



## KNOW THE SIGNS & SYMPTOMS

Hypophosphatasia (HPP) and Low Alkaline Phosphatase (Alk Phos)

# 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).<sup>1</sup>**

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.

**START**



# 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

Patient Symptoms    Patient History    Patient Labs    Make the Connection



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# Q.1 Patient Symptoms

## Have your patients reported experiencing any of the following?

(Select all that apply)

### Bone/muscle pain

Joint, bone, or muscle pain, muscle weakness, fractures, and chronic fatigue are symptoms you may commonly see.<sup>1,2</sup> 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**.<sup>2</sup>

Patients may be taking pain medication to cope.<sup>1</sup>

### Limited mobility

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.<sup>1</sup>

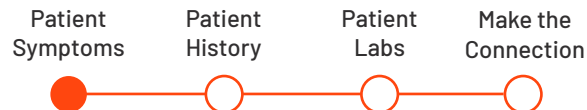
Patients may be using assistive devices, such as canes.<sup>2</sup>

### Interruption of daily activities

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.<sup>2</sup>



# Q.2 Patient History

Exploring your patients' history may provide additional clues to help you make a proper diagnosis.<sup>1</sup> Have they had, or do they have, any of the following?

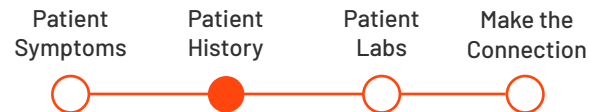
(Select all that apply)

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



← NEXT →

# Q.2 Patient History

Exploring your patients' history may provide additional clues to help you make a proper diagnosis.<sup>1</sup> 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.<sup>1</sup>

- Lack of response to common treatments for other conditions (possible misdiagnoses)

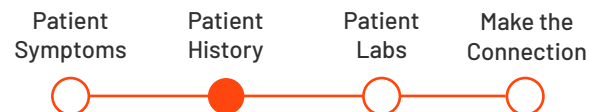
While a diagnosis of fibromyalgia or osteoporosis may seem to fit the profile for some of these patients, if they aren't responding to common treatments for these conditions, this may be a sign to look for another diagnosis. **As the symptoms of HPP are similar to those of other diseases, it may be mistaken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

- 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.<sup>1</sup>

- 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.<sup>1</sup> **According to two patient surveys, patients with HPP experience approximately 13 fractures on average during their lifetime.**<sup>3</sup>

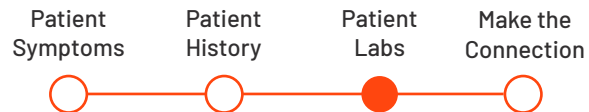


# Q.3 Patient Labs

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)



← CONNECTION TO HPP →

# Q.3 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.<sup>1,4,9</sup>



← CONNECTION TO HPP →

# Q.3 Patient Labs

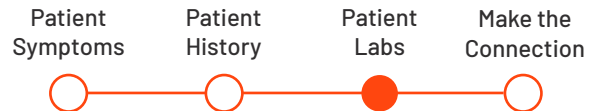
Look for a standard value on a complete metabolic panel (CMP). For each patient you're considering, which one of the following groups applies?

## Adult

In adult patients with perplexing symptoms, look for alkaline phosphatase enzyme activity **values that are <40 U/L.**<sup>1,4-8\*</sup>

\*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.

