Totem: The University of Western Ontario Journal of Anthropology

Volume 20 | Issue 1 Article 7

7-1-2012

Diffuse Idiopathic Skeletal Hyperostosis and the Osteological Paradox

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Abstract
Diffuse idiopathic skeletal hyperostosis (DISH) is of interest to bioarchaeologists due to its strong associations with male sex, increased age, and potential associations with obesity, related metabolic conditions, and high social status. However, these possible associations and DISH's contested status as a pathologic condition raise issues concerning how DISH must be viewed through the lens of the osteological paradox, particularly relating to selective mortality and heterogeneity of frailty. This article explores these concerns by examining recent clinical and bioarchaeological research on the symptomatology, etiology, and epidemiology of DISH and examines how bioarchaeologists should approach the paleoepidemiological interpretation of DISH.

Keywords
Diffuse idiopathic skeletal hyperostosis (DISH), osteological paradox, paleoepidemiology, vertebral conditions

Acknowledgements
The author is the recipient of funding from the Manitoba Graduate Scholarship (MGS) (2008-2010), Social Sciences and Humanities Research Council (SSHRC) (2009-2010), Manitoba Health Research Council (MHRC) (2010-2012), and Western Regional Training Centre for Health Services Research (WRTC) (2010-2011). The author reports no conflicts of interest.

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Introduction

Diffuse idiopathic skeletal hyperostosis (DISH) was first recognized by Forestier and Rotés-Querol (1950) as a vertebral condition distinct from degenerative joint disease (Crubézy and Trinkaus 1992). DISH manifests as the complete and total fusion of the spine and the ossification of the anterior longitudinal spinal ligament and paraspinal ligament. It particularly affects the anterio-lateral aspect of the thoracic vertebrae, and large flowing 'candlewax' osteophytes (bony growths) appear on the right side of the spine. Extraspinal manifestations are also common and frequently manifest in: the pelvis including 'whiskering' ossification at the iliac crest, iliolumbar ligament, and ischial tuberosity, the trochanters of the femur (Arriaza 1993), the insertion of the Achilles tendon and the planter fascia into the calcaneum, the triceps tendon into the olecranon process, the insertion of the patellar tendon (Rogers and Waldron 2001), the deltoid tuberosity, and the shaft of long bones (Arriaza 1993). Although this condition is referred to by numerous terms in the literature, DISH is the most accepted term in clinical medicine and paleopathology.

Bioarchaeological studies of DISH extend across a diverse temporal and geographical range. It has been found in Neanderthal remains from the Middle Paleolithic in Iraq and the Late Pleistocene in Crimea (Crubézy and Trinkaus 1992; Trinkaus, Maley, and Buzhilova 2008). DISH was present in an Egyptian mummy (Chhem, Schmit, and Faure 2004) and has been found often in Egyptian and African case studies (Hussien et al. 2009; Dupras et al. 2010). It was present in both the New and Old Worlds from 5000 years ago (Arriaza 1993) and in Japan from the Jomon period (Oxenham, Matsumura, and Nishimoto 2006). DISH has also been researched in Medieval Dutch sites (Mays 2000; Verlaan, Oner, and Maat 2007), in first and second century Lithuanian sites (Jankauskas 2003), in Meriotic Nubians, and in Medieval Switzerland (Kramer, Lagier, and Baud 1990). DISH was also reported from Italy (Canci et al., 2005; Fornaciari et al., 2009), and scattered cases continue to be reported from China (Hukuda et al. 2000). The area which has produced the most research is Northwestern Europe, particularly Britain (Rogers, Waat, and Dieppe 1985; Waldron 1991; Mays 2000; Rogers 2001; Rogers and Waldron 2001).

DISH is of particular interest to mortuary archaeologists, and anthropologists in general, due to its strong correlation with advancing age, the male sex, and, possibly, high caloric intake, which may be indicative of high social status (Rogers and Waldron, 2001). DISH's distinguishing characteristics, its idiopathic nature, its frequent asymptomatic status, and its association, if not causal relationship, with numerous metabolic disorders, raise intriguing possibilities as to how DISH should be viewed within a paleoepidemiological context. These characteristics of DISH result in unique opportunities and limitations in its incorporation in studies designed to determine or compare the health statuses of past populations. These studies must attempt to reconcile the skeletal biases that have come to be collectively known as the osteological paradox, and DISH is uniquely situated for consideration of two of these potential biases: hidden heterogeneity of frailty and selective mortality (Wood et al 1992). This review will address current research on the etiology and epidemiology

of DISH, before examining how current clinical research can inform bio-archaeological studies on how DISH relates to selective mortality and how studies including DISH can attempt to reconcile biases introduced by heterogeneity of frailty.

