Soft Bones
Finding the Key to HPP

SOFT BONES HYPOPHOSPHATASIA GLOSSARY

Alkaline phosphatase (ALP)
Enzyme that controls a chemical that blocks skeletal calcification

Enzyme
A protein that breaks down certain chemicals (substrates)

Hypophosphatasia (HPP)
Hypophosphatasia (HPP) is the rare genetic form of rickets or osteomalacia that features paradoxically low serum alkaline phosphatase (ALP) activity.

BONE BIOLOGY

Chondrocytes
Cartilage cells found in growth plates of growing children

Collagen
Most abundant protein in bones, skin, muscles, and tendons

Ectopic
“Out of place or position” (for calcium – outside of the skeleton)

Hydroxyapatite
Crystals of calcium and phosphate deposited into collagen to make bones strong

Osteoblasts
Cells that form bone

Osteoclasts
Cells that break down bone

Premature Tooth Loss
Loss of a “baby” tooth without trauma before the 5th birthday

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DOCTORS AND MEDICAL SPECIALISTS INVOLVED IN HPP CARE

Endocrinologist
Diagnoses and treats hormone and metabolic disorders, including HPP

Medical Geneticist
Diagnoses, counsels for, and treats inherited diseases, including HPP

Nephrologist
Treats kidney diseases

Neurologist
Treats brain, seizures, and other nerve problems

Ophthalmologist
Treats eye problems

Orthopedist
Surgeon who manages bone, joint, ligament, muscle, and tendon diseases

Physical Therapist
Provides non-surgical therapy to improve or restore mobility and treat pain

Rheumatologist
Treats inflammation and joint diseases

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GENETICS IGENETIC TERMINOLOGY

Autosomal Inheritance
Two most common patterns of disease inheritance

Compound Heterozygosity
Presence of two different copies of a gene

Founder Mutation
Genetic defect from distinct geographical regions

Genotype
Genetic make-up of a person

Heterozygosity
One distinctive copy of a gene

Homozygosity
Presence of identical gene copies

Missense (Point) Mutation
Change of a single DNA

Phenotype
What the disease looks like overall

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POSSIBLE COMPLICATIONS OF HPP AND OTHER BONE DISORDERS

Craniosynostosis
Premature fusion of growth plates in the skull; can cause pressure on the brain and require surgery

Hypercalcemia
Elevated blood calcium

Microfractures
Microscopic fractures

Nephrocalcinosis
Calcium-phosphate (mineral) in the kidneys

Osteoarthropathy
Loss of joint cartilage causing arthritis

Osteomalacia
Softening of bones from too little deposited hydroxyapatite crystals

Pseudofractures
X-ray feature of osteomalacia (soft bones) in adults

Rachitic Chest
Pulled-in sternum or “pigeon breast” deformity from rickets (soft bones during growth)

Rickets
Softening and weakening of bones during growth from too little hydroxyapatite deposition

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TESTS

Alkaline Phosphatase Blood Test
Measures ALP activity in blood serum. Patients with HPP have low ALP levels for their age

ALPL Gene
Mutation (defect[s]), 1 or 2, in this gene underlie HPP

Bone Biopsy
Taking a small sample for microscope examination

Bone Scan
Small amount of radioactive dye injected into a vein that detects where abnormalities are in the skeleton

Chemicals (Substrates) That Accumulate in HPP
- Pyridoxal 5' phosphate (PLP): a form of Vitamin B_6
- Inorganic pyrophosphate (PPi): the blocker of bone mineralization
- Phosphoethanolamine (PEA): often elevated in HPP blood or urine

DXA (DEXA)
X-ray to measure bone mineral density

PTH and 25-Hydroxyvitamin D
Hormones that regulate blood calcium levels

Radiograph
An x-ray

Renal (Kidney) Ultrasound
Sonar method to check for kidney calcification or stones

Serum Calcium
Blood test to diagnose or monitor blood calcium level for many bone diseases

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TREATMENT OF HPP

Asfotase Alfa (trade name Strensiq™)
ALP replacement therapy given by injection. Approved to treat pediatric-onset HPP

Supportive
Good dental care, analgesics if sufficient for mild occasional aches or pains

TYPES OF HPP

Adult Hypophosphatasia
Typically presents in middle age; sometimes misdiagnosed as osteoporosis

Benign Prenatal Hypophosphatasia
Common pediatric HPP. Skeletal changes (limb shortening and bowing) in the womb or noted at birth, and then improving spontaneously. Not as severe as perinatal HPP

Childhood Hypophosphatasia
Manifests after age 6 months and before age 18 years

Hypophosphatasia Carrier
Has single HPP mutation, but is healthy

Infantile Hypophosphatasia
Manifests after birth but before age six months

Odontohypophosphatasia
Mildest HPP: Tooth problems only

Perinatal Hypophosphatasia
Most severe HPP; strikingly apparent at birth

Pseudohypophosphatasia
Extremely rare. Like infantile HPP, but blood ALP normal or elevated