</td>
<td>90</td>
</tr>
</tbody>
</table>

*Limitations: An ALP level of below 40U/L is not conclusive for diagnosis of HPP. Patient should be evaluated for other symptoms of HPP and differential diagnoses should be ruled out. Check with your lab for their appropriate age- and sex-adjusted reference range.
If you suspect that one of your current patients has HPP, check their CMP history.

A persistently low alk phos value of <40 U/L* for adults suggests an HPP diagnosis.4–9

*Limitations: An alk phos level of below 40 U/L is not conclusive for diagnosis of HPP. Patient should be evaluated for other symptoms of HPP and differential diagnoses should be ruled out. Check with your lab for their appropriate age- and sex- adjusted reference range.


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