New and Emerging Prospects for the Paleopathological Study of Starvation: A Critical Review

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ABSTRACT

Starvation represents a significant contributor to morbidity and mortality, past and present, and is therefore of critical importance to the field of paleopathology. Scholars have previously argued that while critical to understanding past human health, starvation is often not directly observable in skeletal remains. But is this assessment still valid today? In re-evaluating this assessment, this paper discusses new developments in the analysis of (1) the "hunger osteopathies" (osteoporosis with some overlay of osteomalacia), (2) skeletal signs of arrested growth such as Harris lines and Linear Enamel Hypoplasia (LEH), and (3) carbon and nitrogen stable isotope analysis of skeletal remains. Periods of starvation are known to cause these visible and chemical alterations within skeletal remains, but these phenomena are complex, multi-etiological, and approaches to evaluate them are often fraught with a lack of standardization and specificity. An interdisciplinary approach synthesizing multiple lines of osteological and dental evidence, borrowing anatomical and medical research, and implementing new advancements in computer modeling, imaging modalities, and chemical micro-sampling may theoretically aid in inferring starvation bioarchaeologically.

Keywords: bioarchaeology, paleopathology, osteoporosis, osteomalacia, Harris lines, linear enamel hypoplasia, stable isotopes

INTRODUCTION

Starvation is a key contributor to mortality and morbidity, past and present. Due to the significance of starvation to human health in past populations and the breadth to which starvation impacts the skeleton, it is a topic of utmost importance in paleopathology and the subject of much discussion. According to some scholars, however, the prospects of diagnosing starvation bioarchaeologically are extremely bleak. In a review of approaches to interpreting famine, Johanna Morgan (2013) argued that in the absence of documentary data, it is impossible to interpret famine bioarchaeologically. This leads to the following question: in the constantly changing and evolving discipline of paleopathology, is this assessment still valid?

Numerous methodological advancements in paleopathology have been published since 2013. This review paper will discuss and analyze three common approaches to studying starvation from skeletal remains and assess whether these new advancements in paleopathology and bioarchaeology have the potential to challenge Morgan's (2013) hypothesis.

In this paper, I will first introduce the topic of starvation and discuss some widespread theoretical considerations and constraints, such as the osteological paradox, which limit the paleopathologist's ability to directly observe many pathological conditions on skeletal remains. Next, I will discuss three common approaches to the bioarchaeological study of starvation (the "hunger osteopathies," signs of arrested growth, and stable isotopic analysis), focusing particularly on the problems of these approaches and any new and emergent techniques which may refine them.

It should be noted that definitions of starvation vary widely across the literature, even within the fields of bioarchaeology and paleopathology (Horocholyn and Brickley 2017). Within the context of this paper, starvation will refer specifically to severe protein-calorie malnutrition, in which the energy the body expends is more than the energy it takes in, resulting in severe wasting and general undernutrition (Waterlow 1972). This definition contains a suite of various starvation states, including marasmus (generalized starvation and wasting, characterized by an emaciated appearance) or kwashiorkor (caused by a pronounced lack of protein in the diet and characterized by an abdominal edema; Waterlow 1972).

BACKGROUND

Starvation, or severe undernutrition, is a pervasive health issue for humans both past and present. Today, an estimated 52 million children under the age of 5 years are considered starved to the point of "wasted" (severely low weight-for-height; WHO 2018). As Webb and colleagues (2018) put it, ironically, "today's world is characterized by the coexistence of agricultural bounty and widespread hunger and malnutrition" (1).

Individual contexts such as medical conditions such as digestive disorders like Crohn's Disease, ulcerative colitis, celiac disease, and irritable bowel syndrome (IBS), cancers, and mental illnesses such as eating disorders (anorexia nervosa and bulimia) or depression, and abusive or negligent circumstances can result in starvation (Kastin and Buchman 2002; Mattar et al. 2011; Piercecchi-Marti et al. 2006; Santarpia, Contaldo, and Pasanisi 2011; Smoliner et al. 2009). On a more social or populational level, widespread causes for starvation include famine (extreme food scarcity), natural disaster, social conflict, warfare, and poverty (Kufour 1994; Sen 1981).

