Bioarchaeological Implications of a Differential Diagnosis of Diffuse Idiopathic Skeletal Hyperostosis (DISH) in *Gorilla gorilla gorilla*

THESIS

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Abstract

Since its identification in the 1950s as a systemic skeletal disorder, the etiology of Forestier’s disease or diffuse idiopathic skeletal hyperostosis (DISH) has remained unclear. Clinical studies have attempted to illuminate risk factors and associated pathological conditions without consensus. Prevalent in modern populations, DISH has been documented in multiple bioarchaeological populations as well as the fossil record (Rothschild 1987). Its antiquity has been established, yet the anthropological literature contains only one published case of DISH in a non-human primate, a 42 year old captive *Pongo pygmaeus pygmaeus*. Medical records from captivity, macroscopic diagnostic criteria, computed tomography (CT) and histological data are used here to differentially diagnose and document DISH in a captive female *Gorilla gorilla gorilla* as a proxy for an archaeological situation. Furthering our understanding and interpretation of the process this disease takes through three dimensional CT reconstruction and accompanying histological analysis of ectopic growth, this paper examines the use of conventional macroscopic identification of DISH and attempts to build bioarchaeological knowledge of diagnostic signatures of the disease. While investigating DISH in past populations, clinical studies must be referenced in order to interpret lifestyle risk factors in skeletal populations. Combining clinical data with human and captive non-human primate
skeletal and lifestyle data will aide in further clarification of behavioral reconstructions of past populations. This paper will attempt to diagnose DISH in a gorilla through examination of multiple avenues of diagnostic criteria any of which may be available to the bioarchaeologist working with archaeological remains. Although DISH is a systemic condition characterized by disrupted bone metabolism resulting in abnormal growth, the focus of this research will remain on the vertebral column manifestations. Histological appearance of vertebral ectopic lesions will be documented. Increasing awareness of DISH in human and non-human primates will lead to a more accurate paleopathological differential diagnosis.
Dedication

This document is dedicated to my family and friends who have become family.
Acknowledgments

The author would like to thank Dr. Clark Spencer Larsen from the Ohio State University for his guidance, patience and access to wonderful resources during the process of this evolving research. Thank you to Dr. Matthew Allen of the Department of Veterinary Medicine for his collaboration and generosity. Dr. Michael Barrie provided me with valuable records of the life of my gorilla. Much gratitude to Mandy Agnew for patiently teaching me a new method and aiding me in the interpretation of samples. Lastly, the author would like to thank Drs. Samuel Stout, Paul Sciulli, and Scott McGraw for their input and service.
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CHAPTER 1: INTRODUCTION

