What causes Dental Manifestations?

Individual without XLH

- Normal FGF Regulation
- No Dentinal Defects

Individual with XLH

- Elevated FGF Levels
- Reduced Renal Resorption of Pi
- Hypophosphatemia
- Normal or Hypoplastic enamel
- High pulp horns extend up to ODL
- Increased globular dentin
- Poorly calcified dentin
- Insults to tooth (Microbial, thermal, etc)
- Poor dentinal resistance to the insults
- Pulpal irritation and abscesses

Recommendations for Dental Management

- Early Diagnosis and Management
- Team Approach
- Communication between Health Care Providers
- Frequent Recall Visits
- Sealants on the Primary and Permanent Molars
- Fluoride Therapy
- Pulpectomy vs. Extraction based on Age and Clinical Diagnosis
- Space Maintainers
- Dental Implants
- Root Canal Therapy and Crowns should be Considered

Dental Manifestations of X-Linked Hypophosphatemia

The XLH Network, Inc.
911 Central Avenue, #161
Albany, NY 12206

Implications for Prevention & Treatment of XLH

www.xlhnetwork.org
What is XLH?

X-Linked Hypophosphatemia (XLH) is an X-linked dominant disorder resulting in dental and skeletal abnormalities.

XLH is the most frequent form of inherited rickets and osteomalacia.

Loss-of-function mutations in the PHEX gene (expressed in odontoblasts, osteocytes, and osteoblasts) result in elevated circulating levels of FGF23, a protein that acts on the kidneys and reduces tubular phosphate reabsorption.

Inheritance:
X-linked dominant form

Prevalence:
Approximately 1 in 20,000

A similar phenotype can be seen in less common disorders such as:
- Autosomal Dominant Hypophosphatemia Rickets (FGF23 Mutations)
- Autosomal Recessive Hypophosphatemia Rickets (DMP1 Mutations)
- Sporadic cases with similar phenotype

Etiology and Pathogenesis

Mutations

PHEX gene located on Chromosome X and expressed in:
- Osteocytes
- Osteoblasts
- Odontoblasts
- Ovaries
- Lungs

XLH is characterized by diminished proximal renal tubular phosphate transport due to elevated FGF23 leading to:
- Hypophosphatemia
- Phosphate wasting
- Impaired 1,25(OH)2VitD synthesis
- Diminished Pi gut absorption

Diagnosis

<table>
<thead>
<tr>
<th>XLH</th>
<th>Clinical</th>
<th>Radiographic</th>
<th>Biochemical</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Serum Calcium</td>
<td>Frayed and widened growth plates</td>
<td>Normal</td>
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<tr>
<td></td>
<td>Serum Phosphorus</td>
<td>Bowing of lower extremities</td>
<td>Low</td>
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<tr>
<td></td>
<td>25-OHD</td>
<td>Normal</td>
<td></td>
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<tr>
<td></td>
<td>1,25(OH)2D</td>
<td>Low/Normal</td>
<td></td>
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<tr>
<td></td>
<td>FGF23</td>
<td>High/Normal</td>
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<tr>
<td></td>
<td>PTH</td>
<td>Normal/Slightly High (in children)</td>
<td></td>
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<tr>
<td>Serum alkaline phosphate</td>
<td>High/Normal</td>
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</tbody>
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**XLH - Dental Findings**

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Radiographic</th>
<th>Histologic</th>
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</thead>
<tbody>
<tr>
<td>Spontaneous abscess in absence of dental caries</td>
<td>Reduced density of trabeculations</td>
<td>Enamel: Normal or Hypoplastic</td>
</tr>
<tr>
<td>Delayed eruption</td>
<td>Loss of Lamina dura</td>
<td>Dental: Large tubular clefts extend to pulp</td>
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<tr>
<td></td>
<td>Parapapillary radiolucency in absence of dental caries</td>
<td>Increase globular dentin</td>
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<tr>
<td></td>
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<td>Partially mineralized dentin</td>
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<tr>
<td></td>
<td></td>
<td>Pulp: Large pulp chamber</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High pulp horns extend up to DEJ</td>
</tr>
</tbody>
</table>