

SKELETAL EVIDENCE OF VITAMIN D DEFICIENCY IN EUROPE

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Introduction

Vitamin D deficiency is the major cause of rickets and osteomalacia, bone diseases which lead to several deformities of the skeleton. This paper gives a review about skeletal evidence of both diseases in Europe. First, it is necessary to explain the main principles of vitamin D metabolism in order to understand causes and effects of vitamin D deficiency. These aspects are followed by a description of both rickets and osteomalacia especially regarding macroscopic changes in bone as well as those only recognisable through radiographic methods. Furthermore, the given information will be underlined by results and photographs of some selected analyses of historical records. Even if there are some studies suggesting that not only vitamin D deficiency causes rickets or osteomalacia, but also dietary calcium deficiency, solely the vitamin D dependent aspect of these diseases is described within that paper. The same applies to acquired or genetically based disorders of the calcium or phosphorus metabolism leading to rickets and rachitic changes, respectively, as for instance hypophosphatemic rickets or hypophosphatasia, as well as to tumor-induced oncogenic osteomalacia/ rickets (see Berry et al. 2002, Mughal 2002).

Vitamin D metabolism

The source of vitamin D, which is not a real vitamin but a hormone, is 7-dehydrocholesterol (provitamin D₃) which is located in the skin. Under exposure to sunlight, this form is transformed into the active form vitamin D₃, also called cholecalciferol. The amount of produced vitamin D₃ depends on several factors as for instance season, pigmentation or time of exposure to sunlight. Another source of vitamin D but of more less importance is our diet. Vitamin D₃ or also vitamin D₂, called ergocalciferol, a derivation of the plant sterol ergosterol which is produced under ultraviolet irradiation, are supplied in our food. Groceries like milk, eggs, liver or oily fish like tuna are possible sources of small amounts of vitamin D.

Subsequently, provitamin D₃ is transported to the liver where it is hydroxylated into 25-hydroxyvitamin D (25OHD). After its transport to the kidneys, this 25OHD is converted into 1.25-dihydroxyvitamin D (1,25D) or calcitriol, the active metabolite under control of parathyroid hormone (PTH). The described metabolism can be seen in Figure 1.

Active vitamin D has different effects on body. It enhances the absorption of calcium and phosphorus in the intestine by stimulating the conversion of intestinal cells to calcium binding cells whereby an increased transfer of calcium in the gut is achieved. Concerning its effects on bone, vitamin D is necessary for adequate mineralisation of bone matrix, as it is an important factor to maintain the serum calcium level as well as the serum phosphorus level. In the process of bone remodelling, osteoclasts remove bone substance. The resulting lacunas are filled in with unmineralised bone matrix, called osteoid, which is normally subsequently mineralised by calcium-phosphorus compounds.

The synthesis of the metabolically active form, calcitriol, is enhanced by the presence of parathyroid hormone (PTH), hypocalcemia and hypophosphatemia. And vice versa, hypercalcemia and hyperphosphatemia lead to suppression of this renal metabolite.

Vitamin D deficiency

Like it was already said, vitamin D metabolism starts with the conversion of provitamin D caused by ultraviolet irradiation. Is there no adequate exposure, depending on season, time of day or even cultural customs, the production of vitamin D can be affected negatively. The inadequate exposure to sunlight results in a greater importance of diet. Pettifor (2004) quoted that the development of rickets is mostly prevalent between 3 and 18 months of age. Thus, he mentions exclusive breast-feeding⁽¹⁾ as one possible factor leading to rickets as well as maternal vitamin D deficiency.

Apart of the stated factors leading to vitamin D deficiency there are also liver and kidney disorders impairing the conversion of vitamin D in its active metabolites, genetically based, as for instance pseudovitamin D deficiency rickets (see Mughal 2002) or acquired which thus can result in rickets or osteomalacia. But these syndroms shall not be explained further within that paper.