1.1 Diffuse Idiopathic Skeletal Hyperostosis (DISH)

The systemic skeletal condition presently known as diffuse idiopathic skeletal hyperostosis (DISH) has been identified in medical literature as early as the 19th century (Smythe and Littlejohn 1998; Forestier and Rotes-Querol 1950). However, it was not until 1950, when Forestier and Rotes-Querol systematically studied an ankylosing disease with differential clinical and post-mortem presentation from ankylosing spondylitis, that “senile ankylosing hyperostosis” or Forestier’s Disease was first characterized in the medical literature (Forestier and Rotes-Querol 1950; Utsinger 1985). Forestier and Rotes-Querol (1950:329) provided the first definition of the spinal disorder with an emphasis on “(a) the hyperostosis, a most striking pathological element, and (b) two constant clinical features: spinal rigidity and advanced age.” Using nine clinical cases and two autopsy specimens of individuals aged between 50 and 73 years, “an irregular flowing outgrowth alongside the anterior aspect of the vertebrae and the disks of the dorsal spine” as in a “candle wax” pattern was observed (Forestier and Rotes-Querol 1950:322). Forestier’s disease became known as diffuse idiopathic skeletal hyperostosis (DISH) in the 1970s when systemic entheseal reactions were also observed though not considered pathognomonic (Resnick et al. 1975).
The fundamental diagnostic criteria of DISH have remained constant in the medical literature with only minor revisions. Clinical radiographic diagnosis is generally based on the prevailing criteria taken from Resnick and Niwayama (1976) and is delineated in Table 1 (Sarzi-Puttini and Atzeni 2009). DISH differs quantitatively and qualitatively from other forms of spinal spondylosis and “represents regional ossification encompassing ligaments, paraspinal connective tissue and annulus fibrosis, and periosteal new bone formation on the anterior aspect of the vertebral body” (Resnick and Niwayama 1976:567). In addition to the work of Resnick and Niwayama, current clinical literature has included the following diagnostic criteria: (1) ossification of at least four contiguous vertebral bodies; (2) vertebral patterning most likely to begin on the right antero-lateral thoracic spine then affecting the lumbar spine and cervical spine bilaterally; (3) preservation of the intervertebral disc space; (4) non-involvement of articular facets; (5) and extraspinal manifestations that include enthesophytes of the iliac wing and ischial tuberosity, calcification of the sacrotuberous and iliolumbar ligaments, calcaneal spurs, hyperostosis around the glenoid and distal clavicle, olecrenon spurring, cortical thickening of the tubular bones of the hand, and periarticular osteophytes, particularly about the hip (Hannallah et al. 2007; Belanger and Rowe 2001). The disease shows a predilection for the axial skeleton (Sarzi-Putini and Atzeni 2009). Although a systemic condition, the involvement of the vertebral column is ubiquitous with or without peripheral ossifications. Clinical diagnosis is made through a variety of radiological
methods most often plain radiographs and/or computed tomography (CT). The classic “candle wax” pattern of ossification can be seen both photographically and radiographically in a human vertebral column in Figure 1. The ossification is typically though not exclusively limited to the right antero-lateral side in the upper and middle thoracic spine thought to be a product of the pulsating aorta, but begins to extend bilaterally in the lower thoracic and lumbar spine (El Miedany et al. 2000).

<table>
<thead>
<tr>
<th>Site</th>
<th>DISH</th>
<th>Ankylosing Spondylitis</th>
<th>Intervertebral Osteochondrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebral bodies</td>
<td>&quot;Flowing&quot; ossification and hyperostosis; large osteophytes; bony ankylosis (radiographic)</td>
<td>Thin syndesmophytes; osteitis with vertebral body &quot;squaring;&quot; extensive bony ankylosis (radiographic and pathologic); &quot;bamboo&quot; appearance</td>
<td>Sclerosis of superior and inferior surfaces of vertebral bodies</td>
</tr>
<tr>
<td>Intervertebral Discs</td>
<td>Normal or mild decrease in height</td>
<td>Normal or convex in shape</td>
<td>Moderate to severe decrease in height</td>
</tr>
<tr>
<td>Apophyseal Joints</td>
<td>Normal or mild sclerosis; occasional osteophytes</td>
<td>Erosions, sclerosis and bony ankylosis</td>
<td>Normal</td>
</tr>
<tr>
<td>Sacroiliac Joints</td>
<td>Para-articular osteophytes</td>
<td>Erosions, sclerosis and bony ankylosis</td>
<td>Normal</td>
</tr>
<tr>
<td>Extraspinal Manifestations</td>
<td>Para-articular osteophytes; ligament calcification and ossification; hyperostosis</td>
<td>&quot;Whiskering&quot; arthritis</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Table 1: Differential diagnostic criteria of spinal pathologies. Adapted from Resnick and Niwayama 1976
Figure 1: Pathognomonic "candle wax" bone growth of DISH anterior thoracic spine (A). Note the right antero-lateral severity and early stages forming left laterally: From Rogers and Waldron 2001. Posterior radiograph lumbar spine showing bilateral ossifications (B). From Belanger and Rowe 2001.

1.2 Demographic characteristics

The prevalence of DISH has been well documented in the clinical literature (Forestier and Rotes-Querol, 1950; Mader and Lavi, 2008; Sarzi-Puttini and Atzeni, 2004; Utsinger, 1985). It is most often found in individuals over 50 years of age and males over females (at a 2:1 rate). Variability in reported rates spans the literature and is population specific. The male to female ratio has continuously proved to be approximately 2:1 with 12-22% of males over 65 years of age and 12-13% of females over 65 years of age afflicted (El Miedany et al. 2000; Ortner, 2003; Verlaan et al. 2007). If considering demographic prevalence at a younger age between males and females, only
3.8% of males aged 40 and 2.6% of females aged 40 present with DISH (Mata et al. 1998). Mata and colleagues (1998) report a prevalence of 2.5% to 10% in patients aged 70 and over. Another clinical study cites between 3% and 30% of males over the age of 50 present with DISH (Hannallah et al. 2007). Despite the discord between specific prevalence rates in clinical populations, DISH does appear to affect males at approximately a 2:1 ratio to females as well as increase in prevalence with age particularly 65 years or older. The prevalence has been documented to vary with age, ethnic origin, geographic location and clinical setting (Mader and Lavi, 2008). Forestier and Rotes-Querol (1950) initially observed the increasing risk of DISH with increasing age, a trend that has since remained constant in the clinical literature (Utsinger, 1985; El Miedany et al. 2000; Ortner, 2003; Verlaan et al. 2007). Mader (2004) and Mader and Lavi (2008) estimate the pathology requires at least ten years for skeletal manifestations to progress to a radiographically recognizable stage. It is possible that the age related aspect could be a product of the asymptomatic early stages of DISH in earlier decades of life.

1.3 Etiology, Behavioral and Lifestyle Risk Factors

Several metabolic, genetic, anatomic, endocrinologic and environmental factors have been implicated in the undoubtedly complex etiopathogenesis of DISH (see figure 2) (Sarzi-Puttini and Atzeni, 2004). Yet, the specific etiology of hyperostosis is still unknown. DISH has been highly associated with the “metabolic syndrome” (MS)
The metabolic syndrome or insulin resistance syndrome is characterized by abnormal insulin metabolism and glucose tolerance, obesity, increased abdominal fat distribution, hypertension, and hyperlipidemia (Mader et al. 2009). These factors significantly increase the risk of developing type II diabetes mellitus, cardiovascular disease as well as DISH (Mader et al. 2009). Early clinical investigations into the bone formation in DISH patients demonstrated abnormal insulin levels in patients after glucose challenge (Littlejohn and Smythe, 1981).

Abnormal levels were found in 17-60% of DISH patients and diabetes in 9% of patients suggesting a relationship between abnormal bone growth, metabolic disruption and growth promoting factors such as insulin (Littlejohn and Smythe, 1981). Elevated serum levels of insulin, a growth stimulator at the physiological level, continuously stimulates tissues, such as bone, that are susceptible to growth modifying influences (Ortner, 2003). Sencan and colleagues (2005) found 12% of patients with type II diabetes mellitus had DISH compared to 6.8% in the control group. Though elevated, this was found to be statistically insignificant as in the clinical comparison of Vezroglou and colleagues (1996) (a prevalence of 8% compared to 3% in the control group). Sarzi-Puttini and Atzeni (2004) cite higher body mass index, higher serum uric acid levels and patients more likely to have diabetes mellitus with DISH patients. In a clinical study of Egyptian patients, 50% (20/40) of patients with DISH were considered overweight with a BMI greater than 30; 45% of patients with DISH (18/40) had hypertension and signs of
coronary artery disease; 60% showed impaired glucose tolerance (El Miedany et al. 2000). However, as will be discussed later, evidence and clinical studies do not support a simple causal relationship.

Figure 2: Metabolic, endocrinological, genetic, environmental interactions in etiology of DISH. From Sarzi-Puttini and Atzeni 2004.

A consensus in rheumatology holds that DISH is likely the result of a complex interaction between metabolic factors and cannot be attributed to a simple explanation (Littlejohn, 1985; Utsinger, 1985; El Miedany et al. 2000; Ortner, 2003). Kiss and colleagues (2002)
in the first matched pair case-control study of DISH patients with vertebral spondylosis patients argue hyperinsulinemia as the variable that links metabolic disturbances with vertebral hyperostosis. Mader and Lavi (2009) support the importance of insulin in the role of the MS and contribution to skeletal hyperostosis. Obesity as a major contributor to the condition along with early life obesity seems to be a risk factor for the development of DISH later in life (Kiss et al. 2002). Investigation into the abnormal metabolic processes contributing to DISH manifestations continues. The type of activity patterns (or lack of activity) associated with development of the MS have been addressed in preventative and therapeutic measures for DISH (Mader et al. 2009). Clinical literature suggests weight loss, aerobic exercise and controlled glucose and insulin levels to reduce the risk of MS and ligamentous ossification (Mader et al. 2009).

1.4 Skeletal Biology

DISH is considered a pathological condition in which a tendency for ossification of ligaments, entheses and joint capsules exists (Ortner 2003, Mader et al. 2009, Waldron 2009). Considered “exuberant” paravertebral bone growth, the spinal changes associated with DISH are the result of anterior longitudinal ligament ossification (ALL) (Waldron 2009). Ossification may be more extensive, though less frequently, including the posterior longitudinal ligament (PLL) and ligamentum flavum (LF) (Ehara et al. 1998). The ALL is a broad fibrous band located on the anterior and antero-lateral aspect of the vertebral column from the atlas descending to the sacrum attached to but set apart from
the vertebral bodies at the articular lip (Resnick and Niwayama 1976, Sarzi-Puttini and Atzeni 2004). Where the ALL attaches to the anterior surface of the vertebral bodies, it forms the periosteum of the spine (Resnick and Niwayama 1976). The loose attachment of the ALL to the vertebral column often results in a characteristic radiolucency or separation between the ectopic growth and the vertebral body (Resnick and Niwayama 1976, Rothschild and Martin 1993); however, in later phases of DISH, this space can be obliterated (Resnick and Niwayama 1976; Fornasier 1983). Ossification appears to begin at the midportion of the vertebral body and the innermost layer of the ALL which then grow across the disc space (often referred to as “bony excrescences”) to meet with the ossifications from above or below vertebrae (Resnick and Niwayama 1976, Rothschild and Martin 1993, Sarzi-Puttini and Atzeni 2004).

The catalyst for universal exuberant ligamentous ossification, not limited to the spine, is thought to be the ability of insulin to promote differentiation of mesenchymal cells into chondrocytes resulting in endochondral ossification (Akune et al. 2001). Exposing mesenchymal cells located in ligaments to insulin, a known bone anabolic agent, may result in ossification (Thomas et al. 1996). Hyperinsulinemia is the increased production of insulin by beta-cells of the pancreas; this response can be triggered by hyperglycemia or the impairment of insulin response in tissues both associated with the MS (Akune et al. 2001). Increased bone mass in patients with hyperinsulinemia associated with type II diabetes mellitus lends support to this relationship (Thomas et al. 1996).
1996). In patients clinically considered to be non-diabetic but whose fasting plasma glucose is elevated, beta-cells upregulate insulin secretion to return to glucose homeostasis (Akune et al. 2001). Thus, the relationship between metabolic disturbances and ligamentous ossification of DISH may be mediated through the role of insulin.

Increased osteoblastic activity mediated through the role of insulin does not explain the characteristic patterning of bone growth in DISH. The localizing or predisposing factor is hypothesized to be hypervascularity of the spine in patients with DISH (El Miedany et al. 2000). Hypervascularity is important for osteoblast proliferation providing the necessary pathways for growth stimulating factors such as insulin to reach the area (El Miedany et al. 2000). Resnick and Niwayama (1976) also noted increased vascularity to the vertebral column in patients with DISH. Radiographic and pathological investigations found increased number and size of nutrient foramina in DISH affected vertebrae versus non-affected vertebrae in the same patient as well as the control group particularly in the thoracic spine (El Miedany et al. 2000). Hypervascularity in the thoracic spine provides excess insulin and insulin-like growth factor (present in patients with metabolic syndrome) to the local microenvironment stimulating osteoblast proliferation in the spine beginning with the ALL (El Miedany et al. 2000). The largest blood vessels were found between T10 and L2 consistent with the areas of the spine most affected by DISH growth (El Miedany et al. 2000). Ossified ligaments contain prominent and large vascular vessels (El Miedany et al. 2000). Whether hypervascularity is a
product of the stresses on the body associated with MS is not well delineated in the study. However, it appears that increased vascularity may contribute to the onset, localization and/or progression of ligamentous ossification by providing an avenue for the increased insulin to affect the area (El Miedany et al. 2000).

1.5 Behavioral Risk Factors Associated with Captive Non-Human Primates

As DISH is related to metabolic disturbances from conditions subsumed under the “metabolic syndrome” such as obesity, heart disease, diabetes mellitus, associated behavioral risk factors have been inferred. Under these clinical guidelines, increased sedentism and nutrient excessive diets coupled with high status life styles may be inferred from the presence of DISH in archaeological populations (Waldron 2009). However, this must be done cautiously and with supporting evidence of high status burials if present (as will be discussed in the subsequent literature review). As in the case of a captive non-human primate, analogous conditions may apply. A decrease in activity in association with a captive lifestyle as opposed to natural habitat activity patterns may parallel increased sedentism in higher status humans. Research on the seasonal variability of natural food resources has shown most great apes face interannual variation in food availability (Masi et al. 2009). Lowland gorillas occupy environments in which food availability is much more variable both seasonally and annually than those of the frequently studied Mountain gorillas (Masi et al. 2009; Remis et al. 2001). Lowland gorillas are thus more mobile in search of variable food resources particularly in times of
patchy fruit distribution (Masi et al. 2009). In response to seasonal variation, lowland
gorillas adjust both their diets and activity patterns (Masi et al. 2009). Gorillas in the
Nouabale-Ndoki National Park, Congo exploited more fruits in their diets in the fruiting
season and more fibrous plants in the off season (Nishihara 1995). Adaptations to
available food resources throughout the year in a natural habitat through mobility are not
required in a captive environment. The non-human primates are well cared for and
environmental challenges to nutrient access is ameliorated in a captive setting.

1.6 Non-human Primate and Human Bone Comparability

Understanding osteoporosis in human populations has stimulated non-human
primate studies of bone turnover and maintenance (Havill 2004). Non-human primate
models have been used to consider osteoporosis due to the close phylogenetic distance to
*Homo sapiens* and similarities in skeletal maintenance and repair (Jerome and Peterson
2001). The similarities in physiology allow for confident extrapolation of results from
studies on non-human primates to human conditions (Brommage 2001). Skeletal
metabolism is similar between non-human primates (particularly Old World monkeys and
greater apes) and humans due to parallels in longer lifespan, reproductive physiology and
endocrinology, and developmental and physiological characteristics (Havill 2004). The
general absence of plexiform bone and presence of Haversian systems in cortical bone
remodeling in non-human primates mirrors skeletal biology seen in humans (Hillier and
Bell 2007; Jerome and Peterson 2001). Havill’s (2004:101) work on the comparability of
rhesus macaques skeletal metabolism as justification for models of “human age related changes and pathologies of bone” is based on the phylogenetic closeness of Old World monkeys (diverging at approximately 25 mya). The divergence of gorillas at a much more recent date (7-8 mya) supports the comparability of skeletal metabolism with humans. Thus, the investigation of the skeletal manifestations of DISH in *Gorilla gorilla* using radiologic and histological methods can provide further understanding of the processes occurring in human samples.

### 1.7 DISH in Non-humans

The clinical literature documenting DISH in humans is extensive composed of mainly radiographic descriptions. The condition has been identified outside of humans using clinical diagnostic criteria. Woodard et al. (1985) diagnosed, with some criticism as to their criteria, DISH in a domestic Labrador retriever. Rothschild (1987) identified multiple nonmarine dinosaurs as having DISH characteristic spinal ligamentous ossification. Peripheral signs of ligamentous ossifications were only present when the vertebral column was affected supporting the ubiquity of spinal involvement with the disease (Rothschild 1987). DISH was also diagnosed in the fossil remains of *Mastodon*, early rhinocera, early camels, saber-toothed tiger, and an extinct horse (Rothschild 1987). Klaver and Kompanje (1996) published the first diagnosis of DISH in a non-human primate, a captive orangutan (*Pongo p. pygmaeus*). The orangutan was diagnosed postmortem with right side T1-T5 vertebral ankylosis in the presence of preserved
intervertebral disc spaces and absence of apophyseal joint changes (Klaver and Kompanje 1996). These characteristics are argued to be in accordance with diagnostic criteria in humans (Klaver and Kompanje 1996). Interestingly, the patterning along the superior aspect of the thoracic spine and sparing the inferior thoracic spine is not frequently found in humans. The blood glucose levels were not available for the orangutan preventing identification of diabetes mellitus or less severe levels of insulin resistance.

1.8 Identifying DISH in the Archaeological Record

The macroscopic standards by which DISH is identified in the bioarchaeological record have been slightly modified from clinical radiographic criteria. Waldron (2009) offers an operational definition of DISH to be used in paleopathology including ossification of four contiguous vertebrae often limited to the right side in the thoracic spine and extra-spinal entheses and ligaments. Frequently, poor preservation of skeletal remains due to taphonomic influences limits the bioarchaeologist’s ability to make a differential diagnosis. In attempts to alleviate such issues, a variety of methods are used in this study to diagnose and document DISH, including macroscopic, radiologic, and histological appearance in a non-human primate specimen. Bioarchaeologists working with skeletal remains have a distinct advantage over physicians diagnosing clinical patients with DISH; diagnostic avenues are not limited to radiographic evidence which carries a decreased sensitivity for earlier stages of the disease process. Computed
tomography (CT) allows for a nondestructive manner in which bioarchaeologists can differentially diagnose DISH against other osteophyte producing spinal pathologies mainly osteoarthritis and ankylosing spondylitis. Description of histological appearance of the hyperostosis in two different planes will serve as a basis for understanding the physiological process of growth. A scarcity of literature on the histological appearance of DISH allows for much to be learned from observational and descriptive science. Histological analysis of ligamentous ossification in the vertebral column, the only portion of the body universally affected by DISH, can expound processes not understood in clinical populations nor included in diagnostic criteria.

This research will implement the use of modern clinical etiological hypotheses and the comprehensive study of the disease in a non-human primate with a documented captive lifestyle to increase the probability of accurate diagnosis in archaeological collections. The presence of DISH in bioarchaeological populations can provide further evidence of activity patterns and lifestyles that may have contributed to clinically known risk factors. A review of archaeological cases will be performed to assess the justification of DISH as an indicator of past life styles. Along with contributing to the anthropological body of knowledge about the past, this research has implications for modern medical understanding of DISH. Due to the limitations of radiologic studies in clinical populations, paleopathological investigations can elucidate the extent, location, and skeletal involvement of the hyperostosis. Diagnosis of DISH in the archaeological
record may be limited by preservational issues where it may be difficult to determine if peripheral manifestations are present (Waldron 2009). The goal of this research is to provide multiple avenues for which to diagnose the condition in attempts to circumvent issues with preservation or mistaken differential diagnoses.
CHAPTER 2: MATERIALS AND METHODS

2.1 Gorilla gorilla gorilla specimen

The skeletal specimen examined here is that of a female Western lowland gorilla (Gorilla gorilla gorilla) born in the wild and taken into captivity at three months old. She was euthanized at age 39 years for inoperable obstetric cancer (Columbus Zoo Pathology report). She was unable to bear offspring but acted as a surrogate mother in captivity at the Columbus Zoo. At time of death, the gorilla weighed 274 pounds (Columbus Zoo Pathology report). The ideal weight determined by veterinarians and keepers was 245 pounds with a range of 235-255 pounds suggesting she was slightly overweight (Dr. Michael Barrie, personal communication 22 January 2010). Upon reviewing the last year of medical records, the gorilla showed symptoms such as difficulty urinating/defecating, occasional loss of appetite, indications of pain (wincing) and vaginal bleeding determined to be products of the abdominal mass identified earlier using CT and exploratory surgery (Dr. Michael Barrie, personal communication 22 January 2010). She was neither diabetic nor did she have any cardiovascular issues. The necropsy was performed in August 2004 at The Ohio State University whereby her remains were macerated. Necropsy results found an inactive ovary (contributing to the female’s infertility) and both intestinal and vaginal masses identified as mesenteric fibromatosis (Columbus Zoo Pathology report). Initial photographic documentation to
demonstrate macroscopic characteristics of the vertebral column was taken before any destructive analyses were performed. The vertebral column was chosen on which to perform both the non-destructive (CT) and destructive (histological) methods due to its universal affectedness in all DISH cases and propensity for better preservation than the appendicular elements.

2.2 Radiography

Two methods of radiological diagnosis were utilized for this study. Antemortem radiographs were provided by the Columbus Zoo for analysis. Additionally, postmortem computed tomography (CT) of the complete vertebral column was performed on the GE Lightspeed eight-slice helical scanner with a resolution of 0.625 mm per slice at The Ohio State University Veterinary School. The following parameters were maintained: 150 MA and 120 Kv. A hydroxyapatite phantom with five increasing densities was placed beneath the vertebral column for future quantitative analyses. The thoracic, lumbar, and sacral spines were articulated and placed prone and head first into the scanner. The cervical spine was articulated and scanned after the thoracic-lumbar-sacral segment. Foam wedges were used to maintain articulation and positioning and prevent movement of the vertebral column so as to avoid attenuation or artifacts. Images were acquired and sent as raw DICOM files to the Mimics FEA/CFD 12 three-dimensional reconstruction software (property of Materialise).
2.3 Histological Sampling

In order to perform histological analysis on the lesions of the vertebral column, a region of interest was chosen based upon the macroscopic and CT evidence of severity. The lumbar region appeared to be the most affected bilaterally and was thus photographed prior to disarticulation (see Figure 3). Using a combination of a dremmel and a band saw, the spinous processes were removed first followed by a sagittal cut through the entire articulated lumbar section resulting in a right lateral segment and left lateral segment (see Figure 4). A dremmel was then used to isolate the region on the right antero-lateral side of L2-L3 through which oblique longitudinal sections would be taken from the thickest part of the lesion. For the left lateral section, a dremmel was used to isolate the region between L3 and L4 for transverse sections to be taken. Both sections contained immediate portions of the vertebral bodies for analysis.
Figure 3: Rt Lateral view of L2-L4 with pencil markings denoting sectioning locations prior to disarticulation (above). Anterior view of L2-L4 with pencil markings denoting location of cuts (below).
Figure 4: Rt Lateral L2-L4 after removal of spinous processes and sagittal cut (from which longitudinal sections will later be taken) (Above). Left lateral L2-L4 after removal of spinous processes and sagittal cuts (from which transverse sections will later be taken) (Below).

The left lateral segment was then sectioned transversely through the midportion of L3 once again prior to embedding due to length and container size constraints. These sections were then embedded in Buehler Epothin (by weight 100g epoxy resin to 30g hardener). A vacuum was repeatedly used to ensure the removal of air bubbles. After approximately 24 hours to allow the Epothin to set, the molds were removed and the sections were glued using “Zap-a-gap” model glue to a glass slide. Using a Buehler
Isomet 1000 precision saw, thick sections were taken from each sample. The sections were ground under water to approximately 70 to 100 microns thick using a Metaserv 2000 grinder/polisher. The slides were treated with xylene to clean and prepare them for examination. Once they were determined to be a sufficient thickness, a coverslip was applied using Permount. The coverslips were anchored to the slides to prevent air bubble accumulation while the Permount dried. Once dry, the clips were removed and the slides were examined under both 4x and 10x microscopy using polarized light. Images were taken using the Spot Basic program.

