

# Hypophosphatasia: To Treat or Not to Treat? A Case Study

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# Conflict of Interest Disclosure

None

A conflict of interest exists when an individual is in a position to profit directly or indirectly through application of authority, influence, or knowledge in relation to the affairs of PENS. A conflict of interest also exists if a relative benefits or when the organization is adversely affected in any way.

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# Case Study

C.P. is a 1yr 11mo old female who was referred by her pediatric dentist for endocrine evaluation associated with premature tooth loss.

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## History

- ▶8.5mo: 2 bottom incisors came in
- ▶10mo: 2 lower teeth laterall came in
- ▶17mo: 2 central incisors fell out
- ▶20mo: full set of teeth came in
- ▶22mo: 2 teeth laterally to her central incisors were pulled due to being lose and fear of aspiration

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## History continued

- ▶No fractures (despite a fall at age 5wk)
- ▶No developmental delay
- ▶No complaints of bone or muscle pain
- ▶No seizures

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## Screening labs

- ▶Normal calcium: 10.0ng/dL
- ▶Normal iPTH: 32.4pg/mL (7.5-53.5)
- ▶Low alkaline phosphatase: 58 U/L (129-291)  
Repeat alk phos also low: 76 U/L
- ▶High vitamin B6: 225mcg/L (5-50)
- ▶High urine phosphoethanolamine: 803nmol/mg Cr.
  
- ▶This confirmed the diagnosis of hypophosphatasia(HPP)
- ▶Of note: skeletal survey was normal

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## What is Hypophosphatasia

- ▶ Potentially life-threatening, systemic, inherited metabolic disorder caused by a loss-of function mutation in the gene encoding tissue-nonspecific alkaline phosphatase (TNALP)
- ▶ The biological hallmark of HPP is low alkaline phosphatase (ALP) activity
  - Low ALP activity results in accumulation of TNSALP substrates:
  - Pyridoxal 5'-phosphate (PLP): major circulating form of vitamin B<sub>6</sub>
  - Inorganic pyrophosphate (PPi): potent inhibitor of mineralization
  - Phosphoethanolamine (PEA): diagnostic marker

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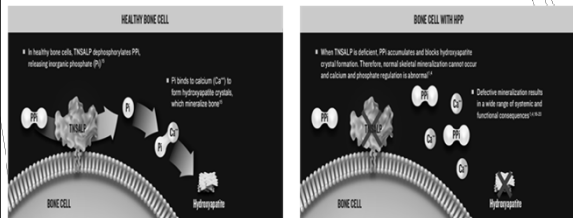
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## What is Hypophosphatasia continued



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## Categories of HPP

- ▶ Perinatal
- ▶ Infantile
- ▶ Childhood
- ▶ Adult
- ▶ Odonto

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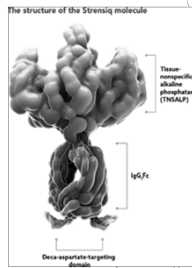
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## New Treatment

- ▶ Asfotase alfa (enzyme-replacement therapy) was FDA approved for treatment of hypophosphatasia in 2015
- ▶ Given SQ 3x/wk
- ▶ Can cause significant site reactions with lipodystrophy/dystrophy



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## To Treat or Not to Treat?

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## Our decision:

- ▶ Hold off on treatment
- ▶ Currently only symptom is premature tooth loss
- ▶ No skeletal manifestations
- ▶ No pain or quality of life limitations
- ▶ Continued close observation (every 6mo)
- ▶ Consider treatment, if it evolves into juvenile HPP with skeletal manifestations and symptoms interfering with quality of life

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Questions, Comments,  
Suggestions?



Thank you

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