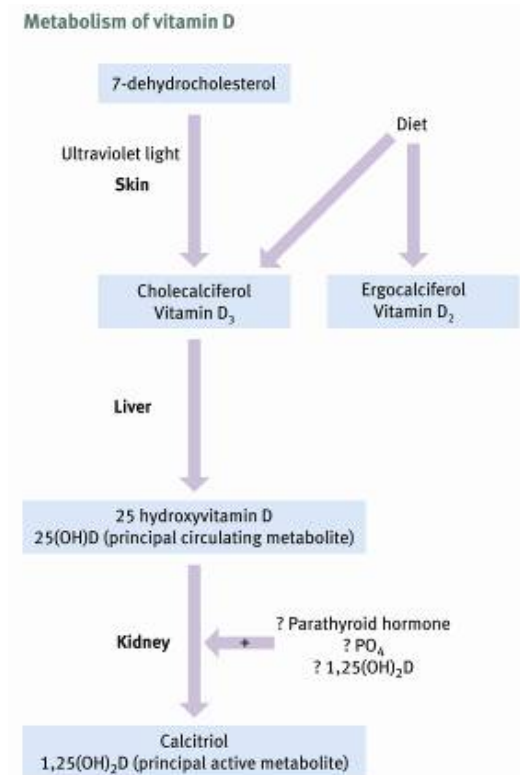


Figure 1: Metabolism of vitamin D (Horner J.).

Rickets

Rickets is a disease mainly caused by deficiency of metabolic vitamin D occurring in infants, young children and adolescents. Although the disease was first described by Daniel Whistler in 1645, Francis Glisson is considered to be its discoverer. In 1650 he published the treatise *De Rachitide* (Dunn 1998). The earliest paleopathological studies on rickets are from the middle of the 19th century, nevertheless there are just a few of reports correlating with the fact that this disease was quite rare prior to the Industrial Revolution. The existing studies mainly are individual case studies within general paleopathological analyses of skeletal collections. Mays et al. (2006) refer on works of Power and O'Sullivan (1992), Gejvall (1960) and Czarnetzki et al. (1985), for instance. Currently there is a greater interest in rickets or also osteomalacia hence several studies investigate the cultural factors effecting the development of diseases. Within that paper, most of all, the studies on populations from England shall be mentioned, especially made by Mays, Brickley and Ives, not only for rickets, but also for osteomalacia.

It is reported that the rate of rickets was higher in 18–19th populations than in Medieval populations, suggesting that factors such as urbanisation, climatic change and rising industrial pollution had effects on the development of these diseases (Mays et al. 2006).

Main characteristics or typical signs of rickets are changes in growth cartilage plates accompanied by swelling of long bone metaphyses and costal rib ends ("rickety rosary" or "rachitic rosary"), flaring of the epiphyses (Fig. 2) and bending of long bones (Fig. 3).



Figure 2: Femur showing anterior bending in subtrochanteric region (Mays et al. 2006).



Figure 3: Femur together with normal comparison (N). Diseased specimen shows marked flaring and cortical porosis in distal part. There is also coxa vara and flattening of bone beneath femoral head (Mays et al. 2006).

Furthermore, disturbances or even complete failure of mineralisation of newly formed osteoid characterise the clinical picture. During the process of bone remodelling there is no replacement of the lacunes, resulting from the work of osteoclast, by mineralized matrix. Therefore, the osteoid remains unmineralized and thus soft, leading to an advanced weakening of the skeleton. Common characteristics are also bowed legs (genu varus, Fig. 4) or knock-knees (genu valgum).

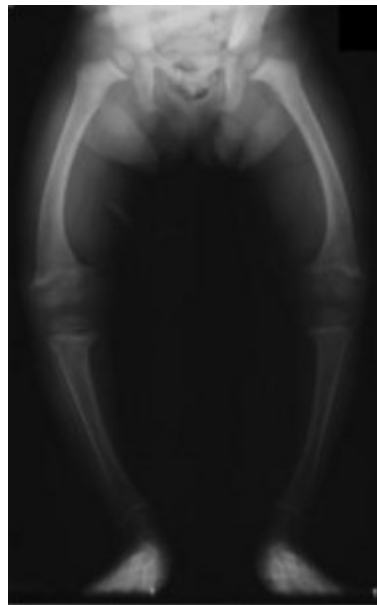


Figure 4: Genu varus. X-Ray of the legs in a 2 year old child with rickets
(<http://content.answers.com/main/content/wp/en/thumb/2/23/190px-XrayRicketsLegssmall.jpg>).

In radiographs the lucent gap between metaphysis and epiphysis is expanded due to a delay of mineralisation. Looser's zones (fissure fractures, pseudofractures) can also be detected frequently. Thacher et al. (2000) mention generalised osteopenia, green-stick fractures, delayed appearance of ossification centres and curved long-bones as further radiographic signs of rickets. Concerning the question whether rickets has some influence on growth, Pinhasi et al. (2006) stated that there are three main factors influencing the degree to which growth faltering or stunting occurs, namely duration, severity and timing of rickets. Furthermore, a possible effect of rickets on growth can be reconciled by catch-up growth and can as well as bone remodelling over a longer period obliterate any signs of rickets. They also refer in their work on Holick (2005), who stated that a lack of vitamin D, especially during infancy as the period of highest growth velocity, results in growth retardation. Nevertheless, Pinhasi et al. showed within their comparative analyse of remains from late-medieval and post-medieval English sites, that there was no statistically significant difference of long-bone diaphyseal length between individuals with and without rickets.