While clearly a vastly important issue in global health today, the existence of starvation is also an important topic for paleopathology, which is defined as the study of disease in the past primarily undertaken through analysis of skeletal remains. The prevalence of starvation likely saw a vast increase following the intensive adoption of agriculture by humans (Berbesque et al. 2014), and it has remained a significant and recurrent mortality crisis for past human societies (Watkins and Menken 1985). Starvation represents an important etiological factor behind numerous pathological conditions that can be observed in the skeletal system. For example, periods of starvation can result in elevated secondary bone loss, cause micronutrient (e.g. vitamin C, vitamin D, calcium, iron, niacin) deficiencies which may manifest skeletally, or cause arrests in skeletal and dental growth (Brickley and Ives 2008; Roberts and Manchester 2005). Additionally, starved individuals are often more susceptible to other insults, such as infectious disease, as immunodeficiency starvation can cause (Gowland 2015, 532; Katona and Katona-Apte 2008; Taylor et al. 2013).

Bone is a tough yet elastic tissue consisting of collagen fibrils and hydroxyapatite mineral, acting as a supportive framework for the body and a reservoir for minerals and nutrients. A dynamic tissue, bone constantly undergoes remodelling, the coupled process by which units called osteoclasts resorb (or remove) bone and units called osteoblasts form new secondary osteons (cylindrical structures constituting the fundamental structural unit of bone) in the resorption spaces (Cooper et al. 2006; Hadjidakis and Androulakis 2006). Both deciduous and permanent teeth consist of a tooth crown and root comprised of the following three distinct tissues: dentine, enamel, and cementum. Beginning in utero, these tissues develop incrementally, with enamel and primary dentine formation ceasing during

childhood, and secondary dentine and cementum continuing to form into adulthood (Bodecker 1925; Grue and Jensen 1979; Lacruz et al. 2017). Stressors or disruptions upon the typical development and dynamics of bone and teeth can result in mascroscopic, microscopic, and chemical irregularities that can be detected by the paleopathologist to make inferences about individual and populational health.

While a critical etiological factor to the field of paleopathology, the skeletal detection of starvation can be challenging and contains many limitations, forming the basis of Morgan's (2013) argument that starvation could not be inferred archaeologically. Many of paleopathology's limitations in this regard are derived from the nature of the skeletal system itself. In 1992, Wood and colleagues introduced the osteological paradox, shedding light on several theoretical issues in paleopathology. They argued that populations within the bioarchaeological record exhibit a hidden heterogeneity of risk and selective mortality, meaning that individuals vary in their susceptibility to illness, and that assessing population health based on the presence or absence of skeletal lesions presents a distorted view of past human mortality and survival. Are skeletal indicators of possible starvation present only because an individual survived the period of physiological stress long enough to develop them? Did starvation directly kill an individual, or did it increase an individual's frailty and susceptibility to other diseases, such as infection? These are important theoretical considerations in paleopathological studies of starvation.

Additionally, there are a finite number of ways that the skeleton can react to disease (Ortner 2009); often times, bony manifestations of disease will not be diagnostic of a condition and rather involve a suite of lytic or sclerotic changes with much overlap in appearance and description. On a similar note, paleopathological conditions linked to starvation often have multiple underlying etiologies, beyond starvation. For example, osteoporosis may be related to age or hormonal changes or develop secondary to nutritional stress, trauma, or infection (Brickley and Ives 2008, 151).

The paleopathological interpretation of starvation is not just limited by the nature of the skeleton itself; there are several limitations inherent in the discipline of paleopathology that have stalled its progress. Zuckerman, Harper, and Armelagos (2016) have argued that the discipline of paleopathology has been hindered by its resistance to draw from or misuse of advancements in other scientific disciplines. Additionally, the assessment of skeletal pathological conditions is impacted by numerous methodological limitations including inter- and intra-observer error, a lack of standardization in methods, and limitations within specific techniques themselves.