Diagnosis of DISH

The clinical diagnosis of DISH is reliant on Resnick and Niwayama's (1976) highly specific criteria:

1. The presence of flowing calcification and ossification along the anterolateral aspect of at least four contiguous vertebral bodies with or without associated localized pointed excrescences at the intervening vertebral body-intervertebral disc junctions.
2. The presence of relative preservation of intervertebral disc height in the involved segment and the absence of extensive radiographic changes of 'degenerative' disc disease, including vacuum phenomena and vertebral body marginal sclerosis.
3. The absence of apophyseal joint bony ankylosis and sacroiliac joint erosion, sclerosis, or-intra-articular osseous fusion.

Few individuals will receive a false positive diagnosis of DISH. However, the diagnostic criteria for DISH are low in sensitivity, and many affected individuals will likely go undiagnosed (Utsinger 1985). In bioarchaeological studies, criteria for a diagnosis of DISH vary between studies and researchers. Some criteria include: fusion of the anterior longitudinal ligament, with no specification for number of fused vertebrae (Kramer, Lagier, and Baud 1990; Arriaza 1993; Arriaza, Merbs, and Rothschild 1993; Maat, Mastwjit, and Van Der Velde 1995); at least two complete bony bridges in the thoracic spine and fusion (Mays 2000), or involvement of four contiguous vertebral bodies (Rogers, Watt, and Dieppe 1985; Waldron 1991; Rogers and Waldron 2001). Less stringent criteria include anterior longitudinal spinal enthesis, or extra-spinal ligament ossification (Jankauskas 2003). Rogers, Shepstone, and Dieppe (1997) believe that the archaeological material may allow for the recognition of the disease at earlier stages than clinical studies. They feel that the ossification of the anterior spinal ligament and extra spinal bone growth are the key pathognomic features for the diagnosis of DISH in skeletal remains.

Conditions to be considered when differentially diagnosing DISH include acromegaly (excess adult growth hormone production), fluorosis (excessive fluoride exposure), ochronosis (excess acid in connective tissues), seronegative spondylo-arthropathies (rheumatoid factor negative joint conditions of the vertebral column), and degenerative osteophytes (Arriaza 1993; Masiero et al. 2006). Seronegative spon-dyloarthropathies typically affect different portions of the spine than DISH. Ankylosing spondylitis (AS) is the seronegative spondyloarthropathy that most closely approximates DISH. However, DISH does not involve apophyseal, costovertebral, and sacroiliac fusion, and the spine retains its flexibility, unlike in AS. Additionally, squaring of the vertebrae does not take place. The longitudinal ligament takes on a thicker appearance, particularly the right side, due to ossification, while the syndesmophytes (bony growths in ligaments) in AS appear thin. Furthermore, DISH predominantly affects middle-aged to older adults, while AS affects the young (Arriaza 1993).

Epidemiology of DISH

Clinically, the prevalence of DISH varies by ethnic group and geography

(Rogers and Waldron 2001). Typically, DISH prevalence increases with age, and the condition is more common in males. The highest prevalence rates were found in two large American populations (Weinfeld et al. 1997). Twenty-five percent (25%) of males and 15% of females over the age of 50 had DISH. Similar rates were found in a Jewish community (Mader et al. 2005), but it is less common in American black, Asian, and indigenous populations (Weinfeld et al. 1997). However, the American Pima have extremely high rates, which were found to increase with age (Spagnola, Bennett, and Terasaki 1978). Rates in Korea were found to be considerably lower, with an overall prevalence of 2.9%, and men approximately seven times more likely to be affected than females. Again, prevalence increased with age (Kim et al. 2004). DISH was found in 3.9% of African blacks taken from a hospital population, which is higher than the prevalence rates for American blacks (Utsinger 1985). A study on the general population in Scandinavia found a prevalence of 3.8% of DISH in men and 2.6% in women. This prevalence also increased with age.