## Pediatric (under 18)



← **CONNECTION TO HPP** →



# Connecting perplexing symptoms to low alkaline phosphatase may lead to an HPP diagnosis.<sup>1</sup>

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.<sup>1,4,5</sup>

← SEE MORE →

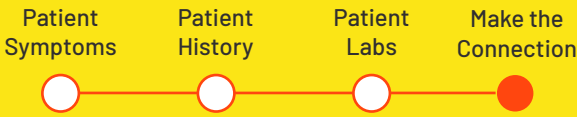


# Alkaline phosphatase plays an important role in bone mineralization and development.<sup>1</sup>

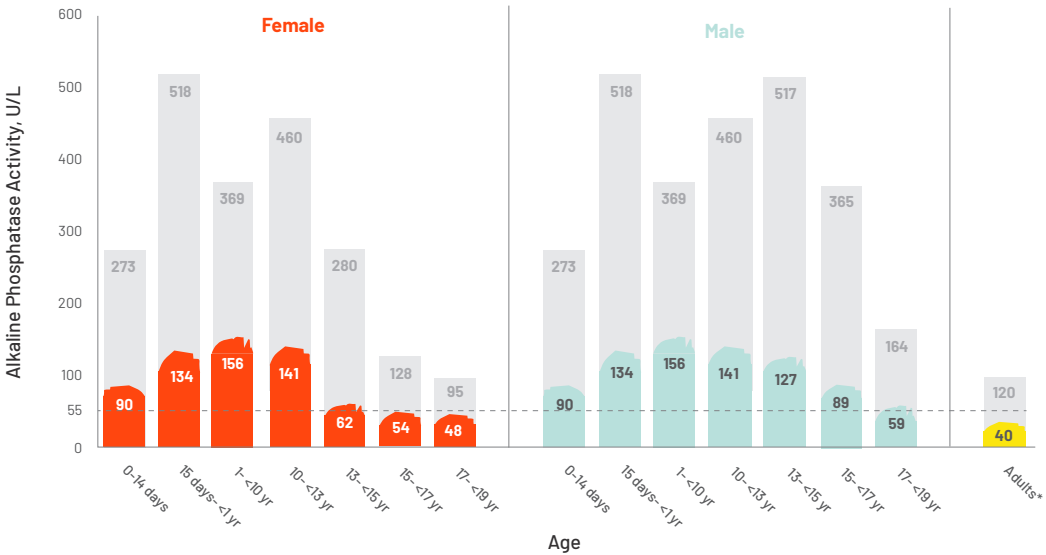
Reduced levels of this enzyme activity disrupt bone mineralization, making it difficult to build strong, healthy bone. This disruption of the bone growth process may result in the life-limiting symptoms your patients experience.

In HPP, a patient's alk phos values will be persistently low throughout their entire life.<sup>1</sup>

It's important to remember that age- and sex-adjusted alkaline phosphatase intervals must be used to determine the low threshold.<sup>4,5</sup>



Age- & Sex-Adjusted Alk Phos Reference Intervals (U/L)<sup>4-9</sup>



- Normal Alkaline Phosphatase
- Low Alkaline Phosphatase in Females and Males <19 years
- Low Alkaline Phosphatase in Adults

\*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.

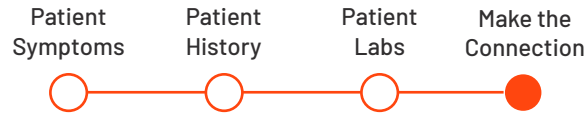
Check with your lab for their appropriate age- and sex- adjusted reference range.

← **CHECK LOW ALK PHOS** →

# 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.<sup>4-9</sup>

← GET MORE INFORMATION ABOUT LOW ALK PHOS →



\*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.

**References:** 1. Bianchi ML, Bishop NJ, Guañabens N, et al. Hypophosphatasia in adolescents and adults: overview of diagnosis and treatment. *Osteoporos Int.* 2020;31(8):1445-1460. 2. Weber TJ, Sawyer EK, Moseley S, Odrlijin T, Kishnani PS. Burden of disease in adult patients with hypophosphatasia: results from two patient-reported surveys. *Metabolism.* 2016;65(10):1522-1530. 3. Weber TJ, Sawyer EK, Moseley S, Odrlijin T, Kishnani PS. Burden of disease in adult patients with hypophosphatasia: results from patient-reported outcome surveys. Poster presented at: The Endocrine Society's 97th Annual Meeting; March 5-8, 2015; San Diego, CA, USA. 4. Adeli K, Higgins V, Nieuwesteeg M, et al. Biochemical marker reference values across pediatric, adult, and geriatric ages: establishment of robust pediatric and adult reference intervals on the basis of the Canadian Health Measures Survey. *Clin Chem.* 2015;61(8):1049-1062. 5. Schumann G, Klauke R, Canalias F, et al. IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37 degrees C. Part 9: reference procedure for the measurement of catalytic concentration of alkaline phosphatase International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Scientific Division, Committee on Reference Systems of Enzymes (C-RSE)(1). *Clin Chem Lab Med.* 2011;49(9):1439-1446. 6. Quest Diagnostics. Alkaline phosphatase. Accessed January 25, 2021. <https://testdirectory.questdiagnostics.com/test/test-detail/234/alkaline-phosphatase?cc=MASTER> 7. Labcorp. Alkaline phosphatase. Updated December 16, 2019. Accessed January 25, 2021. <https://www.labcorp.com/tests/001107/alkaline-phosphatase> 8. ARUP Laboratories. Alkaline phosphatase isoenzymes, serum or plasma. Accessed January 25, 2021. <https://ltd.aruplab.com/Tests/Pub/0021020> 9. Colantonio DA, Kyriakopoulou L, Chan MK, et al. Closing the gaps in pediatric laboratory reference intervals: a CALIPER database of 40 biochemical markers in a healthy and multiethnic population of children. *Clin Chem.* 2012;58(5):854-868.