The following sub-sections will critically assess three different categories of bioarchaeological approaches to studying starvation and discuss whether these approaches support or refute Morgan's (2013) argument in light of new and emerging techniques. It should be noted that it is unlikely that any of these approaches, when used alone, could ever be sufficient enough evidence to indicate periods of starvation within an individual's life. The assumption here is that multiple lines of osteological evidence would always be used in inferring starvation bioarchaeologically as this allows for a greater confidence of properly diagnosing a condition osteologically.

PALEOPATHOLOGICAL APPROACHES TO DETECTING STARVATION

"Hunger Osteopathies": Osteoporosis and Osteomalacia

According to Ortner (2003, 405), starvation results in "hunger osteopathies"—defined as secondary osteoporosis with some overlay

of osteomalacia. Osteoporosis and its precursor condition, osteopenia, are typically characterized by a decrease in bone density and a decline of bone microstructure, often correlated with increasing age or postmenopausal hormone changes (Gregg et al. 1997; Lindsay and Tohme 1990; Vidal et al. 2019). These skeletal changes are related to a shift in remodelling dynamics toward net bone loss, caused by a decrease in bone formation, an increase in bone resorption, or both (Seeman 2003, S3; Donovan et al. 2005). This imbalance of bone remodelling often leads to increased susceptibility for bone fracture, contributing to increased morbidity and mortality (Dempster 2011). Secondary osteopenia and osteoporosis differ from age-related or postmenopausal osteopenia and osteoporosis as they are caused by trauma, nutritional insufficiency, or diseases such as hyperthyroidism, hyperparathyroidism, hypogonadism, idiopathic hypercalciuria, or Cushing's syndrome and occur independent of the aging process (Brickley and Ives 2008, 185; Hudec and Camacho 2013). Several metabolic changes during starvation result in secondary osteoporosis. Reductions in dietary protein leads to a decline in calcium absorption as well as secondary hyperparathyroidism, which facilitates an increase in the rate of bone remodeling (Rizzoli and Bonjour 2004). Additionally, starvation results in estrogen deficiency, thereby causing an increase in osteoclastogenesis (the process of bone resorption), and consequently, an increase in bone loss (D'Amelio et al. 2008; Grinspoon et al. 1999; Rigotti et al. 1984).

Osteomalacia is a pathological condition caused by vitamin D deficiency, resulting in insufficient bone mineralization. This condition is characterized by buckled vertebrae, teeth deformations, antemortem tooth loss, cranial porosity, and deformations or bending to the ribs, sternum, pelvis, sacrum, and long bones (Brickley and Ives 2008, 127–131). However, linear pseudofractures (small, linear fractures which heal poorly) are the hallmark of this condition (Brickley and Ives 2008, 118). Clinically, deficiencies in vitamin D and calcium have also been linked to secondary hyperparathyroidism (Agarwal, Gupta, and Sukumar 2009; Lips 2001), which can cause bone loss, though specific mechanisms of cause and effect are not yet completely understood.

Ortner's "hunger osteopathies" were defined following observations of individuals who experienced starvation during the world wars (e.g. Dalydell and Chick 1921; Maratka 1946). In addition, post-war clinical studies have also repeatedly observed links between anorexia nervosa, osteopenia or osteoporosis, and osteomalacia (e.g. Herzog et al. 1993; Oliveri, Gomez Acotto, and Mautalen 1999; Rigotti et al. 1984; Soyka et al. 1999; Verbruggen, Bruyland, and Shahabpour 1993). The skeletal manifestations of the "hunger osteopathies" can develop later in life, as evidenced by longitudinal studies of child survivors of the Holocaust who went on to develop osteoporosis prematurely (Weisz and Albury 2013). This may be due to the "Barker hypothesis," which proposes that nutritional stress in early childhood or in utero can ultimately "program" an individual's physiology, creating long-lasting repercussions on development and health (Calkins and Devaskar 2011; Gowland 2015).

