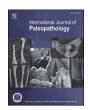
ELSEVIER

Contents lists available at ScienceDirect

International Journal of Paleopathology

journal homepage: www.elsevier.com/locate/ijpp





A macroscopic assessment of porosity and new bone formation on the inferior *pars basilaris*: Normal growth or an indicator of scurvy?

Jack Eggington a,b,*, Rebecca Pitt , Claire Hodson c,c

- a Department of Archaeology, University of Reading, UK
- ^b School of History, Archaeology and Religion, Cardiff University, UK
- ^c Department of Archaeology, Durham University, UK

ARTICLE INFO

Keywords: Scorbutic haemorrhaging Infant Scurvy Microporosity Childhood growth

ABSTRACT

Objectives: This research aims to determine the aetiology of porosity and subperiosteal new bone formation on the inferior surface of the *pars basilaris*.

Materials: A total of 199 non-adult individuals aged 36 weeks gestation to 3.5 years, from a total of 12 archaeological sites throughout the UK, including Iron Age (n=43), Roman (n=12), and post-medieval (n=145) sites, with a preserved *pars basilaris*.

Methods: The pars basilaris was divided into six segments, with porosity (micro and macro) and subperiosteal new bone formation recorded on the inferior surface in scorbutic and non-scorbutic individuals. Scurvy was diagnosed using criteria from the palaeopathological literature that was developed using a biological approach.

Results: There was no statistically significant difference in microporosity between scorbutic and non-scorbutic

Results: There was no statistically significant difference in microporosity between scorbutic and non-scorbutic individuals in four out of the six segments analysed. There was a significant negative correlation between age and microporosity in non-scorbutic and scorbutic individuals. A significant difference in subperiosteal new bone formation was observed between scorbutic and non-scorbutic individuals.

 ${\it Conclusions:}$ Microporosity on the inferior pars basilaris should not be considered among the suite of lesions included in the macroscopic assessment of scurvy in non-adult skeletal remains (less than 3.5 years).

Significance: This study highlights the risk of over diagnosing scurvy in past populations.

Limitations: It is difficult to distinguish between physiological (normal) and pathological (abnormal) bone changes in the skeleton of individuals less than one year of age.

Suggestions for further research: Future research should focus on the analysis of individuals over 3.5 years of age.

1. Introduction

Misdiagnosis and overdiagnosis of palaeopathological changes in non-adult skeletal remains are significant issues within bioarchaeology, particularly regarding the study of infants aged within the first year of life. These individuals often exhibit markers of rapid growth, including porous subperiosteal new bone formation (SPNB) and cortical surface porosity, which are easily mistaken for pathological lesions. As the field of palaeopathology advances, new correlations between skeletal changes and pathological conditions will be established. This has been realised with the adoption of a biological approach, which requires careful observation of lesion location and morphology, coupled with detailed integration of the biomedical literature (Mays, 2018). However,

it is paramount that bioarchaeologists are familiar with the difficulties in distinguishing physiological or 'normal' changes from those which are pathological or 'abnormal' on the immature skeleton. Consequently, differential diagnoses of SPNB and porosity, including consideration of whether these are physiological changes, should be more readily adopted within non-adult research. Interest in the study of scorbutic lesions, caused by vitamin C deficiency, has increased within the 21st century, leading to the proposition of new diagnostic and suggestive criteria (Snoddy et al. 2018; Geber and Murphy, 2012; Simonit et al. 2023; Brickley and Morgan, 2023; Brown and Ortner, 2011). Recently, SPNB and microporosity on the inferior surface of the pars basilaris have been suggested as additional criteria for consideration (Moore and Koon, 2017; Snoddy et al. 2018), despite the limited understanding of the

E-mail address: j.eggington@pgr.reading.ac.uk (J. Eggington).

^{*} Correspondence to: Department of Archaeology, School of Human and Environmental Sciences,. University of Reading, Whiteknights, PO Box 227, Reading RG6 6AB, UK.

age-related and physiological changes this anatomical area undergoes. To advance non-adult palaeopathology, it is vital that bioarchaeologists define and distinguish between physiological and pathological skeletal changes and development, especially when considering fetal, perinatal, and infant individuals under one year of age.

1.1. Pars basilaris anatomy

The pars basilaris, also known as the basilar part of the occipital bone, is a small, dense bone located anteriorly to the foramen magnum at the base of the cranial vault. It fuses with the pars lateralis posteriorly between the ages of five and seven years, and anteriorly to the body of the sphenoid bone between 11 and 16 years in females, or 13 and 18 years in males (Scheuer and Black, 2004, 79). Two deep neck muscles attach to the inferior surface (Fig. 1), aiding flexion of the head and neck: the rectus capitis anterior muscle and longus capitis muscle. The rectus capitis anterior inserts on a crest of the bone, with the longus capitis inserting on the posteromedial portion (Krmpotić-Nemanić et al., 2006). Both muscles originate from the anterior surface of the cervical vertebrae and are supplied by arteries from that region (Sakamoto, 2012). Additionally, a ridged fibrous band of tissue attaches on the anteromedial portion of the pars basilaris at the tuberculum pharyngeum (Fig. 1). This is known as the pharyngeal raphe, serving as the origin and insertion for several muscles to aid with neck movement, including the inferior pharyngeal constrictor muscle, the middle pharyngeal constrictor muscle, and the pharyngeal constrictor muscle (Shimada and Gasser, 1988), which are supplied by the ascending pharyngeal artery.

Prominent crests situated at both sides of the tuberculum pharyngeum are common on the non-adult *pars basilaris*, and have been recorded in individuals up to five years of age (Krmpotić-Nemanić et al., 2006). A semilunar or triangular fossa for the attachment of the *longus capitis* muscle is also noted, with potential slight elevation of the area in some cases (Poirier et al., 1892). However, the anterior crest where the *rectus capitis anterior* muscle attaches is not well developed in infants (defined as an individual under the age of one year), as the tone of this muscle requires time to change and develop (Krmpotić-Nemanić et al., 2006); thus, morphology of the *pars basilaris* naturally alters as neck movement develops.

Consideration for how the *pars basilaris* changes in response to neck muscle development is important for understanding expected morphology. Cervical muscles that enable movement of the head are relatively weak at birth, meaning that the head of the newborn must be

fully supported for the first month of life, or it will flop (Osagie and Givler, 2022). Beyond the first month, muscles become strong enough to briefly lift the head, but it is not until three to four months old that minimal control is achieved. It will take until five to six months for the neck muscles to develop enough to fully hold the head up (Javadifar et al., 2016; Lier, 1988; Öhman and Beckung, 2008; Pineda et al., 2016). It is worth acknowledging that an infant has limited ability to move its head within the first five to six months of life, and this is reflected in the limited bony landmarks present on the *pars basilaris* at this early stage.

1.2. Vitamin C deficiency (scurvy)

Scurvy is a chronic nutritional deficiency caused by prolonged lack of vitamin C (ascorbic acid) in the diet. Metabolism of vitamin C is required to maintain healthy collagen production, in addition to formation of connective tissues in the skin, blood vessels, cartilage and osteoid. Consequently, a deficiency can disrupt the collagen matrix, weaken blood vessels, and compromise the immune system (Armelagos et al., 2014; Brickley et al., 2020; Crandall and Klaus, 2014). The risk of haemorrhage is thus far greater in scorbutic individuals. Even the smallest of muscular activities, such as eye movement, can damage connective membranes and cause bleeding into neighbouring tissues, resulting in the presence of blood outside of the circulatory system and eliciting periosteal inflammation (Rana et al., 2009; Brickley and Mays, 2019). This inflammation is a consequence of blood pooling beneath the periosteum, forcing it to elevate from the cortical surface of the bone, subsequently stimulating the proliferation of periosteal new bone in response to both physiological stress and extravasated blood (Golriz et al., 2017; Rana et al., 2009; Thompson et al., 2022; Morrone et al., 2021; Brickley & Mays, 2019; Snoddy et al., 2018). Bleeding as a result of muscular activity can also cause musculoskeletal pain, degeneration of connective tissues, and hemarthrosis (Brickley et al., 2020).

Humans cannot manufacture vitamin C endogenously and are therefore solely reliant on dietary sources to obtain the required quantities (Crawford, 1988). A critical intake of vitamin C to prevent scurvy can be as low as 10 mg per day (Basu and Schorah, 1982). Current medical recommendations suggest a higher dosage of 40–50 mg for non-adults, to not only prevent deficiency, but also because of vitamin C's physiological and antioxidant benefits (Monsen, 2000; Jacob and Sotoudeh, 2002).