The prevalence of DISH in the past may be underestimated due to confusion with AS (Rogers, Watt, and Diepe 1985). Regardless, clinically established prevalence rates should not be directly compared with bioarchaeological prevalence rates. Many clinical prevalence rates for DISH are based on inherently biased populations. Additionally, radiological examination will inevitably result in underestimation compared to dry bone analysis (Maat, Mastwjit, and Van Der Velde 1995). In addition to these diagnostic and epidemiological issues, the bioarchaeological study of DISH is complicated by its uncertain etiology.

Etiology of DISH

Despite numerous attempts to elucidate the causative mechanisms, the etiology of DISH remains uncertain. Hypotheses have included genetic, dietary, toxic, anatomic, environmental, endocrinological, and metabolic factors (Sarzi-Puttini and Atzeni 2004). Despite the breadth of research and the factors considered, none of these proposed hypotheses have adequately, and without contradiction, been linked to DISH causation. The most likely causative hypotheses, which have been proposed in paleopathological, epidemiologic, and clinical research will be examined.

Vitamin Toxicities

Hypervitaminosis A has been implicated as a possible cause of DISH (Pennes et al. 1984; Abiteboul and Arlet 1985). The data currently available on the diets of the populations most susceptible to DISH do not support the hypothesis that an excess of vitamin A was consumed. Additionally, Harvey (1993), and a more recent study found no association between bone changes and chronic, low-dose retinoid therapy, the administration of Vitamin A-related chemicals for the treatment of psoriasis (Halverstam, Zeicher, and Lebwohl 2006). In their comprehensive review on DISH found in UK monastic sites, Rogers and Waldron (2001) have speculated that the frequent identification of DISH in monks may be attributed to the monks' consumption of insufficient vitamin A. Vitamin A deficiencies may affect eyesight, and one common contemporary treatment was liver ingestion (Oxenham, Matsumura, and Nishimoto 2006). This treatment, if taken in excess, may have caused hyperovitaminosis A, thereby furthering the monks' susceptibility to DISH. A study on DISH in Japan during the Jomon period, however, found no evidence of Hypervitaminosis A among subadults,

suggesting either that the population consumed a different diet throughout life or that Hypervitaminosis A was not an issue, despite the presence of DISH (Oxenham, Matsumura, and Nishimoto 2006).

Physiological Factors

Another posited mechanism of DISH development relates to spinal function. The proposed mechanism is that thoracic immobilization may predispose to DISH by enhancing the likelihood of connective tissue transforming into bone. However, this etiology appears unlikely, given the lack of cartilage fusion between the sternum and the lower five thoracic vertebrae that allows for the inherent thoracic spine flexibility (Sarzi-Puttini and Atzeni 2004). This proposed mechanism also does not explain the manifestation of DISH in the lumbar or cervical spine or throughout the body. Recent research into genetic susceptibility of DISH appears more promising in delineating DISH etiology.

Genetic Factors

Further clinical tests are required to determine the exact relationship between genetics and DISH, although current research has indicated that it is likely a disease with autosomal dominant inheritance (Utsinger 1985; Oxenham, Matsumura, and Nishimoto 2006). DISH has been found to have varying levels of incidence in different ethnic groups. Africans have lower levels of DISH than Europeans and Israelis, and the manifestation of DISH in East Africans involves more common ossification of the posterior longitudinal intervertebral ligaments than in European populations. Obesity has also been shown to associate with European sufferers of DISH but not with Japanese individuals with DISH (Mays 2000), possibly suggesting genetic variants in DISH etiology.

The presence of the gene for the HLAB27 tissue type is associated with a number of erosive arthropathies (joint diseases) such as seronegative spondylo-arthropathies and gout. It has also been explored as a causative factor for DISH (Mays 2000). The alleged relationships between tissue type HLAB27, gout, and DISH have not been evident in all clinical studies. While populations containing individuals with DISH have also been shown to contain individuals who suffered from seronegative spondyloarthropathies and gout, co-morbidity of DISH and these other erosive arthropathies was not found (Mays 2000). Studies conducted on modern Pima Indians, who have an increased prevalence of DISH and tissue type HLA-B27, did not find a significant correlation between the two conditions (Spagnola, Bennett, and Terasaki 1978).

