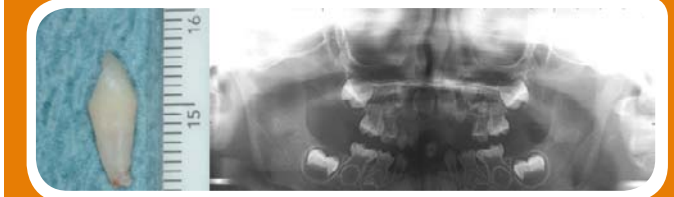
Early loss of primary and/or permanent teeth



The clinical phenotype in images

The hypophosphatasia patient was 3 years old when the radiograph was taken, and spontaneously lost teeth 71 and 81 at 14 months; teeth 72 and 82 at 22 months and teeth 51, 61, 62 and 63 à 34 months. Other dental abnormalities were present, such as reduced enamel and dentin thickness, bell-shaped crowns, significant cervical constriction, thin roots and hyper-development of the pulpal spaces. Tooth 83 was removed at 4 years of age, due to its mobility. Note that the root is intact.

The diseases

What is early loss of primary and/or permanent teeth?

Either partial or generalized early loss of primary and/or permanent teeth, whether associated with an inflammatory and infectious context or not, in children and young adults, is always the warning sign of an underlying systemic disease such as, for example, hypophosphatasia or immune deficiencies found in cyclic neutropenia, Papillon-Lefèvre syndrome, Chédiak-Higashi syndrome or Ehlers-Danlos syndrome (VIII, IV).

How many people are affected by these rare diseases?

In the case of hypophosphatasia, prevalence is estimated at 1 in 300,000 for the most severe forms, and at 1 in 6,370 for the milder forms including the odontological forms, while Papillon-Lefèvre syndrome is rarer, with a prevalence of 0.25 cases in 100,000.

What causes these diseases?

Hypophosphatasia is a rare genetic disorder that is inherited in autosomal dominant and recessive patterns, characterized by impaired bone and tooth mineralization linked to a deficiency and reduction of the alkaline phosphatase enzyme activity in the serum. It is caused by mutations in the ALPL gene coding for tissue-nonspecific (liver/bone/kidney) alkaline phosphatase, found in enamel, dentin, the cementum, the alveolar bone, etc.

Papillon Lefèvre syndrome is transmitted in an autosomal recessive pattern; it is linked to mutations in the CTSC gene coding for cathepsin C, a lysosomal enzyme implicated in the immune and inflammatory response.

What are the clinical manifestations of these diseases?

Hypophosphatasia is a disease with variable severity, which is expressed in six very different clinical forms depending on age at onset of the symptoms: the prenatal (lethal), benign prenatal, infantile, juvenile and adult forms and odontohypophosphatasia, which only affects the teeth.
Bone fragility and deformations can be present in utero or at birth. In the childhood forms, walking is often very difficult or even impossible (limping, crutches or wheelchair); muscle pain and weakness are the warning signs. **Early loss of baby teeth (before 3 years, either of all of the primary teeth or of only teeth in the incisor-canine group) or of permanent teeth is a very important warning sign. The teeth are exfoliated with their roots intact, with no inflammatory context. The teeth begin to loosen, which motivates the patient and his or her family to consult a professional. A radiograph reveals significant alveolar bone loss.**

In the adult form, the early loss of teeth is also a telltale sign. In the adult form, there are no associated skeletal malformations.

The diagnosis is established on the basis of the clinical symptoms and confirmed by the results of biological tests, i.e. low serum alkaline phosphatase, requiring further biological testing and an analysis of the ALPL gene.

From earliest infancy, **Papillon-Lefèvre syndrome** associates palmoplantar keratoderma that may be mild with **gingivitis developing into periodontal disease** with alveolysis and early loss of the primary teeth. This phenomenon is then repeated with the early loss of the permanent teeth.

In half the cases, this syndrome is associated with susceptibility to infection.

Treatment, care and prevention

Early loss of primary and/or permanent teeth may be a sign of a systemic disease and must result in a search in particular for associated signs. This anomaly must be reported to the doctor in charge of the child or adult patient, i.e. the paediatrician, family doctor, geneticist, etc. This medical diagnosis, reinforced by the observations of the dentist, is important for the affected individual and his or her family.

From the point of view of dental care, crucial elements of successful treatment include prevention, with the implementation of an oral health program, multidisciplinary treatment of these dental abnormalities and in particular the aesthetic and functional restoration of the mouth.

In **Alsace** there is a national **Reference Centre for OroDental Manifestations of Rare Diseases** that can be contacted for diagnosis, advises on the treatment and care of patients and/or referrals. In Alsace and France the prevalence of these disorders is unknown. **You can help increase knowledge of this dental disorder and of the associated rare diseases by participating in the registration of patients** in the D[4]/Phenodent patient registry. The creation of this registry was approved by the Consultative Committee for Data Processing in Health Research (CCTIRS) on September 11, 2008 and was authorized by the French Data Protection Authority (CNIL) on May 18, 2009 (registration no. 908416).

Patients and their families may participate in the **Interreg IV/OS A27 project, "Oro-Dental Manifestations of Rare Diseases"**. The objectives of this project are to characterize the clinical manifestations and problems linked to the disease, evaluate their incidence and repercussions in terms of quality of life, attempt to establish a link between certain symptoms and the implicated genes and discover new genes responsible for this disease.

Patient contact

If you encounter any patients affected by the diseases described above

contact@genosmile.eu

The anonymity of the physician, patient and family will be protected in the patient registration process, which will furthermore be carried out with the patient's consent.

Find out more

www.genosmile.eu, INTERREG/OS research project supported by the Faculty of Oral Medicine of the University of Strasbourg.

Orphanet, under hypophosphatasia and Papillon Lefèvre syndrome

The **Hypophosphatasie Europe** association brings together patients and families, healthcare professionals and the general public on the topic of hypophosphatasia.

Centre de Référence des Manifestations Odontologiques de Maladies Rares

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D[4] Diagnosing Dental Defects Database

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