Diagnosis of scurvy can directly determine chronic nutritional deficiency in the skeleton and enable valuable interpretations on

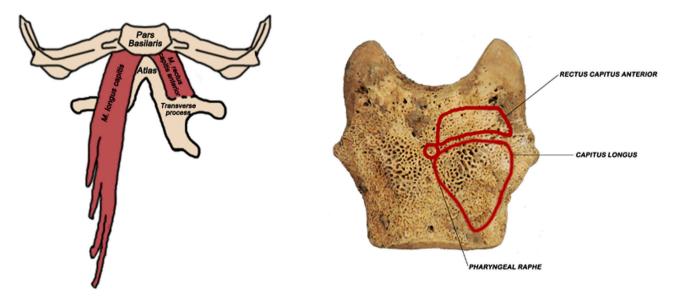


Fig. 1. Muscles attachments on the inferior surface of the pars basilaris. The pars basilaris shown represents the normal morphology of this bone in a perinate (38–42 gestational weeks). The red lines indicate where the muscle attachments and soft tissue structures are located.

communities, including feeding practices (Nicholls et al., 2020), resource availability (Halcrow et al., 2014; Geber and Murphy, 2012; Morrone et al., 2021), socioeconomic status (Newman and Gowland, 2017), and rural vs urban dynamics (Rohnbogner and Lewis, 2017). Prolonged absence of vitamin C for six to ten months can result in scorbutic changes on the non-adult skeleton (Brickley et al., 2020; Crandall and Klaus, 2014; Snoddy et al., 2018), although it has been suggested that manifestations of scurvy can occur in as little as two to four months of inadequate intake (Brickley and Ives, 2006; Snoddy et al., 2018; Hodges et al., 1969). Exclusive lactation in the first six months of life theoretically provides sufficient nourishment for the developing infant (Pérez-Escamilla et al., 2023), so manifestations of scurvy in early life could suggest poor maternal nutritional health, early weaning, or an insufficient weaning diet. Extreme maternal nutritional deficiency during pregnancy can result in congenital scurvy, with osteological changes manifesting in-utero and early postpartum life. This has been observed clinically in neonates within their first month of life (Hirsch et al., 1976), and is increasingly being explored in bioarchaeological contexts (Snoddy et al., 2017; Bourbou, 2018; Morrone et al., 2021).

Late 19th century autopsy reports of diagnosed scurvy cases in nonadults have largely discussed subperiosteal haemorrhaging of long bones and the intracranium, with blood clots being observed across the surface of the brain (Barlow, 1883; Sutherland, 1894). Additionally, Barlow (1883) noted swelling to the periosteum of the scapula and associated blood clots, with one case displaying subperiosteal new bone formation on the anterior surface of the scapula body. Despite this, clinical studies have paid little attention to the underlying bone. Approximately 80% of clinical scorbutic cases develop musculoskeletal alterations (Fain, 2005; Smith et al. 2011; Stark, 2014), which theoretically allows for scurvy to be identified in the skeleton. Through consideration of lesion location and detailed review of the biomedical literature (the biological approach), Ortner and colleagues (Ortner et al. 2001; Ortner and Ericksen, 1997) were able to develop a framework for scurvy diagnosis, and new skeletal lesions have continued to be proposed as part of this suite of features associated with vitamin C deficiency (Snoddy et al. 2018; Geber and Murphy, 2012; Simonit et al. 2023; Brickley and Morgan, 2023; (Brown and Ortner, 2011). Common skeletal changes associated with scurvy include porotic lesions and subperiosteal new bone formation (SPNB) affecting the cranial vault, orbital walls, sphenoid bone, mandible, scapula, and long bone metaphyses and diaphyses (Gulko et al., 2015; Weinstein et al., 2001; Ortner et al. 2001; Ortner and Ericksen, 1997; Snoddy et al. 2018; Brickley et al. 2020). These changes are thought to be the result of an inflammatory response as the periosteum is elevated from the bone surface due to haemorrhaging of blood vessels at muscle origin or insertion sites, with the physiological disturbance to the periosteum causing it to react by proliferating new bone (Ortner and Ericksen, 1997; Ortner et al., 2001; Snoddy et al., 2018). These macroscopic skeletal lesions associated with scurvy have been widely observed archaeologically, but they are not pathognomonic, and several differential diagnoses need to be considered (Brickley et al., 2020).

Moore and Koon (2017) reviewed the *pars basilaris* from 24 non-adult individuals aged between birth and 12 years from the 19th century St. Peter's Collegiate Church cemetery, Wolverhampton. A total of 11 individuals showed areas of 'abnormal' porosity and SPNB at the attachment site of the *longus capitis* muscle, nine of which belonged to individuals diagnosed with scurvy via cranial and post-cranial criteria from the palaeopathological literature (Brickley and Ives, 2006; Geber and Murphy, 2012; Ortner et al., 2001; Ortner and Ericksen, 1997, Ortner et al., 1999). Only three individuals were aged under 1.5 months, despite this being a key period of rapid development for the non-adult skeleton and thus requiring further investigation into growth-related changes. It was subsequently suggested, by applying the biological approach, that these changes on the inferior surface of the *pars basilaris* of the occipital are indicative of scorbutic haemorrhaging. As a result, these 'lesions' have been applied to perinatal and infant skeletons from

archaeological populations in Europe, Asia and South America to support the diagnosis of scurvy (Bourbou, 2018; Larentis et al., 2023; Morrone et al., 2021; Nicholls et al., 2020; Snoddy et al., 2018). The inclusion of lesions on the *pars basilaris* as a diagnostic criterion of scurvy has yet to be tested on a large sample of non-adults of various ages, both with and without other evidence for scurvy.

Further work is required to explore the correlation between porosity and age-at-death, and to define the 'normal' and 'abnormal' appearance of the *pars basilaris* (Martín et al., 2018). Fetal development and early postpartum life are characterised by rapid growth and development, with non-adults having great bone forming potential (Bisseret et al. 2015), making distinction between physiological and pathological changes complex (Lewis, 2017a; Lewis, 2017b; Bisseret et al., 2015; De Silva et al., 2003; Klaus, 2017). Consequently, failure to distinguish between 'normal' and 'abnormal' changes in the non-adult skeleton can result in inflation of suggested health insults experienced by those youngest in society, and an overall misinterpretation of population health.

2. Materials and methods

2.1. Skeletal sample

A total of 199 non-adults (36 weeks gestation to 3.5 years) from Iron Age (n=43), Roman (n=12), and post-medieval (n=145) archaeological sites throughout the UK, with a preserved *pars basilaris*, were analysed for signs of scurvy (Supplementary Information 1: Table 1). Only individuals with at least four bilaterally observable cranial or postcranial elements were included in this study.

Age estimation was determined from dental development (AlQahtani et al., 2010), diaphyseal lengths (Scheuer et al., 1980), measurement of the pars basilaris (Scheuer and MacLaughlin-Black, 1994), plus cranial and vertebral fusion (Scheuer and Black, 2000). Non-adults aged between 36 weeks gestation and 3.5 years postpartum were selected for this study to best capture those experiencing rapid physiological growth (Lewis, 2017a). Additionally, this encapsulates those most susceptible to chronic nutritional deficiency (Barlow, 1883; Snoddy et al., 2018; Brickley et al., 2020). Once age at death had been assigned, all individuals were grouped into four age cohorts: perinate/neonate as defined by 36 weeks to 1.5 months, infant as defined by 1.6 months to one-year, non-adults between 1.1 and 2.0 years and non-adults between 2.1 and 3.5 years.

2.2. Scurvy diagnosis

Multiple disease processes can cause abnormal porosity and SPNB formation on the non-adult skeleton (Klaus, 2017). These may include viral or bacterial infections (e.g. congenital syphilis), leukaemia, trauma, infantile cortical hyperostosis (ICH), and rickets (Lewis 2017a). A thorough differential diagnosis was completed to exclude other possible pathological conditions (Supplementary Information 1).

This study used a threshold system (Vlok, 2023) with weighted criteria based on the palaeopathological and clinical literature (Barlow, 1883; Jaffe, 1972; Geber and Murphy, 2012; Brickley et al., 2020) to determine a 'probable' or 'possible' scurvy diagnosis for each non-adult skeleton. Each criterion was classified as 'diagnostic' or 'suggestive' of vitamin C deficiency based on how frequently the observed pathological features occur in the palaeopathological and clinical literature (Table 1), in addition to the lesion's specificity to scurvy (Schattmann et al., 2016; Snoddy et al., 2018; Brickley et al., 2020). The terminology used to express diagnostic strength was drawn from similar recording schemes in the bioarchaeological literature (Geber and Murphy, 2012; Snoddy et al., 2018). At least three diagnostic or suggestive scurvy features were required for a probable diagnosis (Supplementary Information 1: Table 3). This system requires the presence of more pathological features compared to other studies, in which one or two features are

Table 1
Recording scheme for scurvy features; with reference to the palaeopathological and clinical literature (Barlow, 1883; Jaffe, 1972; Ortner and Ericksen, 1997; Brown and Ortner, 2011; Geber and Murphy, 2012; Crandall and Klaus, 2014; Klaus, 2017; Snoddy et al., 2018; Schattmann et al., 2016).