A thorough compilation of the academic literature surrounding these topics have demonstrated an association between starvation and osteoporosis. But is there any utility in using the "hunger osteopathies" for diagnosing starvation? At first glance, it would seem not, as both osteoporosis and osteomalacia have numerous etiological and risk factors besides starvation (e.g. age, sex, genetics, sunlight exposure, disease). The presence of these pathological conditions does not immediately constitute period(s) of starvation in an individual's life. However, Ortner (2003, 405) argues that a diagnosis of starvation is possible if the "hunger osteopathies" are predominantly found in the spine and occur in younger individuals. These factors allow for the ability to differentiate between osteoporosis and osteomalacia as secondary to starvation, as opposed to other causative factors, such as aging.

Additionally, the opportunity to observe the "hunger osteopathies" may be limited in bioarchaeological contexts as both osteoporosis and osteomalacia do not preserve well. The decrease in the inorganic component of bone associated with both conditions make it more susceptible to taphonomic and diagenetic degradation, the physical, chemical, and biological processes by which skeletal remains have been altered in the burial environment (Baker 1978, 108; Bartosiewicz 2008, 73). On a similar note, osteoporotic bone could be mistaken for taphonomically or diagenetically altered bone (Bartosiewicz 2008, 73). The non-diagnostic nature of osteoporosis and osteomalacia as well as the preservation bias of these conditions limit their application in inferring starvation from skeletal remains.

While these two limitations of complex etiologies and taphonomy to the study of "hunger osteopathies" are unlikely to change, advancements both in age-estimation techniques and in other bone biology fields may improve paleopathology's ability to study osteoporosis and osteomalacia in starvation contexts. According to Ortner, diagnosing osteoporosis and osteomalacia as secondary "hunger osteopathies" becomes more of a possibility if the individuals are younger adults, as age-related changes can be ruled out. However, this is challenging as many skeletal age-estimation techniques have large error rates that require individuals to be placed into wide age categories. Recently there have been developments in skeletal age-estimation techniques that focus on the correlation between age and changes in bone mineral density, degenerative disease, histology, dental pulp changes, and molecular markers (Ubelaker, and Khosrowshahi 2019) that could refine the

estimated ages of skeletal remains. Advancements in these techniques allow for more accurate assessments of whether osteoporosis is primary (age-related) or secondary in nature.

As discussed above, Zuckerman, Harper, and Armelagos (2016) argued that the advancement of the discipline of paleopathology has been historically hindered by its unwillingness to adopt scientific knowledge from other disciplines. However, recent paleopathological literature pertaining to osteoporosis and osteomalacia tells a different narrative, borrowing from skeletal anatomy and clinical studies to advance the discipline's knowledge of these two pathological conditions. For example, in a pilot study, Robertson and colleagues (2018) used a rodent model to examine the interplay between starvation and bone loss with the aim of extending their results to the archaeological record. Using micro-computed tomography (micro-CT), they mathematically and visually tracked changes in bone microarchitecture, observing marked loss in both trabecular integrity and number, and analyzed the corresponding isotopic changes in response to starvation. This study is one such example of an adoption of methods and practices common in other disciplines (e.g. controlled animal models, micro-CT) to advance the paleopathological study of starvation. Further research using animal models and high-resolution microstructural imaging modalities may lead to additional insights in starvation-specific bone microstructural changes or in differentiating taphonomic from osteoporotic changes, which will be useful in the study of the "hunger osteopathies." This study is promising, showing paleopathology's willingness to adopt procedures and knowledge from other disciplines. It represents one example of the new and emerging techniques in paleopathology which can potentially challenge Morgan's (2013) argument that starvation is invisible bioarchaeologically.