Another gene, COL6A1, has recently been shown to have an association with susceptibility to DISH in Japanese, but not Czech, individuals, who do not additionally suffer from ossification of the posterior longitudinal ligament (OPLL). This suggests a possible, very specific, genetic etiology within one ethnic group. Additional support for a genetic etiology is at least one case of a modern, British familial association of DISH (Gorman, Jawad, and Chikanza 2005).

'Bone formers', members of the population who produce excessive osteo-phytes and enthesophytes (bony growths at tendon attachment sites), due to osteo-arthritis, aging, or other conditions, may also be susceptible to DISH. Enthesophyte formation also correlates strongly with the male sex and advanced age. Enthesophyte formation may also result from repeated minor trauma, or in response to the inflammation of the enthesis (attachment site of muscle or ligament to bone) of seronegative spondyloarthropathies (Rogers, Shepstone, and Dieppe 1997; Rogers and

Waldron 2001). Therefore, DISH may be explained as the manifestation of an extreme disposition to bone forming. Beyond genetics, clinical and archaeological researchers have proposed a variety of endocrinological contributors to DISH incidence.

Endocrinological Factors

A great number of studies have also suggested that there is an association between DISH and type II diabetes mellitus or DISH and hyperinsulinemia (excess insulin in blood) (e.g. Hájková, Streda, and Skrha 1965; Littleton 1985; Utsinger 1985; Denko, Boja, and Moskowitz 1994; Kiss et al. 2002; Mader and Lavi 2009). Both of these conditions are frequently associated with obesity in epidemiological studies. Some clinical studies have failed to confirm the association between diabetes and DISH, while recognizing that other metabolic abnormalities related to obesity, including alterations in lipid metabolism, hyperuricaemia (excess uric acid in blood), dyslipidemia (excess lipids in blood), and greater body lipid index are present (Mata et al. 1997; Miyazawa and Akiyama 2006). The relationship between DISH and obesity has been acknowledged since its initial description (Forestier and Rotés-Querol 1950). Given the complex relationships between cardiometabolic conditions and obesity, and the possible associations of DISH with these conditions, diabetes may be a confounding factor in the etiology of DISH, rather than truly implicated in its causation (Daragon et al. 1995).

The relationship between DISH and hyperinsulinemia, hyperuricemia, dyslipidemia, and possibly, diabetes mellitus, are currently best approached from a hypothesis incorporating metabolic syndrome, which is causatively linked to high caloric intake (Jankauskas 2003). The metabolic syndrome is a broad condition, which includes a higher body mass index (BMI), diabetes mellitus, dyslipidemia, hyperuricimea, and hyperinsulinenia (Oxenham, Matsumura, and Nishimoto 2006) or a multi-system hormonal disorder (Denko, Boja, and Moskowitz 1994; Rogers and Waldron 2001). This hypothesis also gathers support from recent studies that have established DISH's association with risk factors for stroke and cardiovascular disease (Mader, Dubenski, and Lavi 2005; Mader et al., 2009; Miyazawa and Akiyama 2006), which are similarly related to metabolism. Again, these associations may be confounded by obesity (Mader, Dubenski, and Lavi 2005).

The proposed mechanism linking metabolic abnormalities and DISH is physiologically complex and has been recently reviewed by Sarzi-Puttini and Atzeni (2004). The initial site of spinal ossification may occur within the innermost layer of the anterior longitudinal ligament, at the vertebral attachment site. Abnormal cell growth and activity occurs at this site, culminating in the spread of vertebral ossification. This localization may be the production of hypervascularity, proliferation and expansion of nutrient foramina, evidence of which, has been detected in DISH afflicted tissues (El Miedany, Wassif, and El Baddini 2000).

Growth factors regulate the growth of osteoblasts (bone forming cells) (Fawcett 1994); and Vetter and colleagues (1986) have demonstrated that chondrocytes and osteoblasts may be stimulated by growth hormone to produce insulin-like factor 1 (IGF-1) and insulin-like factor binding proteins, which induces osteoblastic phosphatase activity and type II collagen. High levels of growth hormone and insulin have been detected in DISH patients (Denko, Boja, and Moskowitz 1994), and this may explain the proliferation and expansion of osteoblasts within DISH sufferers.