Bone element (s)	Lesion type	Diagnostic strength
Sphenoid: greater wing	SPNB/Porosity	Diagnostic
Maxilla: posterior aspect	SPNB/Porosity	Diagnostic
Scapula: supraspinous fossa	Porosity	Diagnostic
Scapula: infraspinous fossa	SPNB/Porosity	Diagnostic
Frontal: orbital roof	SPNB	Diagnostic
Sphenoid: lesser wings	SPNB	Suggestive
Mandible: medial coronoid process	SPNB/Porosity	Suggestive
Sphenoid: foramen rotundum	SPNB	Suggestive
Zygomatic: orbital surface	Porosity	Suggestive
Maxilla: infraorbital foramen	SPNB/ Porosity	Suggestive
Upper/Lower limbs: diaphysis	SPNB	Suggestive
Upper/Lower limbs: metaphysis	Flaring	Suggestive
Maxilla: palate	Porosity	Suggestive
Maxilla/Mandible: alveolar process	SPNB/Porosity	Suggestive
Rib	Flaring/Cupping	Suggestive
Cranial vault	SPNB/Porosity	Non-diagnostic
Ilium	Porosity	Non-diagnostic

considered sufficient for diagnosis (Buckley et al., 2014; Snoddy et al., 2018; Vlok et al., 2023), allowing for a greater degree of diagnostic confidence. All individuals who did not meet this threshold, but displayed at least two suggestive lesions, or porosity on the ectocranial surface of the greater wing of the sphenoid (often considered pathognomonic; Ortner and Ericksen, 1997), were excluded from this study. This was to minimise the risk of the control group (non-scorbutic) containing individuals with scurvy and blurring the analysis. The pars basilaris was not used to diagnose scurvy in this study.

Porosity was considered abnormal when pores were <1 mm in diameter, with vertical walls and a densely clustered appearance (Ortner and Ericksen, 1997). Porosity was recorded by location and healing stage. Porosity was considered 'active' when pores were un-remodelled with sharp margins, 'mixed' when some pores had rounded margins or were completely closed, and 'healed' when all pores were completely closed (Mensforth et al. 1978; Wei and Cooper, 2023). SPNB and porosity were only considered as a scurvy criterion when the lesions were bilateral (Snoddy et al., 2018).

SPNB was recorded across the entirety of the skeleton for all individuals assessed. Recording of SPNB was considered imperative given the common association made between SPNB and haemorrhaging within scorbutic individuals throughout the existing literature (Gulko et al., 2015; Ortner and Ericksen, 1997; Ortner et al., 2001; Snoddy et al., 2018; Weinstein et al., 2001). However, with pervading limitations of distinguishing physiological from pathological SPNB (Kwon

et al. 2002; Rothschild and Jellema, 2020; Shopfner, 1966), the ability for SPNB to provide diagnostic evidence for vitamin C deficiency remains questionable for some locations on the skeleton. As such, a grading system for SPNB was applied following Hodson's (2018) proposed methodology (Table 2). Though this grading system is intended for more general palaeopathological analysis of SPNB, and not solely for the assessment of vitamin C deficiency, no alternative method for attempting to categorise SPNB on non-adult individuals exists. As such, this study records all evidence of SPNB across the skeleton, regardless of aetiology, and thus uses the grading system as a suggestive tool by which to infer physiological or pathological changes.

For this assessment, each grade of SPNB has been defined (Table 2), with the location (skeletal element and aspect), type (woven or lamellar bone), and healing stage (active, mixed, or healed) also noted. Grade categories have been attributed based on margin definition, the number of layers identifiable, and the overall thickness and proliferation of the SPNB. By employing this grading system, this investigation attempts to create a more nuanced interpretation, reflecting the complexities of recording and interpreting SPNB (e.g. as discussed extensively in Weston, 2008; 2012). This grading enables the analysis to avoid a binary system of 'present' or 'absent', which has traditionally been employed (e.g. Mays, 2008; Ortner et al. 2001; Ribot and Roberts, 1996; Simonit et al. 2023). In these cases, the subjectivity and accuracy of these interpretations must be accepted, with little known about the specifics as to how pathological SPNB is being defined and when it is/is not being recorded. Though the grading method implemented here still has a level of subjectivity, it is hoped that the definitions and images provided (Table 2; Fig. 3) will aid the reproducibility of SPNB assessment and thus the resolution of our interpretations.

Given our current general inability to distinguish physiological SPNB from pathological SPNB in young, rapidly growing non-adult individuals, it is likely that SPNB is being both over-recorded and inaccurately interpreted, particularly in instances where no distinction is made between the types and levels identified. As the definition of 'Grade 1 SPNB' used here is most consistent in appearance with physiological SPNB (where SPNB is not clearly apparent, and the margins are difficult to define, typically merging with surrounding cortical bone), it was decided that all individuals with Grade 1 SPNB recorded were removed to ensure that any physiological periosteal changes were excluded from scurvy diagnosis. A score of Grade 2 or Grade 3 SPNB was considered likely pathological. This does not mean that Grade 1 changes are definitively inconsistent with pathological changes, rather that we simply cannot distinguish differences between pathological and physiological changes with this level of accuracy. Consequently, a more cautious approach was favoured by the authors.

Table 2
Grading system for microporosity, macroporosity, and SPNB on the inferior surface of the pars basilaris, recorded for each segment.

Grade				
Bone change	0	1	2	3
Microporosity	No microporosity present	Microporosity (<1 mm) covering localised area of segment	Microporosity (<1 mm) covering the entire face of segment	N <u>/</u> A
Macroporosity	No macroporosity present	Macroporosity (>1 mm) present in localised area of segment	Macroporosity (>1 mm) present over the entire face of segment	N <u>/</u> A
SPNB	No SPNB present. No signs of SPNB, no bone proliferation present. If porosity present, must not be confused with SPNB.	SPNB not clearly apparent, and margins not clearly defined from adjacent normal cortical bone. May appear as SPNB merging/amalgamating with surrounding cortical bone. No difference in colour or surface layer evident. SPNB locally isolated and appears minimally across segment. Grade 1 SPNB may be confused with porosity and normal physiological growth.	Definable area of woven or lamellar SPNB with clear boundaries and likely different colour (greyer in appearance if woven bone. SPNB is a single, clear layer atop the original cortical surface. Clear distinction between cortical bone and SPNB, with minimal remodelling at the margins showing a lack of integration between the two surfaces. SPNB may extend over a large area of the segment.	Clear, multi-layered, or thick layers of woven or lamellar SPNB resting on top of normal cortical bone. SPNB is thicker, creating an expanded and 'inflated' appearance. SPNB will likely cover a large area of the segment and have clear and well-defined margins. SPNB will also likely differentiate in colour from the surrounding cortical bone, again being greyer in colour.

2.3. Recording bone changes on the pars basilaris

The inferior pars basilaris of each individual was examined according to six segments (labelled S1-S6) (Fig. 2) to allow for precise examination of the area where the primary longus capitis muscle attaches (S3-S4). Each segment was graded according to scales for microporosity (<1 mm in size), macroporosity (>1 mm in size), and SPNB (Grades 1–3; Table 2) to observe whether changes occurred across the entire element or within localised areas. Micro and macro porosity was defined by pore size and not by the morphology or orientation of the porosity. Additionally, nutrient foramina were recorded in increments of five (i.e. 1–5) for each segment, classified as isolated pores with a non-clustered distribution that tunnel through the bone cortex. The intracranial surface of the pars basilaris is commonly pitted with nutrient foramina of varying quantity (Cunningham et al., 2016). Examples of the grading system used for microporosity and SPNB on the pars basilaris are presented in Fig. 3.

2.4. Statistical analysis

SPSS version 27 was used to perform three statistical tests. A Mann-Whitney U test was used to assess if there was a statistical difference in porosity and SPNB grade on the inferior *pars basilaris* between scorbutic and non-scorbutic individuals. Effect size was determined using the following equation:

$$r=Z/\sqrt{N}$$

Z is the standardised test statistic and N is the number of individuals analysed. Effect size was interpreted according to Cohen (1988): <0.3 was considered a small effect, 0.3–0.5 a medium effect, and >0.5 a large effect (Supplementary Information 3). The Pearson's Chi-squared was used to test for significant differences in lesion presence between *pars basilaris* segments. A Kendall's tau-b coefficient test was used to assess the correlation between age and expression of porosity on the inferior *pars basilaris*, in scorbutic and non-scorbutic individuals.