Starvation and Development: Signs of Arrested Growth

Starvation, when experienced during an individual's development, can have potent impacts on skeletal growth, as the body no longer has enough energy to expend on growth processes. Consequently, non-specific indicators of stress, particularly those linked to arrested growth, are often used in bioarchaeological contexts to infer periods of stress, such as starvation, from an individual's life. Such indicators include Harris lines of arrested growth or linear enamel hypoplasia (LEH). Mays (1995) argues that dental development is less susceptible to periods of stress than bone; therefore, inconsequential or short-term stress events may result in the formation of Harris lines but not LEH. On the other hand, bones remodel while teeth do not; therefore, childhood Harris lines resorb over time and are replaced with new bone, whereas LEH is a permanent record of physiological stress during development (Grolleau-Raoux et al. 1997). Assessing the presence or absence of each type of these particular stress indicators is therefore potentially useful in inferring the nature or severity of a stress episode. Use of these skeletal indicators to infer starvation in past populations is inherently limited by their non-specific nature; nutritional stress is simply one of many etiological factors that can cause skeletal arrests in growth. Nonetheless, the use of these indicators in conjunction with other skeletal evidence to infer starvation has frequently been employed in past bioarchaeological studies (e.g. Geber 2014; Huumonen et al. 2016; Lobdell 1984) and may continue to be warranted.

Harris lines are observed radiographically as opaque, transverse lines parallel to the epiphyseal plate of bones, and they represent disruptions in longitudinal endochondral bone growth (Mays 1985, 207). Under normal circumstances, cartilaginous cells would proliferate, forming a columnar framework

that would later become ossified through osteoblastic activity (Mays 1985, 208). During disruptions in growth (caused, for example, by a lack of nutrients), cartilaginous growth ceases prior to maturing and osteoblastic activity lessens. Shrunken osteoblasts deposit bone gradually beneath the immature avascular cartilage cap, forming a thin primary stratum of trabeculae (Park 1964, 816-818). When normal cartilaginous and osteoblastic activity resumes (for example, due to the restoration of adequate nutrition), initial osteoblast deposition will occur along the primary stratum until the cartilage template has matured and vascularized, thickening this stratum to where it can be observed radiographically.

Harris lines are sometimes used by bioarchaeologists to indicate periods of starvation and subsequent partial to complete recovery. Early studies linked Harris lines to periods of stress, particularly nutritional deficiency (Park and Richter 1953), though the presence of Harris lines was later expanded by scholars to encompass stressful childhood events such as illness or trauma in addition to nutritional insults. However, later studies have shown that this relationship is not as clear or reliable as initially proposed. Papageorgopoulou and colleagues (2011) show that Harris lines can result from normal growth spurt processes among children who were not under considerable physiological or nutritional stress. Additionally, some children who do suffer from consistent physiological stress do not manifest Harris lines, as partial nutritional recovery is required for their formation (Lewis and Roberts 1997, 583). Therefore, caution should be exercised when analyzing Harris lines and nutritional conclusions should only be drawn when formulated from multiple sources of skeletal evidence.

Enamel hypoplasias are a class of enamel formation defects often caused by a metabolic disruption. During early development, tooth enamel grows incrementally, manifesting as microscopic striae referred to as lines of Retzius. Linear enamel hypoplasia (LEH) can result when non-specific physiological stress disrupts ameloblastic enamel formation, presenting as linear grooves of thinned enamel along the crown of the tooth (Goodman and Rose 1991). While enamel is extremely sensitive to nutritional stress, Goodman and Rose (1991) caution that similar to Harris lines, LEH lacks specificity. In addition to periods of starvation, physiological and external stressors originating from weaning, infection, disease, or the environment are of potential etiological factors behind LEH (Katzenberg, Herring, and Saunders 1996; Méndez Collí et al. 2009).

The non-specificity of these indicators of arrested growth do pose limitations in their use as indicators of starvation. However, if the presence of Harris lines and LEH are used in conjunction with other approaches (e.g. "hunger osteopathies," stable isotopes), there is more potential to establish starvation as an etiological factor for these growth arrests. However, the complex etiologies of these indicators of arrested growth are not the only limitation in the application toward the issue of inferring starvation from the skeleton. There remains numerous data collection and analysis issues in the study of Harris lines and LEH, which impede their paleopathological observation at all, not including their use in inferring starvation-derived stress.