An additional proposed mechanism involves the immune response to the development of an atherosclerotic lesion, an accumulation of plaque in arterial walls (Fawcett 1994). Diabetes mellitus, hyperlipidemia, and hyperinsulinemia are all risk factors for atherosclerosis, the first phase of which involves the formation of a lesion. This injury may result in the accumulation of platelet-derived growth hormone and subsequent osteoblastic proliferation. Also potentially implicated is nuclear-factor kβ, which may stimulate the differentiation of osteoblasts, upon environmental and growth hormone stimuli (Kosaka et al. 2000). Mechanical stress may also serve a function in stimulating osteogenic differentiation in spinal ligament cells (Ohishi et al. 2003).

Matrix Gla protein (MGP) is an extracellular mineral-binding protein present in tissues with a high concentration of bone and cartilage. It has also been hypothesized to play a not yet fully elucidated role in DISH etiology (Sarzi-Puttini and Atzeni 2004), as it is present to a higher extent in patients with DISH than in individuals without DISH. The precise nature of MGP's function is not fully understood but appears to involve the prevention of bone mineralization.

The etiology of DISH remains incompletely understood. Amongst the numerous proposed pathways, the likeliest would seem to involve hormone abnormalities stimulating growth factors and related molecular substances to increase osteoblastic activity. This osteogenesis begins at the innermost layer of the anterior longitudinal ligament and spreads throughout the vertebrae (Sarzi-Puttini and Atzeni 2004). Given the uncertain causation of DISH, it is essential for bioarchaeologists to remember that no associations between metabolic abnormalities and DISH have been completely supported, particularly when they are attempting to assess the possible susceptibilities to DISH in a once-living population.

DISH and Selective Mortality

DISH is generally asymptomatic in modern individuals, and this has called its morbid nature into question (Hutton 1989). It has even been contended that DISH may be an adaptation to increasing longevity and subsequent somatic degeneration, as increased skeletal stress on the body may have resulted in hyperostosis to strengthen and support a weakened bodily frame (Arriaza 1993; Arriaza, Merbs, and Rothschild, 1993). A study designed to determine the relative rate of back ache between those with and without DISH found no significant differences in pain frequency between DISH sufferers and controls, lending credence to the non-morbid theory. However, a subsequent study by Mata and colleagues (1997) found statistically significant increased levels of pain, stiffness, and disability in DISH cases compared to controls. The contention that DISH is a state and not a disease, and that it may even serve as an adaptive function, influences the manner in which it must be perceived in relation to the osteological paradox (Wood et al. 1992).

One component of the osteological paradox, which acts to bias cemetery samples and confuse paleoepidemiological analyses, is selective mortality. Selective mortality operates under the principle that the frequency of skeletons with lesions retrieved from archaeological sites will inevitably overestimate the prevalence of the condition in the once-living population. This is a result of the lesions being indicative of a condition that would have rendered the individual more susceptible to death in some manner, however indirect, than individuals who did not manifest the lesion. If DISH is simply a skeletal peculiarity, which does not influence an individual's health or

functioning, then selective mortality is not in effect. The frequencies of DISH retrieved from burials should thus more accurately reflect the prevalence of DISH in once living populations, taking into account the effects of differential preservation.

Regardless of how DISH relates to the osteological paradox, its status as an actual morbid condition or simply a physiological, clinically irrelevant abnormality, must be established to ensure the validity of paleoepidemiological studies that include DISH as a disease category or use the relative frequencies of DISH in populations to compare health statuses. Its inclusion in paleopathological studies must also be addressed, if it does not, in fact, provide any insight into an individual's, and by extension, a population's, health status. That DISH is associated with metabolic abnormalities does not necessarily establish that DISH compromises health. It is likely impossible from skeletal remains to truly determine the presence or absence of the metabolic condition. In order to properly address this issue, the symptomatology of DISH as demonstrated in modern clinical literature must be assessed.

DISH Symptomatology

Non-specific aching, non-productive cough, dysphonia (voice disorders), foreign body sensation, vertebral artery insufficiency, nocturnal snoring, recurrent laryngeal nerve palsy, Horner syndrome, laryngeal edema (swelling), and spinal cord immobilization have all been attributed to spinal DISH (Marks, Schober, and Swoboda 1998; Karkas et al. 2008; Jeannon et al. 2008). Extraspinal DISH may present as pain, stiffening of the soft tissues, and movement restriction in the fingers, elbow, and shoulder (Childs 2004). Excresences (abnormal outgrowths) may develop in the calcaneous and olecranon, which further limit the range of movement. Additionally, nodular masses may develop in the quadriceps-patellar tendon (Childs 2004). While size of the osteophytes may be a factor in how DISH presents, the more potent criteria appears to be location of the osteophytes, particularly in those instances when DISH has spread into the cervical vertebrae (Seidler et al. 2009).