3. Results

3.1. Osteological analysis

In total, 199 individuals were analysed, with eight excluded from the study because they did not meet the criteria for the scorbutic or non-

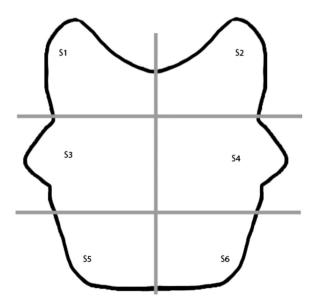


Fig. 2. The inferior surface of the *pars basilaris* divided into six segments (labelled S1-S6) to facilitate recording bone changes.

scorbutic group. The subsequent results will consider the remaining 191 individuals (Supplementary Information 2).

Scurvy (probable or possible) was identified in 11.0% (n=21) of non-adults analysed. The highest rates of scurvy were in infants (1.6 months to one year), with 20.4% (n=9) affected (Table 3). SPNB was observed in all perinates, but often displayed in a uniform layered pattern (Grade 1) indicating physiological growth, rather than a pathological response to disease. Two individuals below 1.5 months of age, from the St. James population, displayed lesions diagnostic of scurvy. Across the entire sample the most frequently observed lesions were abnormal porosity, often combined with SPNB, on the medial aspect of the coronoid process of the mandible (50.0%, n=10), and the supraspinatus fossa of the scapula (47.6%, n=10) (Supplementary Information 2).

3.2. Inter-observer error

A small inter-observer error test was performed using four inferior surfaces of the *pars basilaris* from the Redhill collection. Six observers (including the first author) were invited to score the presence or absence of microporosity, macroporosity, and SPNB on the inferior surface of the *pars basilaris* according to the method outlined in Section 2.3. All observers were postgraduate students who had a similar level of osteological experience. Agreement on the presence of microporosity (86.1%), macroporosity (89.6%), and SPNB (85.4%) was high, allowing for confidence in the method used in this study.

3.3. Bone change distribution on the pars basilaris

Microporosity was the most frequently observed change on the inferior pars basilaris (Fig. 4), with 171 individuals (89.5%) displaying porosity (Grade 1 or 2) on at least one segment (S1 to S6). Microporosity was significantly more common in S3 (83.2%, n=159) and S4 (81.2%, n=155), compared to S1, S2, S5, and S6 ($\rm X^2=6.028, d.f.=1, p=0.014$). New bone formation and macroporosity were less common. Eight individuals (4.0%) displayed new bone formation on the inferior aspect, and two individuals (1.0%) displayed macroporosity on at least one segment.

3.4. Microporosity and pathology status

When individuals were analysed in relation to pathology status, scorbutic and non-scorbutic individuals displayed a similar level of microporosity across segments S1 to S4 with no statistically significant difference. Some variation was noted, for example in relation to S3 for Grade 1 and 2 microporosity, but again, no statistical significance was identified. Grade 1 microporosity was more commonly observed in non-scorbutic individuals (76.5%, n=125) than scorbutic (47.6%, n=10). In addition, Grade 2 microporosity was higher in scorbutic non-adults (28.6%, n=6) than non-scorbutic (7.6%, n=13). A higher prevalence of microporosity was observed in S5 and S6 (76.3% for both) in scorbutic individuals, and this was determined to be significantly different when compared to the non-scorbutic sample (S5 z= -2.458, P= 0.012; S6 z=-2.004, P= 0.045) (Supplementary Information 3).

3.5. Microporosity and age-at-death

When all individuals were analysed by age, the appearance of microporosity was variable across the six segments of the inferior *pars basilaris* (Supplementary Information 3), but the prevalence was greatest in S3 and S4 for all age categories (Fig. 5). Perinates had the highest rates of microporosity across all six segments, with 100% of S3 (n=67) displaying microporosity, and 98.5% of S4 (n=66). The frequency of Grade 2 porosity was greatest in infants aged 1.6 months to one year across all segments, for both scorbutic and non-scorbutic individuals.

Using the Kendall's tau-b coefficient test, there was a significant negative correlation between age and microporosity for S3-S6 at



Fig. 3. Examples of grades 0–2 microporosity and SPNB on the inferior surface of the pars basilaris, with segments S3 and S4 highlighted in the box. Isolated nutrient foraminae are highlighted with red circles.

Table 3Demographic profile and scurvy prevalence of skeletal sample used in study.

Age	Number of individuals (N)	Percentage (%)	Scurvy prevalence (%/n)
Perinate/Neonate (36 weeks to 1.5 months)	67	35.1	3.0 (2)
Infants (1.6 months to 1 year)	44	23.0	20.4 (9)
1.1-2.0 years	57	29.8	12.3 (7)
2.1-3.5 years	23	12.0	8.7 (2)
Total	191		11.0 (21)

 $p{<}0.001$ (S3: $\tau_b=-0.324;$ S4: $\tau_b=-0.326;$ S5: $\tau_b=-0.282;$ S6: $\tau_b=-0.323)$ in the non-scorbutic individuals, indicating that as age increases microporosity prevalence decreases. A negative correlation between microporosity and age was also observed in the scorbutic children for all segments, but this was only statistically significant at confidence interval ${<}0.05$ in S4 and S6 (S4: $\tau_b={-}0.413;$ S6: $\tau_b={-}0.396)$ (Supplementary Information 3: Table 2).

3.6. New bone formation on the inferior pars basilaris

In total, eight individuals displayed SPNB on the inferior pars

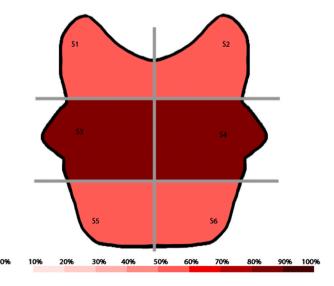


Fig. 4. Percentage prevalence of microporosity (Grades 1 and 2) in segments S1 to S6.

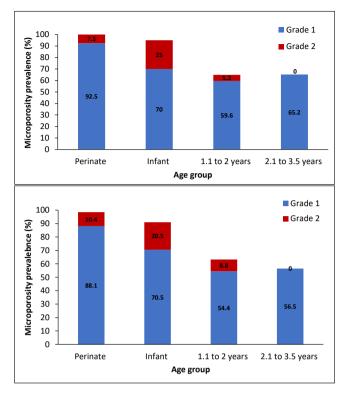


Fig. 5. Microporosity frequency in segment S3 (top) and S4 (bottom) of the inferior pars basilaris, by age.

basilaris, but only those with scurvy (n=3) displayed Grade 2 changes. A significant difference in the SPNB grade was observed between scorbutic and non-scorbutic individuals for all six segments (S1 z=3.549, P=<0.001; S2 z=2.804, P=0.005; S3 z=2.815, p=0.005; S4 z=3.257, P=0.001; P=0.001; P=0.001; P=0.001; P=0.001; P=0.001; P=0.001; S6 0.001; P=0.001; P=0.001; P=0.001; P=0.001; P=0.001; S6 0.001; P=0.001; P=0.

Most individuals displaying SPNB were aged 1.1–2 years (n=5, 62.5%). Five children displayed both SPNB and microporosity on the inferior *pars basilaris*. Only one of these individuals (a 14.5 month- old from St. James, Euston) had Grade 2 SPNB and microporosity.

4. Discussion

4.1. Microporosity on the pars basilaris: an indicator of scurvy?

A higher frequency of Grade 2 microporosity on S3 and S4 in scorbutic individuals of all ages was identified. This could indicate that some observed porosity is due to inflammation of the periosteum triggered by haemorrhaging, and thus warrants further investigation (Supplementary Information 3: Table 6). Additionally supporting this, Grade 2 microporosity was greatest in scorbutic infants aged 1.6 months to one year (40%, n=4). However, it is worth noting that non-scorbutic individuals also displayed a high frequency of Grade 2 microporosity (S3: 20.6%, n=7, S4: 14.7%, n=5), highlighting the difficulty that remains in disentangling its aetiology. Furthermore, a significant difference in microporosity between scorbutic and non-scorbutic individuals was observed on the left and right distal aspect (S5 and S6) of the pars basilaris. This anatomical position is largely absent of muscle structures so the high prevalence of microporosity (76.3% for both) indicates it is unlikely to be caused directly by scorbutic haemorrhaging in this area. Nevertheless, it cannot be ruled out that pooling of blood over the whole inferior pars basilaris could instigate an inflammatory response in anatomical locations that do not have significant muscle attachments (Barlow, 1883). Yet if this was the case, a high prevalence of microporosity would also be expected in segments S1 and S2, and this was not observed (see Section 4.2 below).