Assessing Harris lines comes with a myriad of methodological issues, including inter-observer error and underestimation due to the convention of assessing lines in the anterior-posterior view. These two issues have been addressed recently in scholarly literature. First with regards to the individual error problem, Suter and colleagues (2008) employed a semi-automatic Harris line detection software capable of detecting 60–65% of lines in order to reduce inter-observer error. Second, Harris lines have conventionally been assessed radiographically in the anterior-posterior view; however, in a recently published paper, Scott and Hoppa (2015) found that while it is

conventional to take radiographs of Harris lines in the anterior-posterior view, radiographs in the medial-lateral view actually reveal more lines. This finding potentially addresses the inconsistencies of Harris line formation previously published in the literature. Use of semi-automatic detection software and radiographs in different anatomical views will potentially standardize the assessment of Harris lines paleopathologically and gain more accurate estimates of their prevalence in past populations, and by extension, their use in inferring nutritional stress.

There are also some limitations in observing LEH which in turn, impacts the utility of LEH as a reliable indicator of stress and consequently, starvation. First, analysis of LEH can be hindered by the fact that only some lines of Retzius (and perikymata, their external expressions) are macroscopically visible due to line spacing, line continuity, and teeth curvature (Cares Henriquez and Oxenham 2017). Discontinuous, compact, or nonlinear hypoplastic defects are difficult to detect. Second, macroscopic evaluation of perikymata is not possible if teeth are unerupted or in regions of teeth where perikymata are not externally visible, and semi-destructive microscopic histology is not always an option with valuable bioarchaeological skeletal material. However, recent advancements in analysis of perikymata have addressed these limitations. Henriquez and Oxeham Cares (2017)employed a Micro Polynomial method for cases in which perikymata are not entirely visible on the enamel surface. This method allowed them to detect subtle depressions on the enamel surface in order to examine LEH in such cases when perikymata are not entirely visible but still represent temporary arrests in enamel secretion. With regards to the problem of observing perikymata which are not visually accessible, advancements in high-resolution imaging modalities may prove useful. For example, Le Cabec and colleagues (2015) used

synchrotron radiation micro-computed tomography (micro-CT) to assess perikymata noninvasively and non-destructively within unerupted hominin teeth.

On paper, Harris Lines and LEH represent a useful means to investigate past nutritional stress. However, in practice, the application of these skeletal indicators to study starvation has been hindered by their complex etiologies not specific to starvation and methodological limitations commonly used to assess them. Use of Harris Lines and LEH in conjunction with other approaches to detect starvation may in part address the inability to "pin down" their etiology, and improvements in methods used to detect these growth arrests will refine their use in paleopathology overall. In the last few years, there has been several methodological advancements in detecting skeletal growth arrests. Often, due to issues with observer error and lack of visibility when using conventional methods, Harris Lines and LEH cannot be accurately assessed paleopathologically. The recent techniques pioneered by Cares Henriquez and Oxenham (2017), Le Cabec, Tang, and Tafforeau (2015), Scott and Hoppa (2015), and Suter and colleagues (2008), and have improved the reliability of the assessment of these skeletal growth arrests.

"Wasting Away": Stable Isotopes and Starvation

Stable isotopes of carbon and nitrogen serve as potentially useful indicators of starvation and nutritional stress in past human diets, but in practice, their use has previously been limited by their lack of temporal resolution. In this regard, the discipline has methodologically advanced through the technique of microsampling dental tissues to track shortterm isotopic changes.

The chemical analysis of stable isotopes is widely used in bioarchaeology as a source of information for paleodiet (Harrison and Katzenberg 2003; Prowse et al. 2004; Rissech et al. 2016), environment (e.g. water stress) (Ambrose and DeNiro 1987), breastfeeding and weaning practices (Burt 2013; Fuller et al. 2006), migration and residence (Dupras and Schwarcz 2001; White, Price, and Longstaffe 2007), and body physiology (Katzenberg and Lovell 1999; D'Ortenzio et al. 2015). Carbon and nitrogen isotopes are typically analyzed in making paleodietary inferences, but they are also a potentially useful source of information for interpreting physiological stress, including starvation.