Dysphagia (difficulty swallowing) is one of the most commonly reported symptoms of DISH (Jeannon et al. 2008). Dysphagia can result in difficulty in eating and subsequent weight loss, aspiration, pneumonia, lower respiratory tract infections, and staphylococcus septicaemia (Masiero et al. 2006; Ambrose, Smith, and Cunnane 2008). DISH's exact involvement with dysphagia is unknown. Several possibilities have been suggested including compression of the esophagus, and subsequent inflammation, fibrosis (excessive connective fibre growth), and adhesion. This would compromise the normal gliding movement of the esophagus, through the presence of osteophytes at the cricoid cartilage (Jeannon et al. 2008). Approximately 17 to 28% of individuals with DISH manifest dysphagia (Galiano et al. 2005). This may be an underestimation due to misdiagnosis or being a less significant symptom reported in case series (Eviatar and Harell 1987). While conservative treatments (swallow therapy or dietary modifications) are the most frequent treatment for dysphagia, surgical decompression is necessary in approximately 10% of cases (Galiano et al. 2005). As in most symptomatic responses to DISH, cervical vertebrae osteophytes are implicated more frequently than thoracic or lumbar vertebrae (Nelson, Urquhart, and Faciszewski 2006).

Dyspnea (shortness of breath) is a relatively uncommon symptom of DISH, and sleep apnea may also result from DISH (Naik, Lobato, and Sulek 2004). Dyspnea may occur as the result of compression of

the areodigestive tract or tissue irritation and subsequent inflammation, edema, fibrosis, ankylosis (stiffening) and compression of nerves, which may compromise vocal cord and laryngeal mobility (Giger, Dulguerov, and Payer 2006). Although surgery is, again, advocated in instances of severe airway compression, some patients have died from respiratory arrest immediately post-surgery or from compression of the trachea (Eviatar and Harell 1987).

DISH can also result in dangerous neurological situations, including cervical spine pathology, or spinal cord compression (Pascal-Moussellard et al. 2006). Patients often present with gait disturbance, motor deficiencies, loss of sensation or paraplegia (Pascal-Moussellard et al. 2006). In these cases, soft tissue masses frequently form posterior to the odontoid process (the protuberance of the second cervical vertebrae), which compress the spinal cord. The mass is often formed from connective tissue and cell-degenerated cartilaginous tissue. One possible mechanism for the development of these masses is that a reduction in the mobility of the lower cervical vertebrae places additional mechanical stress on the mobile portions of the cervical spine. The strain placed on these portions of the spine leads to tearing of the ligaments, and a perpetual repair process ensues resulting in the formation of hypertrophic masses of soft tissue (Pascal-Moussellard et al. 2006). Surgical removal of these masses is the accepted mode of treatment in these situations.

Damage caused from trauma to both the cervical and thoracic spine can be enhanced if the spinal segment damaged was an already affected segment, even if the trauma involved is relatively minor or low impact (Hendrix et al. 1994). Paralysis, sensory loss, and death frequently result (Sreedham and Li 2005; Westervald, Verlaan, and Oner 2009). Compared to non-DISH afflicted victims of spinal trauma, DISH patients experienced considerably worse outcomes (Westervald, Verlaan, and Oner 2009). Possible mechanisms to explain this discrepancy in outcomes may relate to the different fracture types experienced by individuals with ankylosed spines compared to those with flexible spines. Although compression fractures often occur in healthy, flexible spines, ankylosed spines may fracture transversely, in much the same way as a long bone (Hendrix et al. 1994). The fused portion of the spine provides a surface upon which more complex fractures can occur.