Overall, microporosity was most frequently observed on the medial inferior surface of the *pars basilaris* (segments S3 and S4) compared to the anterior or posterior aspect (segments S1, S2, S5, S6), with a statistically significant prevalence rate of 83.2% and 81.2% respectively. This corresponds to the attachment for the primary *longus capitis* muscle and the ascending pharyngeal artery which terminates at the base of the ectocranial surface of the skull, passing between muscle and bone (Moore and Koon, 2017). If the biological approach is considered, this provides the necessary anatomical conditions to proliferate an inflammatory response in cases of chronic vitamin C deficiency (Ortner and Ericksen, 1997; Mays, 2018). Additionally, the clinical literature does mention swollen neck muscles, stiffness of the neck and pain in the head that may reflect internal bleeding (Bott, 1911; Sutherland, 1894; Grewar, 1965).

However, it is unlikely that such a high proportion of children would display scorbutic changes on the *pars basilaris* without presenting other diagnostic evidence for the disease on their skull or post-cranial bones. An alternative explanation is that these changes are the result of normal bone-muscle interaction (DiGirolamo et al., 2013), as muscle develops more rapidly than bone in non-adults and has a regulatory role in enhancing bone mineralisation (Kawao and Kaji, 2015; Battafarano et al., 2020).

4.2. Microporosity on the pars basilaris: an indicator of normal growth?

A possible aetiology for the microporosity observed on the pars basilaris is normal cranial development, and this is supported by the significant correlation observed between increasing age and decreasing microporosity for both scorbutic and non-scorbutic individuals. This is particularly apparent in S3-6 for non-scorbutic individuals and S4 and S6 for scorbutic individuals. Additionally, no significant correlation was observed between microporosity and age in S1 or S2 for both scorbutic and non-scorbutic individuals. This could be related to the lack of established muscle structures on this posterior area (where the pars basilaris articulates with the partes lateralis of the occipital to form the foramen magnum) at this age range, as the rectus capitis muscle is much less developed in infants. For all segments, microporosity prevalence decreases with age and appears to plateau after the first year of life (Fig. 5). This possibly relates to the growth rate of the developing child, which decelerates rapidly in the second year of life (Ono and Kronenberg, 2018). While an absence of a significant correlation between microporosity and age in S3 and S5 for scorbutic children was observed, this may be the result of the small sample size tested (n=21). The observed correlation strength remained similar to the non-scorbutic individuals for all segments of the pars basilaris (Supplementary Information 3: Tables 2-3). It is also possible that scurvy does affect this area in some instances, such as in individuals displaying multiple scorbutic lesions, but this cannot be relied upon as a diagnostic criterion.

To the authors knowledge, no research has identified the pattern of porosity expected in normal growth of the non-adult skeleton. This would require the examination of known age individuals, with associated medical records, who did not die of a condition affecting bone remodelling. Despite this, bioarchaeological studies often refer to the porous nature of fetal and infant bone, but the current consensus regarding what is 'normal' and 'abnormal' is difficult to gauge from the literature (Snoddy et al., 2018; Brickley and Mays, 2019), and not always explicitly defined. Ortner and Ericksen (1997) defined abnormal bone porosity as localised pores that are typically less than 1 mm in diameter, penetrating the cortical bone surface. By contrast, when discussing lesions on the ectocranial greater wing of the sphenoid, porosity associated with growth or normal variation was defined by Brickley et al. (2020) as pores greater than 1 mm with a less clustered distribution and an oblique angle of entry (Brickley et al., 2020, from Fig. 6). The microporosity observed in this study is more characteristic of the former description, and yet it seems implausible that such a high prevalence of porosity (89.5%) is primarily associated with a pathological

inflammatory response. These concerns have previously been echoed by Melikian and Waldron (2003), who noted that porosity was as high as 90% in the infant cranial bones (i.e. maxilla palate) of three archaeological populations. It must be considered that in the first two years of life, the neurocranium experiences particularly rapid growth (Humphrey, 1998; Huelke, 1998), potentially contributing to the high rates of microporosity observed across the *pars basilaris* and wider cranium in both the current study and bioarchaeological literature (Snoddy et al. 2018; Vlok et al. 2023).

To date, the normal macroscopic appearance of fetal, perinate, and infant cranial bones has not been well defined. The bioarchaeological and clinical literature does offer some evidence for age-related bone porosity, but this has primarily focused on microscopic intracortical morphology and ontogeny of long bones (Welsh and Brickley, 2023; Cambra-Moo et al., 2014). Substantial cortical porosity has been noted in long bones during rapid adolescent growth (Khosla et al., 2003), with Parfitt (1994) suggesting a link between rapid bone turnover and an increase in cortical porosity. Additionally Welsh and Brickley (2023) found increased intracortical porosity in 0.5–1.9-year-olds in a medieval archaeological sample, suggesting this was the result of a rapid increase in growth velocity associated with weight bearing activities. A thorough exploration of the clinical, anatomical, and bioarchaeological literature could only uncover one reference to age-related infant cranial porosity. The study by Igo et al., (2021) used micro-CT scanning to assess the mechanical properties of the infant skull and determined a high porosity coverage of 36% in the analysis of eight individuals aged four to ten months. The regression model also indicated that porosity decreased by 4% per a month (Igo et al. 2021). Although not directly comparable to the porosity observed on the inferior surface of the *pars basilaris* in this study, the literature supports the possibility that porosity on the external cortical surface of infants could be related to age. Considering this, it is reasonable to conclude that microporosity observed on the *pars basilaris* is largely the result of normal physiological growth in non-adults aged <3.5 years. This highlights the need to further define 'normal' bone changes on the skull with careful consideration of age.

4.3. Changes to the pars basilaris in known individuals

To highlight the suspected normal porous nature of the pars basilaris, a small sample of individuals from the Granada, Spain, collection of identified infants and young children (with known ages and causes of death), were selected. None of these individuals showed changes consistent with scurvy, but microporosity can be clearly observed across the inferior surface of the pars basilaris in four (Individuals G-412, G-154, G-240, G-166) of the six individuals examined (Fig. 6). It is improbable that this microporosity was linked to the cause of death, as the individuals died of acute conditions that were unlikely to have affected bone remodelling on the pars basilaris. The two oldest individuals in the known sample (both aged one year, ten months and six days) displayed minimal changes to the inferior surface. In individual G-211, the microporosity observed had a closed appearance indicating a state of remodelling (Mensforth et al., 1978), whilst individual G-172 displayed no microporosity. This absence of microporosity is possibly age related, which is supported by observations in the archaeological sample, as individuals with no microporosity on the pars basilaris were primarily older than 1.5 years (14/15 in the non-scorbutic group). This



Fig. 6. A range of microporosity expression in known-age individuals from Granada, Spain. From left to right/top to bottom, with age at death, and cause of death: individual G-412, 36 weeks gestation (NA); individual G-154, three days (acute jaundice); individual G-240, three months and 19 days (inguinal hernia); individual G-166, eight months and four days (acute pneumococcal meningitis); individual G-172, one year, ten months and six days (measles); individual G-211, one year, ten months and six days (Acetonemia) (Adapted with permission from photos taken by Álvaro M. Monge Calleja).

adds further evidence to our hypothesis that microporosity on the inferior aspect of the *pars basilaris* is more likely to represent rapid growth at the cranial base in non-adults and is correlated with age, rather than a pathological process. Future work on the development of microporosity in the cranial and postcranial skeleton would benefit from the analysis of a large known skeletal sample of perinates and infants, coupled with a thorough review of the biomedical literature, and consideration of age (Mays, 2018).

4.4. SPNB on the pars basilaris

Only eight (4.2%) of the 191 individuals studied displayed SPNB on one or more segments of the inferior *pars basilaris*. Significantly, the three individuals with Grade 2 changes were diagnosed with scurvy or lesions consistent with the disease (33%). In our sample, Grade 2 SPNB on the inferior *pars basilaris* occurred more frequently than two currently accepted scorbutic lesions: subperiosteal new bone or porosity on the lesser wings of the sphenoid (10.5%, n=2) and the maxillae infra orbital foramen (5.2%, n=1).

Subperiosteal new bone can be associated with normal physiological growth in the non-adult skeleton (De Silva et al., 2003; Bisseret et al., 2015; Lewis, 2017b; Lewis, 2017a), and differentiating this from an inflammatory response is difficult. One scorbutic individual aged 14.5 months from St James, Euston displayed microporosity (Grade 1) in addition to Grade 2 SPNB (segments S1-S5). The expressive nature of these changes on the inferior *pars basilaris* surface suggests a more probable haemorrhagic origin, and this is further supported by the highly diagnostic scorbutic lesions observed on the cranial skeleton (Supplementary Information 1: Fig. 1).