The ratio of two carbon isotopes ¹³C and 12 C, denoted by δ^{13} C, often reflects whether the diet is based more heavily in C₃ or C₄ plants. These plants follow different photosynthetic pathways, meaning they fix CO₂ differently, resulting in different ratios of stable carbon isotopes. C3 plants, such as trees, shrubs, and temperate grasses, fix carbon by the Calvin Benson photosynthetic cycle, and C₄ plants, mostly tropical grasses, fix carbon by the Hatch-Slack cycle (Katzenberg 2008, 423; van der Merwe 1982). As C3 plants are depleted in 13 C relative to C₄ plants, it is possible to infer the relative contributions of each to diet (Katzenberg 2008, 423). Additionally, analysis of $\delta^{13}C$ can aid in differentiating between marine and terrestrial resources, as the main source of carbon for marine resources is dissolved carbonate whereas the main source of carbon for terrestrial resources is atmospheric CO₂ (Katzenberg 2008, 425).

Nitrogen isotopes provide information pertaining to trophic level. The proportion of ¹⁵N to ¹⁴N, represented by the notation δ^{15} N, differ among different plants according to their nitrogen-fixing properties: legume plants fix nitrogen, resulting in a ¹⁵N level close to atmospheric nitrogen levels whereas non-leguminous plants have elevated nitrogen levels (DeNiro and Epstein 1981). δ^{15} N is a valuable reflection of the protein sources of diet and can be used to infer trophic level in diet, as a stepwise 3‰ enrichment occurs with each increase in trophic level due to the fractionation of protein in which amino acids are broken down and synthesized (Katzenberg 2008, 425; Reitsema 2013, 446).

How does this relate to physiological stress and starvation? Insufficient protein in the diet will force the body to catabolize its own tissues for protein. First observed by Hobson and colleagues (1993) in avian tissues, a state of starvation will induce the phenomenon of "wasting away," in which a body catabolizes its own tissues, resulting in an enrichment of nitrogen due to a trophic level increase. This isotopic phenomenon has also been observed in hair, as shown in clinical studies of anorexia nervosa patients (Mekota et al. 2006), and in forensic cases of suspected elder abuse (Baković, Vreča, and Mayer 2017). This process is not strictly linked to starvation, however, studies of bone and hair have shown that a similar effect occurs when individuals experience diseases such as chronic infection (Katzenberg and Lovell 1999), chronic illnesses (such as cancer and related cachexia; D'Ortenzio et al. 2015), or celiac disease (Scorrano et al. 2014). These diseases result when nitrogen enrichment occurs either as a result of the body diverting resources toward an immune or reparative response or due to tissue catabolization from a wasting condition.

However, while theoretically useful in interpreting starvation bioarchaeologically, there are some issues with these methods. As bones constantly remodel, they represent an isotopic average spanning several years (Sealy, Armstrong, and Schrire 1995) and therefore, short-term dietary or physiological changes, including those occurring immediately before death, may not be evident isotopically. This, incidentally, forms the basis of Morgan's (2013) argument that stable isotopes are insufficient indicators of starvation. Scholars have attempted to overcome this limitation by comparing stable isotope levels in teeth and bones (Sealy, Armstrong, and Schrire 1995) or by comparing isotope levels in the developed bone diaphysis to levels in the growing metaphysis (Waters-Rist et al. 2011). However, while constituting a substantial improvement to the isotopic averaging problem, these approaches arguably still lack the temporal sensitivity required to diagnose periods of starvation.

Julia Beaumont and colleagues (2013, 2016) have aimed to overcome this limitation by microsampling tooth dentine to detect short-term isotopic changes. Dentine forms according to both short-period, circadian rhythms (appearing as von Ebner's lines) and long-period rhythms (appearing as Andresen lines) developing in more or less weekly increments (Fitzgerald and Rose 2008, 241–242, 245). By microsampling dentine increments, either manually or with laser ablation methods, it becomes possible to track short-term shifts representing isotopic realities at the time of odontoblast secretion that would not be distinguishable in bone collagen.