This review of the symptomatology of DISH suggests that while it may be frequently asymptomatic, it can manifest in ways that are both detrimental to general health and occasionally life-threatening. DISH then appears to be a distinct clinical entity (Mata et al. 1997), and its cost to quality of life and occasional life-threatening manifestations would seem to preclude it from being an evolutionarily advantageous adaptation (Oxenham, Matsumura, and Nishimoto 2006). This validates the categorization of DISH as a disease process in paleopathological assessments of past population health. It also suggests that DISH can be implicated in the bias produced by selective mortality. Based on this evidence, it seems apparent that DISH does produce sufficient discomfort and disability to contribute to risk of death. Thus, it may be seen in disproportionately higher frequency than would actually have been present in the once-living population. These considerations do not remove the onus on bioarchaeologists to remember that DISH, regardless of how abnormal it may appear in dry bone, may not have been noticed by those individuals who manifested the condition during their lifetimes. Investigations of health that include DISH

must keep these nuances of the meanings of morbidity and health in mind.

DISH and Heterogeneity of Frailty

Hidden heterogeneity of frailty refers to a bioarchaeologist's inability to accurately determine the susceptibility of individuals to particular conditions within and between populations, due to an obvious deficit of information regarding the composition of the once living population. This can result in invalid comparisons of health statuses between archaeological populations (Wood et al 1992). To combat this issue, bioarchaeologists must accumulate as much data as possible on what factors affect frailty in regard to the diseases being included and compared in paleoepidemiological studies. Given DISH's association with males, old age, numerous health conditions, and obesity, it poses challenges as well as provides unique opportunities for paleopathological research.

DISH, Age, and Sex

Despite showing significant ethnic and geographical variation, all researchers concede that DISH is correlated with the male sex and older age (Rogers and Waldron 2001). The difference between the sexes in DISH frequency has been attributed to a decrease in bone formation following postmenopausal hormonal imbalances, female bone gracility (Kramer, Lagier, and Baud 1990), or a difference in bone metabolism between the sexes (Mays 2000). The relationship between advancing age and DISH suggests that earlier populations may have contained lower prevalence rates of DISH than modern populations because of lower life expectancies (Arriaza 1993; Kramer, Lagier, and Baud 1990). The increased levels of DISH compared to decreasing levels of vertebral osteophytosis and vertebral osteoarthritis may be indicative of either the anatomical masking effect of DISH or a correlation between DISH and higher life expectancy (Maat, Mastwjit, and Van Der Velde 1995). It should also be emphasized that rates of DISH in the past may be underestimated due to low levels of skeletal preservation of older individuals. In addition, the inability to accurately and precisely age older individuals may result in age-incompatible samples being compared for determining DISH prevalence rates, which would be particularly detrimental for a disease whose prevalence is as affected by age as DISH (Milner, Wood, and Boldsen 2008). In one highly anomalous study, DISH was not found to correlate with old age in a population buried at Christ Church, Spitalfields (Waldron 1991). Sex and age may serve as important negative criteria in differentially diagnosing DISH. For example, if a young female displays spinal abnormalities, which cannot be positively assigned to a disease category, DISH may be assumed to be a less likely diagnosis. The converse, however, of using sex and age as positive criteria and assuming that all spinal abnormalities in older men are DISH, must never be employed (Rogers et al. 1987).

DISH and Social Status

DISH is thought to be associated with type II diabetes mellitus and obesity. This association has allowed for connections to be made between caloric intake, sedentary lifeways and occupations, and, thus, higher social status. This is premised on the assumption that enhanced caloric intake is implicated in the development of obesity and diabetes. While not an improbable assumption, this association contrasts with modern populations, in which obesity is associated with lower socioeconomic status in developed nations (McLaren 2007). This suggests that bioarchaeologists must be cautious in over-generalizing relationships

as complex as that between nutrition and economic status. Additionally, the debatable nature of the association between DISH and type II diabetes mellitus (Daragon et al. 1995; Vezyroglou et al. 1996; Mata et al. 1997; Miyazawa and Akiyama 2006) may require more circumspect conclusions regarding DISH and social status.

The remains of individuals of higher social status who suffered from DISH include an Egyptian priest, a Saxon bishop, and a Medieval dean, in a study conducted by Rogers and colleagues (1985) on 560 intact skeletons and thousands of disarticulated vertebrae that ranged from the 21st dynasty of Egypt to the mid-nineteenth century. An affluent late Medieval Dutch population examined by Maat, Mastwjit, and Van Der Velde (1995) found an unexpectedly high rate of DISH. The remains of Ramses II and the Medici family also showed signs of DISH (Chhem, Schmit, and Faure 2004; Fornaciari et al. 2009). Correlations between social status and DISH have been made directly in a number of studies. Jankauskas's (2003) study on Lithuanian skeletal remains from the first and second millennia confirmed the correlation between DISH, high social status, old age, and the male sex. Only high status males showed significant differences compared to other status groups. However, there were no differences in levels of DISH dependent upon social status in females. Some researchers have drawn correlations between a high incidence of DISH and Medieval monastic orders, based on historical accounts of their extreme caloric intake and the high frequency of DISH in their remains (Rogers 2001; Rogers and Waldron 2001).