5. Conclusions

Since Moore and Koon's (2017) publication, porosity and SPNB on the inferior pars basilaris have been incorporated into the diagnostic framework for scurvy in numerous bioarchaeological studies (Bourbou, 2018; Snoddy et al., 2018; Morrone et al., 2021; Vlok et al., 2023; Larentis et al., 2023; Karligkioti et al., 2022). However, this study has shown that while microporosity on the pars basilaris may occur in individuals who have scurvy (because they are growing), it is not consistent with the disease, and is difficult to distinguish from porosity related to normal growth. Microporosity prevalence on the pars basilaris decreases with age, and to better understand this relationship, future research should focus on the analysis of individuals over 3.5 years to confirm whether prevalence rates continue to decrease. The expression of SPNB is important when discriminating between physiological and pathological bone changes. Subtle SPNB (Grade 1) should not be recorded as a scorbutic feature, but Grade 2 observations should continue to be recorded in diagnostic scurvy cases to further explore its relationship with the disease. The co-occurrence of SPNB (Grade 2) and microporosity was only noted in one individual and might indicate a haemorrhaging response considering the diagnostic nature of scorbutic lesions observed in the cranial skeleton.

This study highlights the risk of over diagnosing scurvy in past populations. In non-adults younger than 3.5 years the causes of SPNB and porosity must be considered more thoroughly in both the cranial and post-cranial skeleton. Currently, there is an emphasis on pathological porosity and SPNB in the diagnosis of scurvy, with little consideration of normal skeletal responses to physiological growth, and recent work has been quick to apply scorbutic features to perinate and infant skeletal remains (Snoddy et al., 2017; Vlok et al., 2023). There is a need for a standardised recording system for SPNB and porosity in fetuses, perinates, and infants to help determine the difference between bone changes related to growth and anatomical variation, as opposed to pathological processes.

CRediT authorship contribution statement

Jack Eggington: Writing – review & editing, Writing – original draft, Visualization, Software, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Claire Hodson: Writing – review & editing, Project administration, Methodology, Data curation, Conceptualization. Rebecca Pitt: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization.

Acknowledgements

This work was supported by the Arts & Humanities Research Council through the South, West and Wales Doctoral Training Partnership (Jack Eggington) and the British Academy Post-Doctoral Research Fellowship (Claire Hodson). The authors would like to thank the following individuals and institutions for access to skeletal collections: Andrea Bradley (High Speed Railway 2), Louise Fowler and Michael Henderson (Museum of London Archaeology), Ross Turle (Hampshire Cultural Trust), Ben Donnelly-Symes (Northamptonshire Archaeological Resource Centre), Elizabeth Selby (Dorchester Museum), Tabatha Barton (Milton Keynes Museum), and Jo Buckberry (Bradford University). We are also grateful to Álvaro M. Monge Calleja, who provided access to data from the Granada collection of identified infants and young children, Spain. Finally, thanks are due to Mary Lewis (University of Reading) for her valuable comments on the first draft, and Rob Hosfield (University of Reading) for advice on the appropriate statistical tests to use in this study.

Appendix A. Supporting information

Supplementary and supporting data associated with this article can be found in the online version at doi:10.1016/j.ijpp.2024.05.001.

References

- AlQahtani, S.J., Hector, M.P., Liversidge, H.M., 2010. Brief communication: the London atlas of human tooth development and eruption. Am. J. Phys. Anthropol. 142, 481–490. https://doi.org/10.1002/ajpa.21258.
- Armelagos, G.J., Sirak, K., Werkema, T., Turner, B.L., 2014. Analysis of nutritional disease in prehistory: the search for scurvy in antiquity and today. Int. J. Paleonathol. 5, 9–17. https://doi.org/10.1016/j.ijnp.2013.09.007.
- Paleopathol. 5, 9–17. https://doi.org/10.1016/j.ijpp.2013.09.007.
 Barlow, T., 1883. On Cases Described as "Acute Rickets," which are probably a combination of Scurvy and Rickets, the Scurvy being an essential, and the rickets a variable, element. Med. -Chir. Trans. 66, 159.
- Basu, T.K., Schorah, C.J., 1982. Vitamin C in health and disease. Croom Helm Limited.
 Battafarano, G., Rossi, M., Marampon, F., Minisola, S., Del Fattore, A., 2020. Bone control of muscle function. Int. J. Mol. Sci. 21, 1178. https://doi.org/10.3390/ijms21041178.
- Bisseret, D., Kaci, R., Lafage-Proust, M.-H., Alison, M., Parlier-Cuau, C., Laredo, J.-D., Bousson, V., 2015. Periosteum: characteristic imaging findings with emphasis on radiologic-pathologic comparisons. Skelet. Radiol. 44, 321–338. https://doi.org/ 10.1007/s00256-014-1976-5.
- Bott, S., 1911. Extensive blistering occurring in an infant; diagnosis of scurvy. Lancet 177, 878.
- Bourbou, C., 2018. Life and death at the "The Land of Three Lakes": revisiting the non-adults from Roman Aventicum, Switzerland (1st–3rd century CE). Int. J. Paleopathol. 22, 121–134. https://doi.org/10.1016/j.ijpp.2018.06.005.
- Brickley, M., Ives, R., 2006. Skeletal manifestations of infantile scurvy. Am. J. Biol. Anthropol. 129, 163–172. https://doi.org/10.1002/ajpa.20265.
- Brickley, M.B., Ives, R., Mays, S., 2020. The bioarchaeology of metabolic bone disease. Academic Press.
- Brickley, M.B., Mays, S., 2019. Metabolic disease. Ortner's identification of pathological conditions in human skeletal remains. Elsevier. https://doi.org/10.1016/B978-0-12-809738-0.00015-6.
- Brickley, M.B., Morgan, B., 2023. Assessing diagnostic certainty for scurvy and rickets in human skeletal remains. Am. J. Biol. Anthropol. 181 (4), 637–645. https://doi.org/ 10.1002/ajpa.24799.
- Brown, M., Ortner, D.J., 2011. Childhood scurvy in a medieval burial from Mačvanska Mitrovica, Serbia. Int. J. Osteoarchaeol. 21, 197–207. https://doi.org/10.1002/oa.1124.
- Buckley, H.R., Kinaston, R., Halcrow, S.E., Foster, A., Spriggs, M., Bedford, S., 2014.Scurvy in a tropical paradise? Evaluating the possibility of infant and adult vitamin C

