

# Vitamin D resistant rickets

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## Abstract

*Vitamin D resistant rickets is defined by its resistance to the vitamin D treatment generally used in deficiency rickets. Typical signs are observed from the first months of life: radiological signs of defective mineralization on cartilage growth plates (rickets) and bones (osteomalacia) and alterations of the phosphocalcic homeostasis in spite of a satisfactory vitamin D status. The clinical phenotype combines bone deformities, mainly at the lower limbs, and other signs depending upon the etiology of the resistance (see below). Two groups of hereditary resistant rickets should be distinguished: hypophosphatemic rickets and pseudo-deficiency rickets.*

## Keywords

Rickets, osteomalacia, phosphocalcic homeostasis anomalies, hypophosphatemic rickets, pseudo-deficiency rickets

## Definition

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### Hypophosphatemic resistant rickets

Hypophosphatemic resistant rickets is characterized by severe hypophosphatemia and the absence of radiological or biological signs of secondary hyperparathyroidism. Postnatal growth retardation and dental anomalies are the other typical signs. Hypophosphatemic rickets is

mainly due to an alteration in the *PHEX* i.e phosphate regulating endopeptidase homolog, X linked gene on Xp22.1 (X-linked dominant transmission), or to an alteration in the *FGF23* i.e fibroblast growth factor 23 gene on 12p13 (autosomal dominant transmission). Other gene alterations have been suggested, *CICN5* i.e Chloride channel 5 for example which may explain some of the hypophosphatemic rickets with a recessive mode of inheritance. Treatment with phosphates and 1-hydroxylated derivatives of vitamin D from early infancy prevents bone deformities. It also prevents or markedly decreases the statural growth deficit and the occurrence of dental anomalies.

### Pseudo-deficiency rickets

Pseudo-deficiency rickets is characterized by severe hypocalcemia with secondary hyperparathyroidism. Bone deformities concern all the long bones and are associated with bone pain, muscular hypotonia, dental anomalies (enamel hypoplasia), and, in some cases,

neuromuscular signs of hypocalcemia. The mode of inheritance is autosomal recessive. Two alterations in the genes responsible have been identified. They are both located on 12q13:

- Anomalies in the gene encoding the cytochrome P450 of the vitamin D-1 hydroxylase (Pseudo-deficiency rickets type I). A lifelong treatment with 1-hydroxylated derivatives of vitamin D totally prevents or cures the clinical, radiological and biological signs of rickets.
- Anomalies in the gene encoding VDR, the vitamin D receptor (Pseudo-deficiency rickets type II or rickets with resistance to calcitriol). This type of resistant rickets is partially or not responsive even to high-dose treatment with vitamin D derivatives and often requires long-term parenteral calcium supplementation. Alopecia is observed in half of the cases and is not responsive to vitamin D or calcium treatment.