While microsampling dentine was first employed to study weaning practices (see Eerkens, Berget, and Bartelink 2011), Beaumont and colleagues (2013, 2016) used this technique to investigate, with high temporal resolution, the Great Irish Famine (1845-1852). Beaumont and colleagues (2013) discovered likely Irish immigrants within the Lukin St. cemetery (London, England) based on dentine isotopic profiles. Then, in a study of the Kilkenny Union workhouse housing victims of the Irish Famine, Beaumont and colleagues (2016) studied the carbon and nitrogen isotope levels within dentine layers corresponding to approximately semi-annual intervals and compared the dentine levels with those contained within bone collagen. Initial dentine increments showed high $\delta^{15}N$ and low δ^{13} C corresponding to a period of starvation in which nitrogen isotope levels are elevated from "wasting away." Within many individuals, however, there was a shift to higher $\delta^{13}C$ and a fall in $\delta^{15}N$ corresponding to the adoption of the "Indian meal," a maize (C₄ plant) diet imported from America (Beaumont et al. 2016, 13).

These micro-sampling methods may also allow for starvation events to be observed in bone; due to the ability for bone to represent isotopic averages of several years to decades. This is because bone constantly remodels; localized resorption events that break down bone occur in concert with the formation of new osteons (the fundamental structures of bone). Therefore, it may be possible to observe minute and short-term changes in the chemical composition of bone related to nutritional stress by sampling from individual osteons themselves. Scharlotta and colleagues (2013) laser ablation-inductively coupled used plasma-mass spectrometry to evaluate isotopic changes in strontium in bone within a single osteon in order to evaluate changes in migration patterns. This methodology could similarly be applied to evaluate intra-osteonal changes in carbon and nitrogen isotopic related to starvation.

The improvement in temporal resolution of stable isotope analysis to detect periods of nutritional stress is crucial to paleopathological studies of starvation. Prior to the use of either metaphyseal bone collagen sample (e.g. Waters-Rist et al. 2011), or more recently, incremental dentine samples for stable isotope analysis (e.g. Beaumont et al. 2013, 2016), stable isotope analysis of skeletal remains represented a dietary average and therefore was not a useful means to detect short-term dietary changes. The onset of microsampling incremental structures for stable isotope analysis has already shown its potential for the study of starvation bioarchaeologically and therefore challenges the view that starvation is indistinguishable in skeletal remains.

CONCLUSION

In a 2013 review, Morgan argued that in the absence of documentary or iconographic data, famine and starvation are invisible; in other words, skeletal remains do not contain enough information for paleopathologists to infer periods of famine or starvation. This paper, in response, has challenged this argureviewing paleopathological ment by approaches previously used in the study of starvation, discussing both the limitations of each approach as well as showcasing new and emergent techniques that may improve the utility of each approach in inferring starvation. While the study of starvation remains constrained by the above-mentioned limitations, such as the osteological paradox as well as the non-specificity of osteological conditions, recent advancements in the discipline show potential for the study of starvation.

The use of the "hunger osteopathies" (i.e. premature secondary osteoporosis with some overlay of osteomalacia) to infer starvation has been limited by a number of factors. However, improvements in age estimation may help elucidate whether osteoporosis is primary or secondary, and the discipline of paleopathology as a whole has shown a recent willingness to borrow methodological approaches from other fields in order to advance its understanding of these conditions. As non-specific signs of stress with several methodological issues, Harris Lines and linear enamel hypoplasia have numerous issues when used to assess physiological stress. However, recent advancements in standardization and visualization of these growth arrests may increase the overall accuracy of their use in paleopathology, and by extension, studies of past starvation. Stable isotopes of carbon and nitrogen have the potential to represent the phenomenon of "wasting away"; however, bones represent an isotopic average and lack the temporal resolution to reflect short-term dietary and physiological changes. Recent advancements in microsampling incremental structures such as dentine are extremely promising for overcoming this limitation. In sum, taking multiple lines of evidence together presents a stronger case for starvation in the bioarchaeological record that may be further strengthened by the multitude of technological advancements and emergent techniques that the field has adopted

within the last decade. Overall, advancements within the last decade provide an optimistic view of future prospects for the paleopathological analysis of starvation, challenging Morgan's (2013) argument that starvation is invisible bioarchaeologically.

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