- deficiency in the Lapita skeletal sample of Teouma, Vanuatu, Pacific islands. Int. J. Paleopathol. 5, 72–85. https://doi.org/10.1016/j.ijpp.2014.03.001.
- Cambra-Moo, O., Nacarino Meneses, C., Rodriguez Barbero, M.A., Garcia Gil, O., Rascon Perez, J., Rello-Varona, S., D'Angelo, M., Campo Martin, M., Gonzalez Martin, A., 2014. An approach to the histomorphological and histochemical variations of the humerus cortical bone through human ontogeny. J. Anat. 224 (6), 634–646. https://doi.org/10.1111/joa.12172
- Cohen, J. (1988). The effect size. Statistical Power Analysis for the Behavioural Sciences, 77-83.
- Crandall, J.J., Klaus, H.D., 2014. Advancements, challenges, and prospects in the paleopathology of scurvy: Current perspectives on vitamin C deficiency in human skeletal remains. Int. J. Paleopathol. 5, 1–8. https://doi.org/10.1016/j. iipp.2014.04.005.
- Crawford, E.M., 1988. Scurvy in Ireland during the Great Famine. Soc. Hist. Med. 1, 281–300. https://doi.org/10.1093/shm/1.3.281.
- Cunningham, C., Scheuer, L., Black, S., 2016. Developmental juvenile osteology Academic press.
- De Silva, P., Evans-Jones, G., Wright, A., Henderson, R., 2003. Physiological periostitis; a potential pitfall. Arch. Dis. Child. 88, 1124–1125. https://doi.org/10.1136/adc 88.12.1124
- DiGirolamo, D.J., Kiel, D.P., Esser, K.A., 2013. Bone and skeletal muscle: neighbours with close ties. J. Bone Miner. Res. 28, 1509–1518. https://doi.org/10.1002/jbmr.1969.
- Fain, O., 2005. Musculoskeletal manifestations of scurvy. Jt. Bone Spine 72, 124–128. https://doi.org/10.1016/j.jbspin.2004.01.007.
- Geber, J., Murphy, E., 2012. Scurvy in the Great Irish Famine: Evidence of vitamin C deficiency from a mid-19th century skeletal population. Am. J. Biol. Anthropol. 148, 512–524. https://doi.org/10.1002/ajpa.22066.
- Golriz, F., Donnelly, L.F., Devaraj, S., Krishnamurthy, R., 2017. Modern American scurvy — experience with vitamin C deficiency at a large children's hospital. Pediatr. Radiol. 47 (2), 214–220.
- Grewar, D., 1965. Infantile scurvy. Clin. Pediatr. 4, 82-89.
- Gulko, E., Collins, L.K., Murphy, R.C., Thornhill, B.A., Taragin, B.H., 2015. MRI findings in pediatric patients with scurvy. Skelet. Radiol. 44 (2), 291–297. https://doi.org/ 10.1007/s00256-014-1962-y.
- Halcrow, S.E., Harris, N.J., Beavan, N., Buckley, H.R., 2014. First bioarchaeological evidence of probable scurvy in Southeast Asia: multifactorial etiologies of vitamin C deficiency in a tropical environment. Int. J. Paleopathol. 5, 63–71. https://doi.org/ 10.1016/j.iipp.2014.01.004.
- Hirsch, M., Mogle, P., Barkli, Y., 1976. Neonatal scurvy. Pediatr. Radiol. 4, 251–253. https://doi.org/10.1007/BF02461534.
- Hodges, R.E., Baker, E.M., Hood, J., Sauberlich, H.E., March, S.C., 1969. Experimental scurvy in man. Am. J. Clin. Nutr. 22, 535–548. https://doi.org/10.1093/ajcn/22.5.535
- Hodson, C., 2018. Stressed at Birth: Investigating Fetal, Perinatal and Infant Growth and Health Disruption (Doctoral Dissertation). University of Durham.
- Huelke, D.F., (1998). An overview of anatomical considerations of infants and children in the adult world of automobile safety design. In Annual Proceedings/Association for the Advancement of Automotive Medicine, Association for the Advancement of Automotive Medicine, 42, 93-113.
- Humphrey, L.T., 1998. Growth patterns in the modern human skeleton. Am. J. Phys. Anthropol. 105, 57–72. https://doi.org/10.1002/(SICI)1096-8644(199801)105: 1<57::AID-AJPA6>3.0.CO;2-A.
- Igo, B.J., Cottler, P.S., Black, J.S., Panzer, M.B., 2021. The mechanical and microstructural properties of the pediatric skull. J. Mech. Behav. Biomed. Mater. 120, 1–8. https://doi.org/10.1016/j.jmbbm.2021.104578.
- Jacob, R.A., Sotoudeh, G., 2002. Vitamin C function and status in chronic disease. Nutr. Clin. Care 5, 66–74. https://doi.org/10.1046/j.1523-5408.2002.00005.x.
- Jaffe, H.L., 1972. Metabolic degenerative, and inflammatory diseases of bones and joints. Lea and Febiger. Philadelphia.
- Javadifar, N., Majlesi, F., Nikbakht, A., Nedjat, S., Montazeri, A., 2016. Journey to motherhood in the first year after childbirth. J. Fam. Reprod. Health 10, 146.
- Karligkioti, A., Mardini, M., Christofi, P., Nikita, E., 2022. First bioarchaeological insights to living conditions in Cyprus from Venetian to Ottoman times. J. Archaeol. Sci.: Rep. 45, 103640 https://doi.org/10.1016/j.jasrep.2022.103640.
- Kawao, N., Kaji, H., 2015. Interactions between muscle tissues and bone metabolism. J. Cell. Biochem. 116, 687–695. https://doi.org/10.1002/jcb.25040.
- Khosla, S., Melton III, L.J., Dekutoski, M.B., Achenbach, S.J., Oberg, A.L., Riggs, B.L., 2003. Incidence of childhood distal forearm fractures over 30 years: a populationbased study. Jama 290 (11), 1479–1485.
- Klaus, H.D., 2017. Paleopathological rigor and differential diagnosis: Case studies involving terminology, description, and diagnostic frameworks for scurvy in skeletal remains. Int. J. Paleopathol. 19, 96–110. https://doi.org/10.1016/j. ibn 2015 10.002
- Krmpotić-Nemanić, J., Vinter, I., Ehrenfreund, T., Marušić, A., 2006. Age-related changes in the anatomical landmarks of the osseous epipharynx. Ann. Anat. -Anat. Anz. 188, 459–467. https://doi.org/10.1016/j.aanat.2006.04.005.
- Kwon, D.S., Spevak, M.R., Fletcher, K., Kleinman, P.K., 2002. Physiologic subperiosteal new bone formation: prevalence, distribution, and thickness in neonates and infants. Am. J. Roentgenol. 179 (4), 985–988. https://doi.org/10.2214/ajr.179.4.1790985.
- Larentis, O., Licata, M., Tonina, E., Pangrazzi, C., 2023. Probable micronutrient deficiency diseases in a rural community. The nonadults of Mary's Nativity church, 16th century, Trentino Alto-Adige, Italy. J. Archaeol. Sci.: Rep. 47, 103774 https:// doi.org/10.1016/j.jasrep.2022.103774.
- Lewis, M., 2017a. Paleopathology of children: Identification of pathological conditions in the human skeletal remains of non-adults. Academic Press.

