

CAUTION LOW ALKALINE PHOSPHATASE MATTERS

Missing **LOW ALKALINE PHOSPHATASE (ALP)** could mean missing a diagnosis

Alkaline Phosphatase is involved in essential organ functions throughout the body:¹⁻³ fetal development, skeletal development, neurotransmitter synthesis, liver detoxification, intestinal absorption, lung function, and kidney/urinary mineral balance.

HPP is a metabolic disorder characterized by LOW ALP activity

Patients with HPP may experience unpredictable, devastating, and life-limiting consequences, including:⁴



**PREMATURE
TOOTH LOSS**



**SHORT STATURE
AND/OR UNUSUAL
GAIT**



**MUSCLE WEAKNESS
AND/OR FATIGUE**



**CHRONIC MUSCLE/
JOINT PAIN**



**SKELETAL
DEFORMITIES AND/
OR FRACTURES**

• In adults, low ALP activity is **<40 U/L^{5,a}**

• Age- and sex-adjusted ALP reference intervals must be used in children^{6,7}

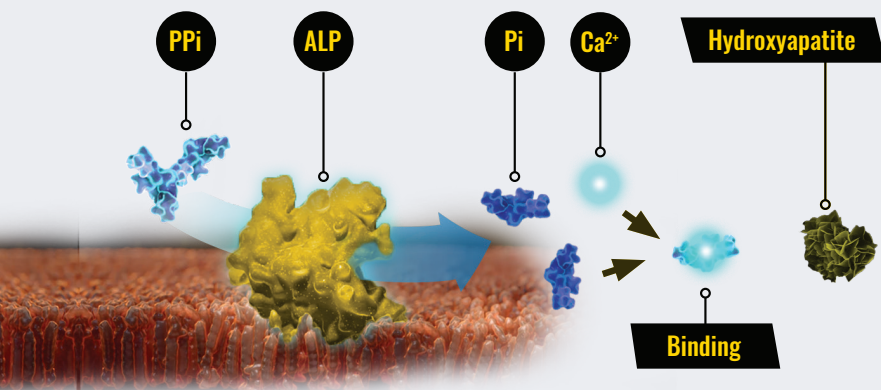
**Patients with any of these key signs/symptoms
and LOW ALP should be evaluated for HPP⁴**

^aExample cutoff from Abbott Laboratories; adult ALP ranges are lab-specific and may vary.

**LOW ALP should raise
the concern for HPP**

Business Card Holder

LOW ALP? Think HPP!



IN HEALTHY BONE: Alkaline phosphatase splits inorganic pyrophosphate (PPi), releasing inorganic phosphate (Pi) that binds with calcium (Ca^{2+}) to form hydroxyapatite⁸

IN HPP: *ALPL* mutation causes **low alkaline phosphatase** activity and diminished bone mineralization⁸

LOW ALP Differential Diagnosis⁹

Transiently Low	<ul style="list-style-type: none"> • Osteogenesis imperfecta type II • Profound hypothyroidism • Cushing disease • Bisphosphonate therapy • Adynamic renal osteodystrophy 	<ul style="list-style-type: none"> • Milk-alkali syndrome • Vitamin D intoxication • Vitamin C or other nutritional deficiencies • Wilson disease • Celiac disease
Precipitously Low	<ul style="list-style-type: none"> • Cardiac bypass surgery • Major trauma or surgery • Multiple myeloma or other cancers 	<ul style="list-style-type: none"> • Transfusion (often massive) • Acute caloric restriction
<u>PERSISTENTLY</u> Low	<ul style="list-style-type: none"> • Cleidocranial dysplasia 	<ul style="list-style-type: none"> • Mseleeni joint disease
Hypophosphatasia (HPP)		

References: 1. Whyte MP. *Ann N Y Acad Sci.* 2010;1192:190-200. 2. Whyte MP. *Endocr Rev.* 1994;15(4):439-461. 3. Buchet R, et al. *Methods Mol Biol.* 2013;1053:27-51. 4. Bishop N, et al. *Arch Dis Child.* 2016;101(6):514-515. 5. Alkaline phosphatase assay [package insert]. Abbott Park, IL: Abbott Laboratories; 2007. 6. Offiah AC, et al. *Pediatr Radiol.* 2019;49(1):3-22. 7. Colantonio DA, et al. *Clin Chem.* 2012;58(5):854-868. 8. Rockman-Greenberg C. *Pediatr Endocrinol Rev.* 2013;10(suppl 2):380-388. 9. McKiernan FE, et al. *J Bone Miner Res.* 2014;29(7):1651-1660.



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