These associations have been contested by some researchers with regard to past populations. A study by Mays (2000) found a rate of DISH greater to modern rates in a Medieval London cemetery that could not possibly have suffered from high levels of obesity. Higher levels of DISH, however, were found in the cemetery housing the remains of wealthier individuals than the cemetery composed of poor peasants' remains.

The presence of DISH in a Middle Paleolithic Neanderthal from Iraq and possible DISH from a skeleton from a Late Pleistocene Neanderthal from the Crimea (Trinkaus, Maley, and Buzhilova 2008) also helps to refute the over-simplification that DISH only affects older, affluent men. Crubézy and Trinkaus (1992) contend that the condition may have been present at a reasonable prevalence during this time, based on the possible diagnosis of DISH in the specimens Shanidar 4 and AL-288-1. Deliberate burials were present in this era, and some fossils found during this era were middle-aged. Thus, DISH may have been present earlier, but evidence may not have preserved. The presence of DISH in later skeletons, in which further dietary information is available, allows for the consideration of dietary associations with DISH in past populations.

DISH and Diet

The association between DISH and obesity provides bioarchaeologists with one of the few opportunities to study even a proxy of obesity in the past. Caution must be used to not over-generalize or simplify this association. DISH has been found in many circumstances in the past, including amongst Neanderthals (Crubézy and Trinkaus 1992); Trinkaus, Maley, and Buzhilova 2008), which were unlikely to have experienced particularly high rates of obesity. The best approach may be to examine the specific diets of those that experience high rates of DISH. The best opportunity for this may be in the numerous monastic studies in which a high prevalence of DISH has been found (Mays 2000; Rogers 2001; Rogers and

Waldron 2001; Verlan, Oner, and Maat 2007).

Harvey's (1993) study of the diet of Medieval British monasteries has shown that monks initially practiced austere eating restrictions before allowing their diet to become increasingly relaxed and secularized. They enjoyed a large proportion of fish and meat, particularly mutton, but also beef, pork, veal, and goose. Four meat dishes were served at dinner (lunch) and another was served at supper. Animal fat was also served independently. For example, a dish called principal pudding was composed of 6 lbs. of currants, 270-300 eggs, a significant portion of bread crumbs, and at least 18 lbs. of suet. Also composing a large portion of the daily diet of monks was dairy produce, bread, and alcoholic beverages, whereas fruit and vegetables did not significantly contribute to diet. Isotopic analyses from DISH sufferers from a monastic site from York confirmed the high levels of animal protein and marine foods in the diet (Müldner and Richards 2007).

It is important to note that while conventional wisdom may suggest that a diet high in animal fats will naturally result in obesity, this view is not without its critics. For example, a recent review has questioned this position (Myerstud et al. 2008). Modern areas of conflicting evidence must be taken into consideration by bioarchaeologists before making any over-generalizations concerning the animal fat content of the diet of an individual in whose remains DISH is present.

Conclusions

DISH is a common condition, with a distinct manifestation, poorly understood etiology, and numerous associated comorbidities. These comorbidities provide bioarchaeologists with the opportunity to develop hypotheses concerning hidden susceptibilities within skeletal samples relating to obesity, social status, age, and sex. While frequently asymptomatic, DISH still would have produced some measure of ill-health and threat of death in its sufferers. Thus, skeletal populations in which DISH is present will be biased by selective mortality. As the etiology of DISH is not yet fully understood, bioarchaeologists must exercise caution in attempting to uncover hidden heterogeneities of frailty, which may render some populations more susceptible to DISH than others. Paleoepidemiologists can benefit from increasing clinical knowledge in associated conditions, which may help to establish models for identifying frailty in regard to DISH. In turn, bioarchaeologists may aid clinicians in identifying early stages of the disease, in order to help definitively establish early mechanisms of DISH manifestation.

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