- Lewis, M.E., 2017b. Fetal paleopathology: An impossible discipline. Anthropol. fetus: Biol., Cult., Soc. 112–131.
- Lier, L., 1988. Mother-infant relationship in the first year of life. Acta Paediatr. Scand. Suppl. 344, 31–42. https://doi.org/10.1111/ji.1651-2227.1988.tb10859.x.
- Martín, A.G., Rodríguez, F.R., Cambra-Moo, O., Pérez, J.R., Martín, M.C., 2018.
 Comment upon" Basilar portion porosity: A pathological lesion possibly associated with infantile scurvy. Int. J. Paleopathol. 20, 114–115. https://doi.org/10.1016/j.ijpp.2017.09.003.
- Mays, S., 2008. A likely case of scurvy from early Bronze Age Britain. Int. J. Osteoarchaeol. 18 (2), 178–187. https://doi.org/10.1002/oa.930.
- Mays, S., 2018. How should we diagnose disease in palaeopathology? Some epistemological considerations. Int. J. Paleopathol. 20, 12–19. https://doi.org/ 10.1016/j.ijpp.2017.10.006.
- Melikian, M., Waldron, T., 2003. An examination of skulls from two British sites for possible evidence of scurvy. Int. J. Osteoarchaeol. 13, 207–212. https://doi.org/ 10.1002/pa.674
- Mensforth, R.P., Lovejoy, C.O., Lallo, J.W., Armelagos, G.J., 1978. Part two: the role of constitutional factors, diet, and infectious disease in the etiology of porotic hyperostosis and periosteal reactions in prehistoric infants and children. Med. Anthropol. 2 (1), 1–59. https://doi.org/10.1080/01459740.1978.9986939.
- Monsen, E.R., 2000. Dietary reference intakes for the antioxidant nutrients: vitamin C, vitamin E, selenium, and carotenoids. J. Acad. Nutr. Diet. 100, 637.
- Moore, J., Koon, H.E., 2017. Basilar portion porosity: a pathological lesion possibly associated with infantile scurvy. Int. J. Paleopathol. 18, 92–97. https://doi.org/ 10.1016/j.ijpp.2017.05.010.
- Morrone, A., Törv, M., Piombino-Mascali, D., Malve, M., Valk, H., Oras, E., 2021. Hunger, disease, and subtle lesions: Insights into systemic metabolic disease in fetal and perinatal remains from 13th-to 15th-century Tartu, Estonia. Int. J. Osteoarchaeol. 31, 534–555. https://doi.org/10.1002/oa.2970.
- Newman, S.L., Gowland, R.L., 2017. Dedicated Followers of Fashion? Bioarchaeological Perspectives on Socio-Economic Status, Inequality, and Health in Urban Children from the Industrial Revolution (18th–19th C), England. Int. J. Osteoarchaeol. 27, 217–229. https://doi.org/10.1002/oa.2531.
- Nicholls, R., Buckberry, J., Beaumont, J., Črešnar, M., Mason, P., Armit, I., Koon, H., 2020. A carbon and nitrogen isotopic investigation of a case of probable infantile scurvy (6th–4th centuries BC, Slovenia). J. Archaeol. Sci.: Rep. 30, 102206 https://doi.org/10.1016/j.jasrep.2020.102206.
- Öhman, A.M., Beckung, E.R., 2008. Reference values for range of motion and muscle function of the neck in infants. Pediatr. Phys. Ther. 20, 53–58 https://doi. org10.1097/PEP.0b013e31815ebb27.
- Ono, N. & Kronenberg, H.M. (2018). Developmental biology of musculoskeletal tissues for tissue engineers. Developmental Biology and Musculoskeletal Tissue Engineering, Elsevier. https://doi.org/10.1016/B978-0-12-811467-4.00001-2.
- Ortner, D.J., Butler, W., Cafarella, J., Milligan, L., 2001. Evidence of probable scurvy in subadults from archaeological sites in North America. Am. J. Biol. Anthropol. 114, 343–351. https://doi.org/10.1002/ajpa.1046.
- Ortner, D.J., Ericksen, M.F., 1997. Bone changes in the human skull probably resulting from scurvy in infancy and childhood. Int. J. Osteoarchaeol. 7, 212–220. https://doi.org/10.1002/(SIC01099-1212(199705)7:3<212::AID-OA346>3.0.C0:2-5.
- Ortner, D.J., Kimmerle, E.H., Diez, M., 1999. Probable evidence of scurvy in subadults from archaeological sites in Peru. Am. J. Biol. Anthropol. 108 (3), 321–331. https://doi.org/10.1002/(SICI)1096-8644(199903)108:3<321::AID-AJPA7>3.0.CO:2-7.
- Osagie I.E., Givler D.N. (2022). Infant head lag. In: StatPearls. StatPearls Publishing, Treasure Island (FL); PMID: 33620859.
- Parfitt, A.M., 1994. The two faces of growth: benefits and risks to bone integrity.
 Osteoporos. Int. 4, 382–398. https://doi.org/10.1007/BF0162220.
 Pérez-Escamilla, R., Tomori, C., Hernández-Cordero, S., Baker, P., Barros, A.J., Bégin, F.,
- Pérez-Escamilla, R., Tomori, C., Hernández-Cordero, S., Baker, P., Barros, A.J., Bégin, F., Chapman, D.J., Grummer-Strawn, L.M., McCoy, D., Menon, P., 2023. Breastfeeding: crucially important, but increasingly challenged in a market-driven world. Lancet 401, 472–485. https://doi.org/10.1016/S0140-6736(22)01932-8.
- Pineda, R.G., Reynolds, L.C., Seefeldt, K., Hilton, C.L., Rogers, C.E., Inder, T.E., 2016. Head lag in infancy: what is it telling us? Am. J. Occup. Ther. 70 (1), 8. https://doi.org/10.5014/ajot.2016.017558.
- Poirier, P., Charpy, A., Nicolas, A., Prenant, A., Jonnesco, T., 1892. Traité d'anatomie humaine: Tome premier. L. Battaille et Cie.
- Rana, R.S., Wu, J.S., Eisenberg, R.L., 2009. Periosteal reaction. Am. J. Roentgenol. 193 (4), 259–272. https://doi.org/10.2214/AJR.09.3300.
- Ribot, I., Roberts, C., 1996. A study of non-specific stress indicators and skeletal growth in two mediaeval subadult populations. J. Archaeol. Sci. 23 (1), 67–79. https://doi. org/10.1006/jasc.1996.0006.
- Rohnbogner, A., Lewis, M.E., 2017. Poundbury camp in context- a new perspective on the lives of children from urban and Rural Roman England. Am. J. Phys. Anthropol. 162, 208–228. https://doi.org/10.1002/ajpa.23106.
- Rothschild, B., Jellema, L., 2020. Periosteal reaction recognition and specificity assessed by surface microscopy. Int. J. Osteoarchaeol. 30 (3), 355–361. https://doi.org/ 10.1002/oa.2864.
- Sakamoto, Y., 2012. Spatial relationships between the morphologies and innervations of the scalene and anterior vertebral muscles. Ann. Anat. -Anat. Anz. 194, 381–388. https://doi.org/10.1016/j.aanat.2011.11.004.
- Schattmann, A., Bertrand, B., Vatteoni, S., Brickley, M., 2016. Approaches to cooccurrence: Scurvy and rickets in infants and young children of 16–18th century Douai, France. Int. J. Paleopathol. 12, 63–75. https://doi.org/10.1016/j. ijpp.2015.12.002.
- Scheuer, L., Black, S., 2000. Development and ageing of the juvenile skeleton. Human Osteology in Archaeology and Forensic science. Cambridge University Press, pp. 9–22.

- Scheuer, L., Black, S., 2004. The Juvenile Skeleton. Elsevier.
- Scheuer, L., MacLaughlin-Black, S., 1994. Age estimation from the pars basilaris of the fetal and juvenile occipital bone. Int. J. Osteoarchaeol. 4, 377–380. https://doi.org/
- Scheuer, J.L., Musgrave, J.H., Evans, S.P., 1980. The estimation of late fetal and perinatal age from limb bone length by linear and logarithmic regression. Ann. Hum. Biol. 7, 257–265. https://doi.org/10.1080/03014468000004301.
- Shimada, K., Gasser, R.F., 1988. Variations of the pharyngeal raphe. Clin. Anat. 1, 285–294. https://doi.org/10.1002/ca.980010405.
- Shopfner, C.E., 1966. Periosteal bone growth in normal infants: a preliminary report. Am. J. Roentgenol. 97 (1), 154–163.
- Simonit, R., Maudet, S., Giuffra, V., Riccomi, G., 2023. Infantile scurvy as a consequence of agricultural intensification in the 1st millennium BCE Etruria Campana. Sci. Rep. 13 (1), 21396 https://doi.org/10.1038/s41598-023-48455-0.
- Smith, A.G., Di Primio, Humphrey-Murto, S., 2011. Scurvy in the developed world. Can. Med. Assoc. J. 183, 752–755. https://doi.org/10.1503/cmaj.091938.
- Snoddy, A.M.E., Buckley, H.R., Elliott, G.E., Standen, V.G., Arriaza, B.T., Halcrow, S.E., 2018. Macroscopic features of scurvy in human skeletal remains: A literature synthesis and diagnostic guide. Am. J. Phys. Anthropol. 167, 876–895. https://doi. org/10.1002/aipa.23699.
- Snoddy, A.M.E., Halcrow, S.E., Buckley, H.R., Standen, V.G., Arriaza, B.T., 2017. Scurvy at the agricultural transition in the Atacama Desert (ca 3600–3200 BP): nutritional stress at the maternal-foetal interface? Int. J. Paleopathol. 18, 108–120. https://doi.org/10.1016/j.ijpp.2017.05.011.
- Stark, R.J., 2014. A proposed framework for the study of paleopathological cases of subadult scurvy. Int. J. Paleopathol. 5, 18–26. https://doi.org/10.1016/j. iipp.2014.01.005.
- Sutherland, G., 1894. On haematoma of the dura mater associated with scurvy in children. Brain 17, 27–36.

- Thompson, J.E., Power, R.K., Mercieca-Spiteri, B., Magnussen, J.S., Pardey, M., Buck, L. T., Stock, J.T., McLaughlin, T.R., Stoddart, S., Malone, C., 2022. Analysis of periosteal lesions from commingled human remains at the Xaghra Circle hypogeum reveals the first case of probable scurvy from Neolithic Malta. Int. J. Osteoarchaeol. 32 (1), 18–37. https://doi.org/10.1002/oa.3040.
- Vlok, M., 2023. The use and misuse of threshold diagnostic criteria in paleopathology. Am. J. Biol. Anthropol. 181 (2), 326–335. https://doi.org/10.1002/ajpa.24721.
- Vlok, M., Oxenham, M.F., Domett, K., Trinh, H.H., Minh, T.T., Mai Huong, N.T., Matsumura, H., Huu, N.T., Nguyen, L.C., Willis, A., 2023. Scurvy in the tropics: Evidence for increasing non-adult micronutrient deficiency with the transition to agriculture in northern Vietnam. Am. J. Biol. Anthropol. 180, 715–732. https://doi. org/10.1002/aipa.24698
- Wei, X., Cooper, D.M., 2023. The various meanings and uses of bone "remodeling" in biological anthropology: A review. Am. J. Biol. Anthropol. 182 (2), 318–329. https://doi.org/10.1002/ajpa.24825.
- Weinstein, M., Babyn, P., Zlotkin, S., 2001. An Orange a Day Keeps the Doctor Away: Scurvy in the Year 2000. e55-e55 Pediatrics 108 (3). https://doi.org/10.1542/peds.108.3.e55.
- Welsh, H., Brickley, M.B., 2023. Pathology or expected morphology? Investigating patterns of cortical porosity and trabecularization during infancy and early childhood. Anat. Rec. 306 (2), 354–365. https://doi.org/10.1002/ar.25081.
- Weston, D.A., 2008. Investigating the specificity of periosteal reactions in pathology museum specimens. Am. J. Phys. Anthropol. 137 (1), 48–59. https://doi.org/ 10.1002/aipa.20839.
- Weston, D.A., 2012. Nonspecific infection in palaeopathology: Interpreting periosteal reactions. In: Grauer, A.L. (Ed.), A Companion to Paleopathology. Wiley Blackwell, Chichester, pp. 492–512. https://doi.org/10.1002/9781444345940.ch27.