Another work was published by Ortner and Mays (1998). They set ten characteristic changes of bone often occurring in rickets: cranial vault porosity, orbital roof porosity, deformed mandibular ramus, costochondral rib flaring, costochondral rib porosity just as deformity of leg and arm bones, long-bone thickening, long-bone metaphysical porosity and porosity or roughening of bone underlying long-bone growth plates. That does neither mean that the manifestation of all these signs has to occur simultaneously, nor that they are diagnostic by their own. They rather appear in a kind of combination which on its whole enables to recognise rickets.

Rickets can be divided into active cases and healed ones, identifiable by the kind of change of bone. Signs of active cases are for instance porosity of cortical bone both in cranial and post-cranial material and porosity or roughening of bone beneath the epiphyseal growth plates. On the other hand, in healed cases the signs of vitamin D deficiency can be found, but there is a lack of porous cortices and growth plate abnormalities.

In 2006 the article “Skeletal manifestation of rickets in infants and young children in a historic population from England” was published by May et al. (2006). They investigated the skeletal remains of 164 immature individuals of which 21 showed signs of rickets. Apart from a macroscopic investigation they also made radiographs of post-cranial elements, thus examining changes in the internal bone structure. Distinguishing between active and healed cases, they could find porosity of cortical bone in the active cases, more frequently in post-cranial than in cranial material, just as superficial porosity/roughening of the ends of the long-bone diaphysis underlying the epiphyseal growth plates. These changes can be seen in Figures 5 and 6.

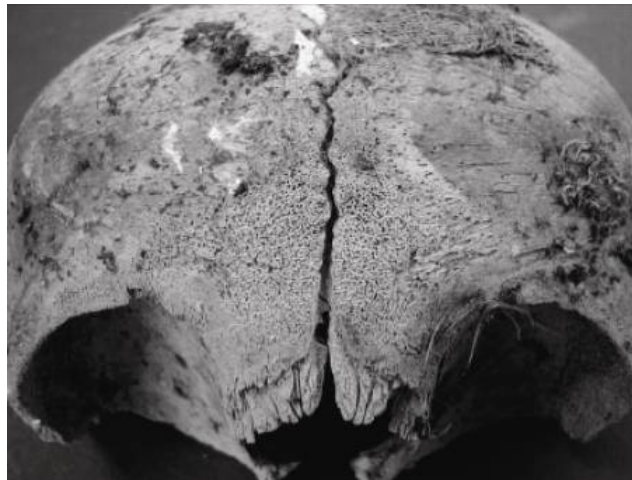


Figure 5: Frontal bones: porosity in glabella region (Mays et al. 2006).

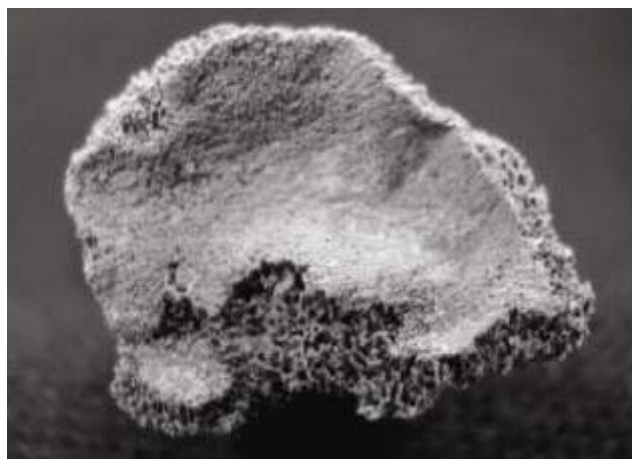


Figure 6: Distal radius: slight roughening of bone underlying growth plate. Porosity on anterior part of surface (toward bottom of photograph) is postdepositional. There is also marked concavity (“cupping”) of bone end (Mays et al. 2006).

Another investigation on rickets was made by Gonzáles Martín et al. (1999). They analysed four collections from the second century BC., the Medieval, the 11th to the 13th century and from modern times, respectively, excavated in different parts of Spain. To quantify the frequency of rickets the number of those immature individuals was counted who showed three or more of the following criteria: ectocranial porosity, porosity of the orbital roof, deformity of the long-bones, flaring of the chondrocostal rib ends and local porosity, flaring of the long-bone metaphyses (copped metaphyses) and local porosity, persistence of the anterior fontanelle and cranial tabes.

Gonzáles Martín et al. could provide evidence of rickets in Spain in different cultural populations not only since Medieval times but also since the Bronze Age.

Finally there shall be mentioned that most cases of rickets are diagnosed on mature skeletons or even older juveniles. Thus, in such cases bending deformities can be demonstrated as they may be indicators of healed rickets.

Osteomalacia

Osteomalacia is also a disease mainly caused by vitamin D deficiency. In contrast to rickets it does not occur in infants, but in adults. The picture of the disease correspond to that of rickets but here the growth cartilage plates are not involved due to the fact that it first occurs after their closure. The number of identified cases affected by osteomalacia is even smaller than that of rickets.

Skeletal deformities in osteomalacia are rarer than in rickets. These bone deformities caused by inadequate mineralisation of osteoid lead to skeletal weakening, particularly of the limbs, vertebrae, ribs and pelvis. Apart of these changes the most important characteristic of osteomalacia is the occurrence of so called Looser's zones (pseudofractures). These are accumulations of non-mineralised or poorly mineralised osteoid which can be recognised on radiographs as zones of increased radiolucency. Owing to minimal trauma these pseudofractures can then progress to full fractures. During such a fracture the involved skeletal parts can be displaced in their position. In cases where the vitamin D deficiency goes on for longer periods the fracture may unite, but osteomalacia keeps on being identifiable since the surrounding fracture callus remains unmineralised. Accordingly, a mineralised callus indicates that the deficiency has been overcome. Looser's zones mostly occur in the superior and inferior pubic rami, the medial femoral neck and medial sub-trochanteric region, the ribs, the clavicles and the outer border of the scapula (Baburaj; Reid 2004, Brickley et al. 2005). They usually appear bilaterally and symmetrically, perpendicularly to the cortical margins of the bone.

Exemplary for osteomalacia in historical skeletal records, some aspects of the study conducted by Brickley et al. (2005) are quoted following. Within that investigation the skeletal remains of 28 individuals from two historical collections with documented osteomalacia⁽²⁾ were analysed. They could identify Looser's zones in scapulae, as well as exaggerated posterior curvature of the scapula (viewed from medial side) as a result of softened bone. Regarding this characteristic Brickley et al. (2004) mention that the normal individual variation can complicate the identification of that feature. Apart of these two criteria they recognised a third one which is not as frequent as the others: the buckling or folding of the superior border of the scapula towards its body caused by the loss of structural integrity due to the bone softening (Fig. 7). Even the evaluation of this feature can be difficult since the bone can be very thin whereby the buckling can lead to post-mortem fragmentation soon after the burial.



Figure 7: Scapula from the Galler Collection with anterior collapse and buckling of the superior border towards the body.apula (Brickley et al. 2005).

The analysis of the vertebrae indicated changes due to osteomalacia. For instance, many of the investigated individuals showed severe kyphosis, accompanied by wedging of the vertebral bodies which is called 'biconcave codfish appearance' (Francis & Selby 1997 in Brickley et al. 2005) (Fig. 8). With affliction of the lower lumbar vertebrae the pelvic canal can be obstructed. Furthermore the vertebrae can fold in on itself.

Regarding the ribcage, they noticed ribs with a straightening of their lateral border resulting in a squarer rib neck angle than normal. Furthermore fractures were present in many cases, mostly reunited, showing small spicules of disorganised bone along the edges of the fracture. The sternum of one specimen was severely curved throughout the manubrium and the body, also displaying anterior-posterior bending which has negative consequences for the cartilage and rib articulations.



Figure 8: Section through the axial skeleton demonstrating wedging of the vertebral bodies, anterior kyphosis, curvature of the sacrum and multiple rib fractures (Brickley et al. 2004).

The pelvis showed different changes ranging from severe deformities to only milder ones. Frequently, the iliac crests were folded over into the body of the ilium. Cortical thinning as well as the buckling of the iliac crest, are results of inadequate mineralisation and thus leading to an inability of the bone to withstand the muscle pulls. Many specimens showed a decreased antero-posterior length of the ilium and obstruction of the pelvic inlet linked to several other deformities as for instance severe angulation of the sacrum. Changes in pelvis and sacrum also led to size reduction of the pelvic outlet. Furthermore, deformities of the pubic symphysis may occur in individuals affected by osteomalacia. So it is possible that the symphyseal faces begin to project towards anterior. Severe cases of osteomalacia show anterior protrusion of the pubic rami and the superior pubic rami can be pushed against each other resulting in buckling of the symphyseal face. So the contact with the cartilage remains maintained. Finally they could find Looser's zones, usually appearing in the superior and inferior pubic rami, which often led to true fractures as can be seen in Figure 9. But Brickley et al. defer to the fact that particularly this part of the skeleton frequently is damaged during processes related to excavation, thus post-depositional fractures always should be considered as possible.

Deformities of the acetabulae can be seen in severe cases of osteomalacia, as well as in some cases thickening of bone having consequences on the position of the femoral head. Regarding the sacrum, as already mentioned above, there can be an angulation which usually affects the inferior margin of the third sacral segment and the sacral body can be displaced anteriorly. These criteria could both be observed within the quoted investigation and are seen to come from greater muscle and ligament bearing on the body of the sacrum thus stabilising the pelvis. Even the evaluation of sacral angulation can be difficult because it normally varies, especially regarding sexual dimorphism and also post-depositional breaking can lead to wrong estimation.

Finally, some changes in the long-bone due to osteomalacia shall be focused. The feature most frequently seen in the investigated remains was antero-lateral bending of the proximal third of the femoral metaphysis. Some specimens showed a prominent bony ridge, frequently on the lateral part of the anterior femoral side. Furthermore, pseudofractures of the femoral neck as well as of the subtrochanteric region could be identified.



Figure 9: Pseudofractures that have developed into true fractures at predilected sites of the superior (a) and inferior (b) pubic ramus (Brickley et al. 2005).

Another study on osteomalacia was published by Brickley et al. in 2007. Here, a sample of 136 individuals out of 857 was investigated. Within that study, they analysed post-cranial features macroscopically according to those criteria given in the paper appeared in 2005, just as they made radiographs to identify pseudofractures, lesions occurring bilaterally resulting from weakened bone.⁽³⁾ Brickley et al. took radiographs of different parts of the skeleton, such as from scapula, ribs, tibia and proximal ulna and femur. Figure 10 shows the inferior aspect of a rib shaft taken from the mentioned paper illustrating a linear raised ridge of bone spicules as a result of an underlying pseudofracture.

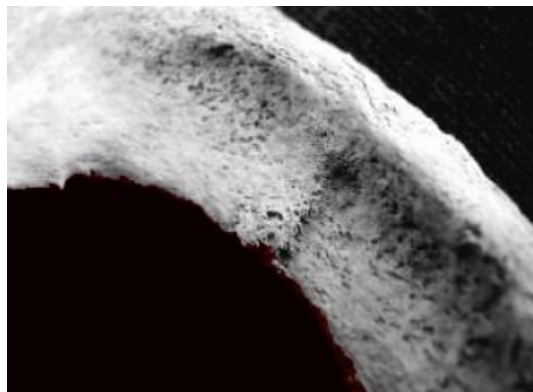


Figure 10: Inferior aspect of rib shaft with a linear raised ridge of bone spicules indicating an underlying pseudofracture (Brickley et al. 2005).

Conclusion

Vitamin D deficiency as a result of inadequate exposure to sunlight or even nutritional deficiency could be described to be one of the possible causes leading to rickets and osteomalacia. Besides the typical bone deformities, caused by the decreased rate of bone mineralisation, also other characteristics of the diseases were shown with the aim to give some kind of survey about the topic. Nevertheless, there should be pointed out, that these skeletal disorders are often difficult to recognise since usually not only a single criterion makes them identifiable, but a combination of several features, as well as the state of preservation often makes an investigation impossible. At least, in case of rickets the fragility of immature skeletons frequently prevents to fully analyse a certain skeletal population and weakened bones in osteomalacia are also less likely to survive for an investigation. Thus, until now there is only a few number of studies on rickets and osteomalacia in archaeological specimens and the situation will probably remain this way.

Annotations

(1) Breast milk contains as little concentrations of vitamin D³ that it is not enough to cover the infant's requirement. Although, they are protected from vitamin D deficiency during the first months, hence vitamin D metabolites can cross the placenta. Concerning this discussion, read more about in Pettifor (2004).

(2) It is about the Galler Collection in Basel and the collection in the Federal Museum for Pathological Anatomy, Vienna.

(3) Brickley et al. mention that pseudofractures are not only criteria for osteomalacia, but also for such corresponding with osteogenesis imperfecta, Paget's disease, congenital syphilis, osteomyelitis and osteopetrosis, for instance. They refer to Steinbach et al. (1954) who said that the pseudofractures in these cases not occur symmetrically and at sites being predilected.

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