What causes Dental Manifestations?

Individual without XLH

PHEX

Odontoblast

Normal FGF Regulation
No Dentinal Defects

Individual with XLH

PHEX

Odontoblast

Elevated FGF levels
Reduced Renal Resorption of Pi
Hypophosphatemia

Normal or hypoplastic Enamel
High pulp horns extend up to DEJ
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 versus Extraction based on age and clinical diagnosis
- Space Maintainers
- Dental Implants
- Root Canal Therapy and Crowns should be considered
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 FGF-23, 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

**XLH** is characterized by diminished proximal renal tubular phosphate transport due to elevated FGF-23 leading to:

- Hypophosphatemia
- Phosphate wasting
- Impaired 1,25(OH)₂VitD synthesis
- Diminished Pi gut absorption

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Radio graphic</th>
<th>Biochemical</th>
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<tbody>
<tr>
<td>Rickets-bow or knock-knee deformity</td>
<td>Frayed and widened growth plates</td>
<td>Serum Calcium Normal</td>
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<td>Craniosynostosis</td>
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<td>Serum Phosphorus Low</td>
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<tr>
<td>Short Stature</td>
<td>Bowing of lower extremities</td>
<td>25-OHD Normal</td>
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<td>Dental Findings</td>
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<td></td>
<td>Periapical radiolucency in absence of dental caries</td>
<td>1,25(OH)D Low/Normal</td>
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<td>FGF23 High/Normal</td>
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<td>PTH Normal/Slightly High (in children)</td>
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<td>Serum alkaline phosphatase High/Normal</td>
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**XLH - Dental Findings**

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<thead>
<tr>
<th>Clinical</th>
<th>Radiographic</th>
<th>Histologic</th>
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<tbody>
<tr>
<td>Spontaneous abscess in absence of dental caries</td>
<td>Reduced density of trabeculations</td>
<td>Enamel Normal or Hypoplastic</td>
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<tr>
<td>Delayed eruption</td>
<td>Loss of Lamina dura</td>
<td>Dentin Large tubular clefts extend to pulp</td>
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<tr>
<td></td>
<td>Periapical radiolucency in absence of dental caries</td>
<td>Wide predentin layer</td>
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<td>Increased globular dentin</td>
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<td></td>
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<td>Partially mineralized dentin</td>
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<tr>
<td></td>
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<td>Pulp Large pulp chamber</td>
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<td></td>
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<td>High pulp horns extend up to DEJ</td>
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</tbody>
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**Mutations**
PHEX gene located on Chromosome X and expressed in: