



**Vitamin D Deficiency: New Perspectives Under Past Light**

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## **Description of symposium/ Purpose of Handout**

By bringing health, biomedical and natural science researchers together with paleopathologists (those that study health, disease and life histories in the past), the symposium ‘Vitamin D Deficiency: New Perspectives Under Past Light’ and linked special issue of the International Journal of Paleopathology (IJPP) will advance knowledge of how social and cultural factors linked to vitamin D deficiency have shaped the evolution of humans and social systems in past societies.

A large number of events have taken place in the last 15 years considering vitamin D from a biomedical and health science perspective, but this will be the first interdisciplinary event in the world to specifically consider vitamin D and deficiency in the context of the social sciences and humanities.

Contributions fall into four sections:

**Section One:** Presentations from contributors in natural and health sciences will consider what paleopathologists can learn from recent developments in the understanding of vitamin D. Papers will also cover information that can be derived from other species that can contribute to paleopathological research, particularly interpretations that can be made. The speakers include leading scholars such as Stephanie Atkinson and Glen Jones who have led research into vitamin D metabolism and deficiency in the current Canadian community.

**Section Two:** The second section takes the form of poster presentations. Posters will be in place all day, but there will be dedicated time for viewing with authors present. Authors will each be allotted five minutes to share information on the key contribution that the technique they are discussing contributes to understanding aspects of past cultures. Techniques to be covered include stable isotopes, x-ray, micro-CT, histological, macroscopic and shape analysis.

**Section Three:** The final series of presentations will enable those who have used information on vitamin D deficiency in past communities to exchange knowledge with delegates. The paper by Brickley et al. comprises the largest investigation of vitamin D deficiency in a past society to date. Simon Mays, who has worked on vitamin D deficiency for many years, will consider contributions that ancient texts can make to our understanding of past societies. Papers will consider archaeological human remains from a wide range of spatial and temporal contexts and go beyond descriptions of pathology to consider issues such as gender and social inequality.

**Open Section:** Posters that explore other aspects of paleopathological work on vitamin D deficiency.

### **This handout contains:**

A timetable for the symposium including scheduling of the short presentations for the posters in Section 2.

Abstracts of the contributions presented at the PPA meeting in New Orleans.

Definitions provided by contributors for terms they will be using in their papers and posters.

## Section 1 Podium Presentations (8:30 -9:50am)

### New Developments in Health and Natural Sciences: Opportunities for Paleopathologists

Chair: Jane Buikstra

#### 8:30 Introduction. Megan Brickley.

#### 8:35 The discovery and synthesis of the nutritional factor, Vitamin D. Glenville Jones

Although vitamin D deficiency, or rickets (osteomalacia in adults), was first recognized over 350 years ago, it was only about 100 years ago that vitamin D, the nutritional factor responsible, was discovered. This discovery was made more difficult by the fact that the substance could be synthesized in human skin through exposure to UV light and could also be present in the diet in animal-derived (D3) and plant-derived forms (D2). Prior to 1920, the frequency of vitamin D deficiency in the general population of industrialized cities was high and it was not unusual to see the bow-legged individuals. Women who experienced rickets in childhood showed pelvic deformities that made child-bearing difficult. The discovery of vitamin D led to the widespread fortification of foods such as dairy products in developed nations and the virtual eradication of rickets in those countries. Vitamin D3 was first chemically synthesized in the 1930s and its metabolism to the active form 1,25-dihydroxyvitamin D3 and its mode of action in calcium and phosphate homeostasis was elucidated in the latter half of the 20th century. The pharmaceutical industry has now synthesized multiple vitamin D analogs that mimic the effects of vitamin D on the body and are used therapeutically in diseases such as bone disease, chronic kidney disease and psoriasis. Accordingly, nutritionists, physicians, chemists and biochemists played critical roles in the rich history of vitamin D and these will be honored in this presentation.

Definitions provided:

1. Vitamin D deficiency - Disease in which there is a shortage of vitamin D as indicated by a serum 25-OH-D3 measurement below 20 ng/mL (50 mol/L) in which there is defective mineralization of bone (osteoid) accompanied by symptoms associated with rickets or osteomalacia.
2. Rickets - Childhood version of vitamin D deficiency in which the defective mineralization results in bowing of long bones and widening of certain joints e.g. costochondral joints of ribcage.
3. Osteomalacia - Adult version of vitamin D deficiency analogous to rickets causing defective mineralization of the adult skeleton seen in bone histomorphometric studies.
4. Vitamin D - A nutritional term used to describe any anti-rachitic substance that resolves vitamin D deficiency. Especially used to describe substances that cure rickets in young animals.
5. Cholecalciferol or vitamin D3 - An anti-rachitic substance made in the skin or in the diet with a chemical structure also described as vitamin D3 with the same side chain as cholesterol.
6. Ergocalciferol or vitamin D2 - An anti-rachitic substance derived from plant-material in the diet with a chemical structure also described as vitamin D2 with the same side chain as ergosterol.

#### 8:50 Vitamin D's role in health and disease: Does the present inform the past? Stephanie Atkinson and Laura Lockau

The acknowledged role of vitamin D in the support of growth and maintenance of bone is well understood. However, emerging ecological and observational evidence has unveiled the potential for vitamin D deficiency to be an etiological factor in cancers, immune disorders, cardiovascular diseases, abnormal glucose metabolism and neurodegenerative diseases. Investigating the association of vitamin D status in humans to these conditions will provide a framework for analyzing and understanding these relationships in archaeological skeletal samples. Not all conditions leave evidence in the skeleton and it is critical to consider all conditions that may have affected past peoples. Surveys of nutrition status of Canadians reveal that vitamin D status is significantly affected by ancestry, latitude, food source

availability and dietary beliefs/practices, all of which are pertinent in consideration of vitamin D availability in the past populations. This paper will review recent developments in the understanding of health consequences of vitamin D and how this new knowledge can be applied for use by paleopathologists.

Definitions provided:

1. Vitamin D deficiency – Measured by serum 25-hydroxyvitamin D < 30 nmol/L as defined by DRI for vitamin D (IOM, 2011)
2. Vitamin D insufficiency – 30-40 nmol/L (as above)
3. Vitamin D sufficiency - > 50 nmol/L (as above)
4. Rickets - Softening and weakening of bones in children, usually because of an extreme and prolonged vitamin D deficiency.
5. Osteomalacia - Softening of the bones caused by impaired bone metabolism primarily due to inadequate levels of available phosphate, calcium, and vitamin D.
6. Health - Level of functional and metabolic efficiency of a living organism.
7. Disease - Is a particular abnormal condition, a disorder of a structure or function that affects part or all of an organism.
8. Vitamin D state/ status – Measure that reflects the state of vitamin D health – deficient, insufficient, sufficient, toxic
9. Nutrition status – Measure that reflects the state of health for overall nutrition or for one particular nutrient.
10. Non-bone functions of vitamin D – Refers to biological actions of vitamin D such as antiproliferative, anti-inflammatory, and immunomodulatory.
11. Biological plausibility – Evidence for a functional role.
12. All-cause mortality - Used by epidemiologists, or disease-tracking scientists, to refer to death from any cause. In clinical trials it is used as an indicator of the safety or hazard of an intervention.
13. Vitamin D recommendations – Recommendations for the amount of vitamin D to be consumed by populations and individuals from food and supplements based on a biochemical or functional indicator of adequacy.
14. Developmental origins of health and disease (DOHaD) - A multi-disciplinary field that examines how “environmental factors acting during the phase of developmental plasticity interact with genotypic variation to change the capacity of the organism to cope with its environment in later life.” (Gluckman, Peter and Mark Hanson, eds. 2006 The developmental origins of health and disease: and Overview, in Developmental Origins of Health and Disease. Peter Gluckman and Mark Hanson, eds. Pp.1-5. Cambridge: Cambridge University Press.)

#### **9:05 The pathology of vitamin D deficiency in animals: a comparative overview.** Elizabeth Uhl

Vitamin D is critical to calcium and phosphate homeostasis and is thus crucial for both the formation of bone and bone remodeling in a wide variety of species. Vitamin D deficiency diseases impact amphibians, reptiles, birds and mammals, however there is variation between species in both the ability to make vitamin D and susceptibility to dietary deficiency. For example, while most herbivores are able to produce vitamin D<sub>3</sub> in response to sunlight, exposure to UV light does not increase dermal vitamin D<sub>3</sub> concentrations in dogs and cats, which in the wild met their requirements through a carnivorous diet. Nutritional deficiencies can induce rickets in cattle, sheep and goats, but the disease is rare, especially in modern times. Pigs are more susceptible to nutritional vitamin D deficiency as they grow rapidly and are weaned early. Horses are less susceptible as they naturally have higher serum calcium concentrations as well as vitamin D levels that are lower than those associated with rickets in other animals. Environments also shaped susceptibility, as llamas and alpacas out of their natural high altitude intense solar radiation environments are highly susceptible to vitamin D deficiency. While susceptibility varies, the pathology

of rickets and osteomalacia is similar across species, although fibrous osteodystrophy may also be present. Studies in animals, including lion cubs in the London zoo in 1889, have been critical to understanding the pathogenesis of vitamin D deficiency diseases in both animals and humans.

Definitions provided:

1. Vitamin D deficiency - Level of vitamin D deficiency due to either a nutritional or genetic cause that is severe enough to induce bone lesions.
2. Rickets - A metabolic bone disease of the developing skeleton affecting many animals including humans. It is characterized by abnormal endochondral ossification at growth plates and defective bone formation. It is caused by defects in mineralization.
3. Osteomalacia - A metabolic disease of mature animals and humans characterized by defective mineralization of newly formed osteoid. The pathogenesis and non-growth plate bone lesions are the same as those of rickets.
4. Nutrient deficiency/ Nutritional deficiencies - A directly or indirectly induced dietary deficiency severe enough to induce bone disease.
5. Metabolic bone disease - A broad term for abnormalities affecting multiple bones that are most commonly caused by nutritional and/or hormonal abnormalities. Some can be reversible once the underlying defect is corrected.

**9:20 Vitamin D metabolism in feral and captive nonhuman primates as an evolutionary approach to understanding vitamin D in humans.** Toni Ziegler, Amita Kapoor, Neil Binkley, Jane Phillips-Conroy, Clifford Jolly & Jeffrey Rogers

Evolutionary approaches to understanding human vitamin D requirements and disease states have a basis in nonhuman primate vitamin D states. A newly developed LC/MS/MS (liquid chromatography / mass spectrometry) vitamin D panel measures vitamin D and its metabolites, 25(OH)D3 & D2, and 24,25 dihydroxyvitamin D3 & D2 is used to compare captive and feral baboon species with present day humans who have high level exposure to the sun. Savannah baboons, as with early hominids, are covered with hair and skin color varies between species. Levels of traditional living East African tribesmen have levels of 25(OH)D3 that are higher than humans living in North America and Europe (28-68 ng/ml in tribesmen; 20 – 40 ng/ml in North America; Luxwolda et al., 2012). Baboons from several species that live in the sun-drenched savannahs of East Africa show 25(OH)D3 levels higher than humans (mean  $90 \pm 5.07$  ng/ml) and are similar to levels found in captive baboons (*Papio Anubis*,  $88.11 \pm 4.86$ ). Baboon species show different levels of vitamin D in the wild ( $P < 0.001$ ) with *P. anubis* showing significantly lower levels than *P. hamadryas* and *P. cynocephalis*. The *P. anubis* species has the darkest skin color of the three species indicating that as in humans, baboons have evolved different coloration dependent upon sun exposure and environment. This work was funded by NSF BCS-1029363 to JPC, CJ, JR, TZ and the WNPRC NIH P51ODO11106 for Assay Services to TEZ.

Definitions provided:

1. Vitamin D sufficiency - Demonstrating adequate metabolic processing of vitamin D.
2. Health- Effect of appropriate levels of vitamin D on physical health.
3. Metabolic process for vitamin D - The enzymatic conversions of vitamin D to other D forms.
4. Cholecalciferol - Vitamin D3.
5. 25 hydroxyvitamin D - Circulating form of vitamin D.
6. 24,25 dihydroxyvitamin D: Hydroxylated form from 25 hydroxyvitamin D.
7. 1,25 dihydroxyvitamin D - Bioactive vitamin D that acts as a hormone in the body.

**9:35 Discussion: How can current research in biomedicine and non-human species contribute to understanding and interpreting vitamin D deficiency in past communities?**

**9:50- 11:00 Break and Poster Session 1            *Magnolia Ballroom***

**Section 2 Poster Presentations (10:05 – 10:50):**

**The Use of New Techniques to Learn More About Past Communities**

**Chair: Tracy Prowse**

- 10:05 The Shape of Things to Come: Growth in Children with Rickets. Sarah Stark, Sonia Zakrzewski & Simon Mays (7)\*
- 10:10 Re-examination of the skeletal manifestations of rickets on immigrants from the historic population from St. Matthew, Quebec City (1771-1860). Marie-Hélène B-Hardy, Zocha Houle-Wierzbicki, Jacinthe Vigeant, Emeline Raguin & Isabelle Ribot (5)
- 10:15 The Rachitic Tooth: The Use of Radiographs as a Screening Technique. Lori D’Ortenzio, Isabelle Ribot, Benoit Bertrand, Bonnie Kahlon, Emmy Bocaege, Emeline Raguin, Annabelle Schattmann & Megan Brickley (4)
- 10:20 Vitamin D deficiency in St-Etienne de Toulouse, France: Investigations using Micro-CT. Bonnie Kahlon, Benoit Bertrand, Antony Colombo, Hélène Coqueugniot, Chris Knüsel, Lori D’Ortenzio & Megan Brickley (3)
- 10:25 Radiographically recognizable? An investigation into the appearance of osteomalacic pseudofractures. Emma Jennings, Jo Buckberry & Megan Brickley (2)
- 10:35-10:50 Discussion: How can technical advances improve our understanding of past (*Azalea Ballroom*)

\* Indicates poster number.

**Open Section Poster Presentations:**

1. The relationship between vitamin D deficiency and leprosy in two English medieval populations. Sofia-Anna Papadopoulou & Jo Buckberry (6)
2. The Art of Diagnosing Rickets: a Test Against a Subadult Portuguese Sample in the Scheuer Collection. Jennifer Austen & Craig Cunningham (8)

**Posters: Abstracts and Definitions provided**

**The Shape of Things to Come: Growth in Children with Rickets.** Sarah Stark, Sonia Zakrzewski & Simon Mays

Normal juvenile development requires adequate nutrient intake, but there is limited understanding of how such deficiencies affect growth trajectories. Growth is commonly studied using linear long bone measurements, but these lack shape information. In the current study, size is studied through linear measurements and shape is examined using geometric morphometrics, thereby enabling an integrated study of bone growth and morphology. A dataset of femora (n=25), tibiae (n=31), and humeri (n=36), from 47 juveniles ranging from infancy to twelve years old, was collected from medieval Wharram Percy. Three-dimensional models were created using structured-light-scanning. Morphometric analysis revealed differences in the long bone growth patterns between children suffering from rickets and those without apparent skeletal markers of disease. This trend was most pronounced in the tibia and may reflect changes in functional loading to this bone.

#### Definitions Provided

1. Geometric Morphometrics - A mathematical and statistical tool-kit to quantify shape by removing size, rotation, and orientation of an object.
2. Developmental Trajectories - The relationship of changing shapes with age.
3. Principal Component Analysis - A statistical technique that visualizes the variation of shape within a multivariate data-set.

#### **Re-examination of the skeletal manifestations of rickets on immigrants from the historic population from St. Matthew, Quebec City (1771-1860).** Marie-Hélène B-Hardy, Zocha Houle-Wierzbicki, Jacinthe Vigeant, Emeline Raguin & Isabelle Ribot

The aim of this paper is to present two unique historic specimens from the protestant cemetery of St-Matthew (Quebec City), who developed vitamin D deficiency at different stages of their life and/or possibly in various places. In fact, according to historical sources as well as isotopic studies, St-Matthew's population (buried between 1771 and 1860) was mainly composed of first generation immigrants from the British Isles or Northern Europe. The growing Quebec City often attracted people seeking for better living conditions in the New Continent.

A full portrait including archaeological, osteological, palaeopathological and chemical data (i.e. burial place within cemetery, age, sex, dietary and mobility pattern) is presented for one child and a young adult. Biographical interpretations are discussed, in order to explore whether these individuals developed vitamin D deficiency onsite, or before arrival in the city in the case of first- generation migrants. Their health status might therefore reflect previous environment.

#### Definitions provided:

1. Vitamin D deficiency - Vitamin D deficiency is medically diagnosed when blood concentrations of 25(OH) D is lower than 50 nmol/L (Stroud et al. 2008). Concentrations between 50 nmol/L and 100 nmol/L would be considered Vitamin D insufficiency. As we are working with archaeological specimens, and therefore do not have access to blood samples, vitamin D deficiency is not easy to diagnose. However, vitamin D deficiency will cause changes in handling of calcium and phosphorus that will induce pathological changes to the skeletons, like we see in rickets or osteomalacia for example.
2. Rickets - Rickets is a metabolic disease resulting in the hypomineralization or defective calcification of bones during an individuals' growth that leads to bone deformities and sometimes even fractures. It can be due to Vitamin D, phosphorus or calcium deficiency, caused by insufficient sun exposure, poor dietary intake or genetic predispositions. To diagnose rickets on skeletons, we use the list of macroscopic, radiological and histological features proposed by Brickley & Ives (2008: 103-108).
3. Residual rickets - Term used to describe the observation of some of the effects of rickets on an adult individual who seems to be healed from the condition at the moment of his death. According to Brickley et al. (2010), those observations can be expressed with a certain range of variation, but often implicate a number of bones. The most common changes are tibiae with medial bending, femurs with anterior bending and remnants of bony ridge on the anterior aspect of femurs. Pattern of residual rickets is similar to the pattern of observed deformities in children's rickets. To diagnose residual rickets on skeletons, we use the list of macroscopic and radiological features proposed by Brickley & Ives (2008: 110-112).
4. Health - We used the term health as a state of physical, mental and social well-being. With that said, it should be noted that the requirements for an individual to feel healthy can vary greatly between cultures and time periods. To estimate past health is quite a challenge, as disrupting factors do not always leave traces on the skeleton.
5. Comorbidity - Presence of more than one disease or disorder occurring at the same time in one individual. The two (or more) conditions can co-exist, but be independent from one another or be related to a primary condition.

6. **Status** - We use the term in a socio-economical perspective: It would refer to the place or position of an individual or a group relative to another. It would usually refer to socio-economic position or social status of an individual within its group or population.

**The Rachitic Tooth: The Use of Radiographs as a Screening Technique.** Lori D'Ortenzio, Isabelle Ribot, Benoit Bertrand, Bonnie Kahlon, Emmy Bocaage, Emeline Raguin, Annabelle Schattmann & Megan Brickley

Dental literature suggests that vitamin D deficiency can alter the morphology of the pulp chamber in radiographically detectable ways. This study investigates if such changes can be seen in the permanent molars of archaeological individuals. Three modern individuals with medical and dental records established that changes in the pulp chamber could be observed in those with past deficiency (n=2/3). To test the utility of this technique, individuals with clear skeletal evidence of rickets from St. Matthews, Quebec (n=1) and St. Jacques, France (n=4), and those with slight skeletal indicators from Bastion des Ursulines, Quebec (n=6) were analysed. Results showed that 5/5 individuals with clear skeletal evidence of past deficiency and 5/6 with slight skeletal indicators of deficiency displayed constricted and/or misshapen pulp horns.

The exact mechanism for morphological changes in the pulp chamber are not fully understood, but are probably linked to severity of deficiency. To determine how many individuals would be missed by radiological examination, histological assessment was undertaken on individuals lacking both skeletal and radiological evidence of deficiency from Saint-Antoine (n=6) and Pointe-aux-Trembles (n=4), Quebec. Forty percent (4/10) showed histological evidence of slight deficiency, through the presence of interglobular dentin (IGD). Many individuals who have rickets do not show clear skeletal changes as adults and assessment of bowing deformity is difficult in such cases. Results from our investigation suggest that radiograph assessment of teeth could be used as a screening method to elucidate patterns of deficiency in past communities and potentially select individuals for histological or microCT assessment.

Definitions provided:

1. **Vitamin D deficiency** - A low concentration of vitamin D that can cause pathological changes in the skeleton. A prolonged lack of vitamin D affects the absorption of calcium and phosphorous in the intestines resulting in mineralisation defects in bone and teeth.
2. **Rickets** - Childhood condition caused by vitamin D deficiency, characterized by lack of bone mineralisation resulting in bowing deformities.
3. **Osteomalacia** - Vitamin D deficiency that occurs in adulthood, which can result in softening of the bones.
4. **Residual rickets** - Evidence of healed childhood vitamin D deficiency detectable in the adult skeleton.
5. **Interglobular dentin (IGD)** - Conditions that disrupt vitamin D, calcium, and phosphate pathways cause systemic mineralisation defects in teeth known as interglobular dentin (IGD), which is observed as clear bands of bubble-like spaces that follow incremental lines within the dentin matrix.
6. **Pulp chamber** - The dental pulp chamber is localised within dentin of the tooth and contains cells that provide nutritive, sensory, and defensive functions to preserve the vitality of the tooth.

**Vitamin D deficiency in St-Etienne de Toulouse, France: Investigations using Micro-CT.** Bonnie Kahlon, Benoit Bertrand, Antony Colombo, H  l  ne Coqueugnot, Chris Kn  sel, Lori D'Ortenzio & Megan Brickley

Vitamin D deficiency is a product of biophysical and biocultural factors; both are important in determining levels of vitamin D deficiency. Recent work on past communities suggests vitamin D deficiency was more widespread than previously thought; as in the current community urban living and cultural factors could lead to deficiency in those living at low latitudes.

This investigation used a newly developed x-ray screening technique (D'Ortenzio et al. 2017) to select individuals for micro-CT analysis. The individuals analysed lived in the southern French town of Toulouse (43°N) and died between the 9th and 12th centuries A.D. Nineteen individuals that had at least one permanent molar were selected and dental x-rays obtained. Five individuals showed radiological changes consistent with deficiency and these five and three individuals with no changes were selected for micro-CT analysis at 11µm.

Micro-CT analysis showed evidence of interglobular dentine (IGD) mineralisation defects, in four of the five individuals with two having multiple episodes. Examination of the skeletons showed changes consistent with healed rickets in one of these individuals.

Histological assessment of SQ15 who showed x-ray changes, but no evidence IGD using micro-CT, demonstrated that slight IGD was present. IGD was also identified in one of the individuals with no radiological evidence of deficiency. Toulouse was an important regional centre at the end of the 9th century, but conflict in the 10th century brought instability for inhabitants. Our results indicate that socio-cultural practices in Toulouse were such that even at this southerly location vitamin D deficiency was present.

D'Ortenzio L, Ribot I, Bertrand B, Kahlon B, Bocaeye E, Raguin E, Schattmann A, Brickley M. 2017. The Rachitic Tooth: The Use of Radiographs as a screening technique. Poster Presented at the PPA North American Meeting, New Orleans.

Definitions provided:

1. Vitamin D deficiency - Traditionally, vitamin D has been associated primarily with bone health, and it is well understood that vitamin D deficiency leads to rickets in children and osteomalacia and osteoporosis in adults
2. Rickets - A childhood disease that causes a softening of the bones, potentially leading to fractures and deformity. A lack of vitamin D is the prime cause of rickets.
3. Biophysical - Geographical latitude, skin pigmentation, and bioavailability of vitamin D in food sources – and cultural factors that determine individual and population risk such as infant and child feeding practices and behaviours that affect exposure to sunlight.
4. Interglobular dentin (IGD) - Areas of unmineralized or hypomineralized dentin where globular zones of mineralization (calcospherites) have failed to fuse into a homogenous mass within the mature dentin. Interglobular dentin is most frequently seen in the circumpulpal dentin because this irregularity of the dentin is a defect of mineralization and not of matrix formation, the normal architectural pattern of the tubules remains unchanged and they run uninterrupted through the interglobular areas.
5. Pulp chamber - The space in a tooth bounded by the dentin and containing the dental pulp. The portion of the cavity within the crown of the tooth is the pulp chamber; the portion within the root is the pulp canal or root canal.
6. Biocultural Approach - An integration of biology and the many facets of culture, including technology and social behavior.

### **Radiographically recognizable? An investigation into the appearance of osteomalacic pseudofractures.** Emma Jennings, Jo Buckberry & Megan Brickley

Osteomalacia is a type of metabolic bone disease caused by vitamin D deficiency. A deficiency in vitamin D causes defects in the mineralization of osteoid, which overtime leads to weakened bone. In adults, pseudofractures, small, linear cracks in the cortex of the bone, surrounded by irregular, spiculated new bone, are a key feature of osteomalacia.

Radiography is frequently used to definitively diagnose pseudofractures, both clinically and in paleopathology, but little research has been done to determine whether pseudofractures appear similar to

fractures caused by trauma, and in what ways they differ. A radiographic study of the characteristics of pseudofractures was performed on five individuals with clear skeletal features of osteomalacia from archaeological sites in Canada and the United Kingdom dating to the medieval period and the 19th century. The radiographic features of the pseudofractures were compared with healing trauma-related fractures. Preliminary results reveal key differences between pseudofractures and trauma-related fractures. Most surprising is the finding that pseudofractures may not always be visible radiographically, as the new bone formation is too poor a quality to appear radiographically dense like a true fracture callus.

This research has interesting implications for the diagnosis of pseudofractures, both paleopathologically and clinically. Pseudofractures cause ongoing discomfort, so accurate identification is critical for paleopathological work that aims to understand experiences of past individuals with vitamin D deficiency. Full recognition of pseudofractures are required to understand the demographics who were most vulnerable in the past, and the corresponding social and cultural reasons why this may have been so.

Definitions provided:

1. Vitamin D Deficiency - A type of metabolic bone disease resulting from insufficient amounts of vitamin D. Vitamin D deficiency can result in rickets in children, and osteomalacia in adults.
2. Osteomalacia - A type of metabolic bone disease resulting from vitamin D deficiency. It is characterized by defects in the mineralization of osteoid, leading to weakened bone.
3. Nutrient deficiency/ Nutritional deficiencies - In the context of vitamin D deficiency, a deficiency resulting from lack of sunlight or adequate diet, as opposed to a deficiency that is acquired or heritable.
4. Pseudofractures - Cracks in the cortex of bone that are a result of stresses on poorly mineralized bone. These may eventually result in a complete fracture: a hallmark of osteomalacia.

### **The relationship between vitamin D deficiency and leprosy in two English medieval populations.**

Sofia-Anna Papadopoulou & Jo Buckberry

Vitamin D is essential for maintaining a normal immune system, and an insufficiency could have a major effect in the resistance of an individual to invading pathogens. Clinical studies have shown that individuals with Vitamin D deficiency may be more at risk from tuberculosis, but is this pattern observed for other infections? Leprosy is a mycobacterial disease that is manifest on the bones, and is commonly studied in archaeological contexts. Like TB, it is a disease of the poor, and is more severe in individuals with low resistance to the pathogen; however its relationship with Vitamin D deficiency is unknown. The prevalence rates of Vitamin D deficiency (residual rickets and osteomalacia) were compared for adults in two medieval populations: adults with skeletal evidence of lepromatous leprosy from the leprosarium of St James and Mary Magdalene in Chichester (n=62) and adults from the non-leprosy population found in Box Lane, Pontefract (n=52), both in England. Macroscopic analysis identified one probable case of residual rickets Chichester. Two possible cases of osteomalacia, one at each site, were identified, but taphonomic change could not be ruled out in either case. No statistically significant relationship was found between leprosy and Vitamin D deficiency. Analysis of childhood stress markers (cribra orbitalia and enamel hypoplasia) revealed a significant relationship between enamel hypoplasia and leprosy ( $\chi^2=9.832$ ,  $p=0.002$  for canines;  $\chi^2=5.004$ ,  $p=0.025$  for central incisors), suggesting poor childhood health may have predisposed individuals to leprosy. Further study with larger sample sizes is recommended.

Definitions provided:

1. Vitamin D deficiency - Vitamin D is a vital pro-hormone metabolized by the body, and it is provided both in the diet and through sunlight exposure. The deficiency is produced by low levels of vitamin D, causing inadequate mineralization of osteoid. This leads to problematic formation and

development of the bones evident in pathological conditions such as rickets and osteomalacia. It is not fatal.

2. Rickets - A disease of infancy and childhood caused by deficiency of effective vitamin D. In the clinical literature rickets specifically refers to the disruptions in mineralization of the endochondral bone, and therefore it relates specifically to disruptions at the growth plate. In addition to the effects on bone growth, the inadequate maintenance of existing bone tissue leads to deformation of skeletal elements under mechanical forces and bowing of the long bones.
3. Osteomalacia - The condition during which an individual suffers from vitamin D deficiency and presents the pertinent signs mainly during adulthood, an approach that refers to palaeopathological convention. This specification is important, as the term in the clinical literature is usually applied to describe changes in both adults and juveniles. It is a metabolic condition that leads to the replacement of mineralized osteoid with non-mineralized osteoid during normal bone remodeling, mainly causing pseudofractures that tend to become osteomalacic fractures.
4. Residual rickets - This is the condition observed when the individual affected by rickets survives and reaches adulthood. The main remaining skeletal change is the residual bowing of the long bones (predominantly on the lower limbs).
5. Nutrient deficiency/ Nutritional deficiencies - This is a deficiency caused by inadequate absorption of nutrients from the body, and it is primarily triggered because of dietary reasons.
6. Pseudofractures - The small, linear fractures often surrounded by irregular callus observed in areas of poorly mineralized bone when affected by stresses. They are a diagnostic feature of osteomalacia.
7. Comorbidity - The existence of two (or more) pathological conditions simultaneously in an individual. These conditions might be connected, and contribute to the development of each other.
8. Taphonomic change - The damage affecting the skeletal elements after the burial of the individual. The term usually refers to fragmentation and damage on the surface of the bones, as well as missing elements of the skeleton.
9. Leprosy - Leprosy is a chronic mycobacterial disease (predominantly *Mycobacterium leprae*) that affects the peripheral nervous system, the skin and certain other tissues. It has been identified in archaeological as well as present populations.
10. Vitamin C deficiency - Deficiency caused by inadequate dietary consumption of vitamin C, leading to problems in the normal function of the immune system and collagen formation. The pathological condition resulting from the deficiency is scurvy, which was fatal when left untreated in the past.
11. Cribra orbitalia - Presented as thickening of the bone of the orbital roof with a porotic appearance on the surface. It is one of the most commonly found pathological conditions observed in skeletal remains found in an archaeological context, and it is indicative of general stress.
12. Enamel hypoplasia - In palaeopathology is qualified as a stress marker (a condition indicative of physiological stress) that affects the enamel matrix composition, and it manifests in the form of lines, pits or grooves on the enamel surfaces of the buccal portion of the dentition. It is an indicator of systematic growth disturbances during childhood surviving throughout adulthood.

### **The Art of Diagnosing Rickets: a Test Against a Subadult Portuguese Sample in the Scheuer Collection.** Jennifer Austen & Craig Cunningham

Current assessment of vitamin D deficiency in the archaeological record has proved difficult at best. Although this is a more definitive diagnosis in adult material, the identification of rickets in subadults is often uncertain, particularly if limb bowing is absent. The use of large subadult osteological collections combats these difficulties in palaeopathology; the capacity for a large subadult sample size allows easy performance of health assessment in younger age groups. As such, the Scheuer Collection, a large juvenile osteology collection at the University of Dundee, offers a variety of both documented and undocumented subadult material. Utilizing gross macroscopic analysis in the examination of 19

undocumented archaeological subadults from the collection, this project assessed the practicality of this method in the assessment of health. The presence of rickets in relation to other pathological conditions was difficult to determine; as such, only three potential cases could be identified. This is a prime example of the problems facing palaeopathologists today, in part due to the production of nonspecific indicators and the lack of bowing in the limbs in early cases of rickets (Brickley and Ives 2008). These macroscopic, nonspecific indicators are often similarly expressed in other conditions such as scurvy and tuberculosis, and even normal growth (Lewis 2007). Based on information gathered from gross macroscopic analysis, this study reaffirmed the difficulty in diagnosing pathological conditions such as rickets with absolute certainty, and confirms the need for more specific diagnostic criteria, should bowing of the limbs be absent.

Definitions provided:

1. Vitamin D deficiency - When the body has an inadequate supply of vitamin D as a result of lack of exposure to UV rays.
2. Rickets - A form of vitamin D deficiency primarily affecting children from 2 months to 6 years, whereby the deficiency primarily affects mineralization during growth.
3. Healed rickets - When the vitamin D deficiency is resolved long enough for the body to correct (in osteological contexts remodel) any lesions or pathological features produced as a result from the deficiency.
4. Health - The state of physical and mental wellbeing of the individual or population.
5. Nonspecific indicators - Pathological lesions that are associated with multiple conditions (not exclusive to one sole condition).
6. Nutrient deficiency/ Nutritional deficiencies - Where the body lacks the required intake of a nutrient essential for normal body tissues and functions.
7. Disease - Any pathological condition physically affecting the body.
8. Healed/healing- The process in which the body is resolving any pathological conditions that is affecting it.
9. Taphonomic change - Any change to the body postmortem caused by external factors (i.e. environment).
10. Sex - The biological status of an individual based on X and Y chromosomes and secondary sex characteristics.

### **Section 3 Podium Presentations (11:00 -12:45pm):**

#### **Vitamin D a Direct Window on Past Lives: Research Developments in Paleopathology**

**Chair: Susan Pfeiffer**

**11:00 Documentary sources on the early history of vitamin D deficiency disease.** Simon Mays

The presentation will focus on the contribution that historic sources can make to our understanding of vitamin D deficiency disease (rickets, osteomalacia) in the past. Evidence dating from the 2nd – 19th century AD will be considered, but the prime focus will be on 17th-19th centuries AD. Sources will be evaluated critically for the light they can shed on aspects such as the epidemiological patterning in vitamin D deficiency, the health impacts of rickets /osteomalacia, and earlier ideas as to the causes of rickets / osteomalacia. Consideration will also be given to the interface between historic sources and palaeopathology, in particular the extent to which historic sources may be used to generate hypotheses amenable to testing using palaeopathological evidence.

11:15 **Vitamin D deficiency across the Western Roman Empire.** Megan Brickley, Michele George, Simon Mays & Tracy Prowse

The medical writings of Soranus of Ephesus and Galen (both 2nd century C.E.), describe pathological changes in children that are consistent with rickets, but the extent of vitamin D deficiency in the Roman Empire has not previously been systematically pursued. This study set out to investigate vitamin D deficiency using data gathered from 3530 individuals from 15 settlements located between 37°N - 53°N. Sites ranged from rural estates to major urban centers. As expected the highest prevalence was found in juveniles 5.3% (63/1199) with active and healed cases present at most sites, followed by adults with evidence of a childhood episode of deficiency 2% (50/2331), and lowest levels seen for active cases of deficiency in adults 0.6% (15/2331). If consideration is given to skeletal preservation, and individuals that lack the key elements required for a diagnosis are removed, rates of deficiency rise to 9.7%, 2.5% and 0.7% respectively. Data gathered demonstrate that vitamin D deficiency was far more widespread than anticipated being found across the Roman Empire. While latitude is clearly important; the highest levels found in the most northern site (Ancaster in the UK), settlement size and levels of social complexity also play a role. Relatively high levels of vitamin D deficiency were found at Isola Sacra (Italy), and Barcino (Spain), both mid-size port cities located closer to the equator. Through the integration of all forms of evidence available, this project offers new insights into biocultural interactions responsible for the presence of vitamin D deficiency.

Definitions provided:

1. Vitamin D deficiency - Used in reference to Individuals with levels of vitamin D sufficiently low to produce the skeletal changes termed rickets and osteomalacia. Further work is required but it is likely that this will involve serum 25(OH)D levels <15 nmol/L.
2. Rickets - Terminology commonly employed in paleopathology will be employed and rickets will be used to describe skeletal lesions produced by vitamin D deficiency in individuals under approximately 19 years old at death.
3. Osteomalacia - Terminology commonly employed in paleopathology will be employed and osteomalacia will be used to describe skeletal lesions produced by vitamin D deficiency in individuals over approximately 19 years old at death.
4. Healed rickets - Will be used to describe individuals of any age that have lesions indicative of rickets that was not active at the time of death.
5. Pseudofractures - Fractures that occur due to a buildup of osteoid during life.
6. Taphonomic change - All changes (apart from those caused by fire) that occur to mineralized tissues following the death of an organism.
7. Sex - Biological sex (either male or female).
8. Biophysical - Geographical latitude, skin pigmentation, and bioavailability of vitamin D in food sources – and cultural factors that determine individual and population risk such as infant and child feeding practices and behaviours that affect exposure to sunlight.

11:30 **Gender-related risk of vitamin D deficiency development in a Dutch post-medieval farming community.** Barbara Veselka, Lida van der Merwe, Menno Hoogland & Andrea Waters-Rist

Vitamin D is obtained from sunlight and diet, and attaining sufficient amounts is affected by several factors that vary within and between populations. Inadequate levels in childhood can be evident in adults, called residual rickets, via remnant bending deformities of the lower limb. Limited research has explored the impact of sociocultural factors, such as division in activities, on vitamin D levels, especially in rural and small urban Dutch populations. For this paper, five

post-Medieval skeletal collections from different parts of the Netherlands with varying population sizes are analysed: Gouda (n = 46), Roosendaal (n = 45), Silvolde (n = 20), Hattem (n = 30), and Beemster (n = 200). Residual rickets prevalence ranges from 8.7% in Gouda to 14.7% in Beemster and there is a different distribution of affected individuals among the samples. Since none of these populations were highly industrialised communities, typical factors, such as narrow architecture, overcrowding, and air pollution, are unlikely to have been at play in the development of vitamin D deficiency. Rather sociocultural habits are postulated to have contributed to childhood vitamin D deficiency. This is seen in (a) Gouda, where the majority of a high status family showed residual rickets and (b) Beemster, a rural population where women were at a higher risk of developing vitamin D deficiency most likely due to a gender related division in activities. This paper emphasises the need to research small urban and rural populations to enhance our understanding of the sociocultural factors that affect vitamin D levels.

Definitions provided:

1. Osteomalacia - Active vitamin D deficiency in adults.
2. Residual rickets - Remnant lesions of non-adult vitamin D deficiency that is still visible in the skeleton. This may be in the adolescent and adult skeleton.

**11:45 Rare paleopathological insights into vitamin D deficiency rickets, co-occurring illnesses and documented cause of death in mid-19<sup>th</sup> century London.** Rachel Ives

This is the first archaeological study to compare documented causes of illness and death with the skeletal manifestations of vitamin D deficiency rickets in order to better understand disease co-occurrence and frailty in the past.

Vitamin D deficiency rickets was recorded in a large series (n.1033) of low socio-economic status burials excavated from Bethnal Green, London, UK. The burials are tightly dated between AD 1840 and 1855, after the civil registration of births and deaths. Skeletal indicators of rickets were recorded using the criteria outlined in Ortner and Mays (1998), Mays et al. (2006) and Brickley and Ives (2008) and cases were classified by disease stage; active, healing, healed.

A high percentage of juveniles were found with skeletal manifestations of vitamin D deficiency rickets (21.4%, 138/642) and 26% of children with rickets had a documented cause of death. Deaths were frequently associated with respiratory infections and specific childhood illnesses, such as measles, as well as non-specific conditions including hydrocephalus and convulsions. No deaths were documented as due to rickets despite contemporary use of the term in the London Bills of Mortality.

The likely implications of the health associations and the manifestations of rickets are discussed and the integrated analysis of historical sources and paleopathological evidence is critically contextualized in this study. This combined analysis presents new insights into the lives of this socially disadvantaged group and demonstrates the high disease burden carried by children from poor urban families in the mid-19th century.

Definitions provided:

1. Vitamin D deficiency - A deficient amount of the active form of vitamin D (di-hydroxyvitamin D, 1,25(OH)<sub>2</sub>D<sub>3</sub>) that detrimentally impacts the normal functions of vitamin D in the body. In this context, vitamin D deficiency denotes a broad level of deficiency at which the skeleton is affected by the lack of active vitamin D. This term is not used to specify the physiological threshold at which deficiency occurs. There is a gradient in the threshold of adequate vitamin D amounts and level of deficiency that varies across populations groups and is not completely defined in the modern population. Used only to refer to the estimated vitamin D status based on skeletal manifestations.
2. Vitamin D insufficiency - A lower than adequate level of the active form of vitamin D (di-hydroxyvitamin D, 1,25(OH)<sub>2</sub>D<sub>3</sub>) that may limit some normal physiological functions and may put an

individual at risk of developing a deficiency. It is not clear if insufficient levels of active vitamin D can lead to skeletal changes. Used only to refer to the estimated vitamin D status based on skeletal manifestations.

3. Vitamin D sufficiency - An adequate amount of the active form of vitamin D (di-hydroxyvitamin D, 1,25(OH)<sub>2</sub>D<sub>3</sub>) required for the normal function of vitamin D in the body. It is assumed that sufficient amounts of vitamin D were present in the skeletal remains of individuals who do not have manifestations of active/recently active deficiency states (childhood rickets or adult osteomalacia), but this may overlook some individuals who were bordering on insufficient amounts and at risk of deficiency. Used only to refer to the estimated vitamin D status based on skeletal manifestations.
4. Rickets - Used to refer to the skeletal manifestations of vitamin D deficiency that developed during childhood (<18 years). While children with vitamin D deficiency experience cartilaginous disruption (rickets) and skeletal mineralization defects (osteomalacia), the collective term rickets is used to broadly refer to children that had experienced this deficiency during childhood.
5. Healed rickets - Used to refer to individuals in which skeletal changes indicate the residual effects of a vitamin D deficiency (e.g. long bone bending deformities), but in which there are no signs of active/recently active manifestations (e.g. no disruption to the growth plate margins; flaring, porosity, fraying, slit-strut formation, or bone surfaces; porosity, coarsening compared to solid smooth cortical bone surfaces). Used to differentiate between children with active/recently active rickets and children that have recovered from an episode of rickets.
6. Residual rickets - Used to refer to adults with residual manifestations of a vitamin D deficiency (e.g. long bone bending deformities) but without evidence of skeletal mineralization defects indicative of active/recently active deficiency (osteomalacia). Thought likely to represent skeletal changes that occurred during a period of vitamin D deficiency in childhood.
7. Nutrient deficiency/ Nutritional deficiencies - Used to refer to a suite of non-specific dietary deficiencies that are likely to impact on the nutritional status of an individual and lead to dietary deficiencies, malnutrition and/or other pathological conditions. Used where specific dietary deficiencies (e.g. vitamin C, vitamin D, calcium deficiency, iron deficiency) cannot be identified.
8. Comorbidity - Used to refer to the presence of two or more pathological conditions that were active at the same time in an individual.
9. Disease - Pathological conditions capable of detrimentally affecting an individual in terms of their normal physiological function and health.
10. Healed/healing - Skeletal manifestations that demonstrate recovery from the active disease state. In rickets, these manifestations would include recovery of the solid definition of the growth plate, remodeling removal of the frayed and slit-strut formation and re-establishment of solid smooth cortical bone surfaces. Porosity may be present linked to active remodeling activity due to compensatory mechanical remodeling in examples of long bone bending deformity.
11. Sex - The biological sex of an individual (e.g. male or female) is normally estimated in adults using sexually dimorphic key areas of the skeleton, which are not well expressed in juvenile remains. In this known-identity group, the biological sex of the sample of children was determined from their individually associated coffin plates.
12. Biocultural approach - An approach that assesses the biological and cultural interactions that may co-exist in a society/group to influence the risk of disease development.

#### 12:00 **The biosocial context of osteomalacia in the Rima Rau cave site skeletal material from the Cook Islands.** Hallie Buckley, Annie Snoddy & Sian Halcrow

The co-mingled skeletal remains of people interred in the Rima Rau burial cave on the island of Atiu, Cook Islands, Polynesia were investigated in 2012 at the request of the local community. A total of 612 skeletal elements with an MNI of 42 individuals were recorded for demographic and palaeopathological analyses. Skeletal evidence of diseases such as yaws was noted in some skeletal elements as well as possible scorbutic changes in infant and child cranial remains. Of note was a high level of traumatic

injuries (9.3% of skeletal elements). Evidence of poorly mineralized fracture calluses with non-union in some bones, femoral neck fractures, bowing deformities and osteopenia are highly suggestive of osteomalacia in a number of elements. Although vitamin D deficiency is the most common clinical cause of osteomalacia, it is also associated with chronic dietary calcium, and/or phosphorous deficiency. A nutrient rich diet and exposure to sunlight are usually more than adequate on tropical Pacific islands. In this case it seems more likely that there is some form of prolonged nutrient deficiency leading to the pathological changes in this sample. There are a number of local oral histories surrounding the identity of the people that make up this skeletal sample, one of which is that they were the slaves of the chiefs. A tentative aetiology of starvation induced osteomalacia is proposed and will be discussed within the biosocial context of the wider Pacific Islands region.

Definitions provided:

1. Vitamin D deficiency - Physiological state at which overt pathological manifestations occur. Typically serum prohormone levels <25nm/L.
2. Vitamin D insufficiency - Physiological state of deprivation above the threshold for deficiency but below the ideal. Typically serum prohormone levels of 25-50nm/L.
3. Vitamin D sufficiency - Sufficient VD hormone to support all physiological functions that require it. Typically serum prohormone levels of 50-75nm/L.
4. Disease burden - Societal “cost” of disease in terms of morbidity, mortality, and quality of life.
5. Rickets - A term describing the effects of poor osteoid mineralization on endochondral bone growth. As a disease, also includes the juvenile expressions of osteomalacia.
6. Osteomalacia - A term describing the effects of poor osteoid mineralization on the homeostasis of mature bone.
7. Healed rickets - Rickets that are no longer active, osteoid mineralization returned to normal and lesions are resolved.
8. Residual rickets - Residual deformities resulting from rickets during childhood.
9. Health - “State of complete physical, mental, and social well-being” (WHO, 1948)
10. Nonspecific indicators - Skeletal lesions which are common to a number of pathological conditions (e.g. osteopenia) but suggestive of a particular condition when present in conjunction with other lesions.
11. Nutrient deficiency/ Nutritional deficiencies - A lack of a particular nutrient resulting in overt manifestations of disease.
12. Pseudofractures - Radiolucent bands of decreased mineral density occurring in the cortex of bone.
13. Comorbidity - Co-occurrence of more than one pathological condition in an individual.
14. Disease - Any systemic pathological condition (i.e. not traumatic) with a single pathogenesis.
15. Healed/healing: healed - Total lesion resolution; healing = lesion resolution has commenced but is not completed.
16. Taphonomic change - Any change to human remains occurring after death. Includes macroscopic (e.g. PM breaks) and microscopic (e.g. degradation of DNA) changes.
17. Sex - Biological expression of sexual traits (i.e. male, female, and intersex).
18. Gender - Social expression of sexuality; sexual identity.
19. Vitamin D state/ status - Condition in terms of physiologically available active vitamin D hormone at a discrete point in time.
20. Nutrition status - Condition in terms of physiological availability of a particular nutrient at a discrete point in time.

### **12:15 Vitamin D deficiency: new perspectives under past light.** Nina Jablonski

Vitamin D is essential for human health, but getting enough vitamin D has been a challenge for many people in prehistoric and historic times. Understanding the factors influencing vitamin D status contributes greatly to the understanding of past communities at both the individual and group level. In

this paper, I will examine the challenge of vitamin D sufficiency in the evolution of anatomically modern humans, and explore how this challenge has been met through both biological and cultural mechanisms in the course of human dispersals. In this presentation, I will also explore the causes and consequences of vitamin D insufficiency resulting from rapid, long-distance migrations and urbanization over, especially, the last 3,000 years. Drawing together information from the submitted papers, I will provide clear suggestions on how investigators interested in exploring the origins of health and disease in ancient populations can gain insight into the multiple roles played by vitamin D. I will also provide information on the determinants of healthy vitamin D status in people today, and identify the populations at highest risk of vitamin D deficiency as human lifestyles become increasingly different from those of the past.

Definitions provided:

1. Hypovitaminosis D - Describes both vitamin D deficiency and insufficiency.

### **12:30 Discussion: How can we use archaeological human remains to learn more about the past?**

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#### **Special Issue of the *International Journal of Paleopathology* to be co-edited by Megan Brickley & Simon Mays with assistance from Jane Buikstra (EIC)**

Contributions are still invited for the Special Issue of the *International Journal of Paleopathology*. Papers should follow standard guidelines set out on the journal website regarding specifications and length and it will be the responsibility of authors to arrange permissions for figures. Submission of Research Articles, Technical Notes, Brief Communications and Case Studies will be considered. Papers submitted do not need to have been presented at the Symposium in New Orleans and the list and order of authors can change. Submission will be through the journal website.

<https://www.journals.elsevier.com/international-journal-of-paleopathology/>

Please contact Megan Brickley (Brickley@mcmaster.ca) if you are interested in submitting a paper. Papers for the journal special issue will be due **16<sup>st</sup> August 2017**.

Current contributions to the special issue of *International Journal of Paleopathology* not being presented at the Symposium in New Orleans.

Hans de Boer<sup>1</sup> and Lida van der Merwe<sup>2</sup>. Cases of osteomalacia from the first institution for those with mental health problems in the Netherlands. Leiden University<sup>1</sup>, Amsterdam Medical Center, Amsterdam<sup>2</sup>, both the Netherlands.

Judith Littleton. Syndemics in palaeopathology? A Vitamin D case study. University of Auckland, New Zealand.