2.4 Bioarchaeology Review

A review of bioarchaeological literature was performed to investigate the consistency of diagnostic criteria and archaeological context indicative of life style risk factors for DISH. Any skeletal specimen diagnosed and published with DISH was considered. Table 2 serves as a reference for published archaeological cases of DISH. Asterisks denote a lack of explicit supporting archaeological evidence of status or behavioral risk factors such as sedentism.
<table>
<thead>
<tr>
<th>Case/Location</th>
<th>Date</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shanidar 1 Neandertal</td>
<td>46,900-50,600 yBP</td>
<td>Crubezy and Trinkaus 1992*</td>
</tr>
<tr>
<td>Montescaglioso, Magna Graecia</td>
<td>6th century BCE</td>
<td>Canci et al. 2005</td>
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<td>Jevisovice Culture, Zerotic</td>
<td>3rd century BCE</td>
<td>Bozdech 1988*</td>
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<td>Late Jomon, Hokkaido, Japan</td>
<td>1500-300 BCE</td>
<td>Oxenham et al. 2006 (brief reference chart)</td>
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<td>Merotic Nubian, Semna South Sudan</td>
<td>350BCE-350 CE</td>
<td>Arriaza et al. 1993b</td>
</tr>
<tr>
<td>Montescaglioso, Angelo Abbey</td>
<td>1100-1400 CE</td>
<td>Reale et al. 1999</td>
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<tr>
<td>Abbey court, Maastricht, Netherlands</td>
<td>275-1795 CE</td>
<td>Verlaan et al. 2007</td>
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<tr>
<td>Merton Priory, Surrey</td>
<td>1140-1540 CE</td>
<td>Waldron 1985</td>
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<tr>
<td>St. Andrew Fischergate, York</td>
<td>13-14th century CE</td>
<td>Knusel et al. 1997 Muldner and Richards 2007</td>
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<tr>
<td>Dordrecht, Holland</td>
<td>1375-1572 BC</td>
<td>Maat et al. 1995</td>
</tr>
<tr>
<td>Royal Mint Church</td>
<td>~1350 CE</td>
<td>Rogers and Waldron 2001</td>
</tr>
<tr>
<td>Edo, Japan</td>
<td>1700-1799 CE</td>
<td>Suzuki et al. 1993*</td>
</tr>
<tr>
<td>Wells Cathedral (Lady chapel)</td>
<td>13th century CE</td>
<td>Rogers and Waldron 2001</td>
</tr>
<tr>
<td>(Stillington’s chapel)</td>
<td>16th century CE</td>
<td></td>
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<tr>
<td>560 samples various sites</td>
<td>1-1850 CE</td>
<td>Rogers et al. 1985</td>
</tr>
<tr>
<td>Northern Chile: Arika, Chinchorro, Quiani</td>
<td>4,000 yBP</td>
<td>Arriaza 1993a</td>
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<td>Jankauskas 2003</td>
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<td>Jankauskas 2003</td>
</tr>
<tr>
<td>Lithuania</td>
<td>Early Modern</td>
<td>Jankauskas 2003</td>
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Table 2: Bioarchaeological literature review of DISH cases (English literature)
Asterisks denote lack of supporting archaeological evidence.
CHAPTER 3: RESULTS

3.1 Macroscopic Differential Diagnosis

To my knowledge, the gorilla was not diagnosed with any spinal pathology during life. “Candle wax” ossification and complete ankylosis was observed bilaterally of at least four contiguous vertebrae (T12 through L4). In the lumbar spine, neither the vertebral bodies nor the zyapophyseal joints demonstrated any type of degeneration. In addition, the zyapophyseal joints lacked obvious signs of ankylosis unlike the vertebral bodies. The intervertebral disc spaces were relatively maintained throughout the afflicted section. The remainder of the thoracic spine contained anterior ossifications that do not resemble the “dripping candle wax” pattern perhaps indicative of earlier stages of ligament ossification [or another disease process] (see figure 5). T7-T11 show more severe right sided ossifications though less advanced than lower thoracic and lumbar growth. In the same region, there appears to be some left sided ossification as well though not to the extent of the right side. T2 to T3 showed anterior and bilateral ossifications. T3 through T7 showed greater ossifications on the left side compared to the right side in the same vertebrae. The sacroiliac joint did not show signs of inflammation or ankylosis as pathognomonic in ankylosing spondylitis (AS). Thoracic zygapophyseal joints showed slight signs of ossifications but no signs of ankylosis. Olivieri and colleagues (2009) document the slight changes in apophyseal joints
associated with DISH as opposed to the significant ankylosis of these joints in AS. Particularly in the lumbar spine, the ligamentous ossification was exuberant with an “undulating” appearance in contrast to the fine syndesmophytes characteristic of AS (Rothschild and Martin1993:558). Meanwhile, the intervertebral disc spaces are clearly preserved (see figure 5). There does not appear to be any significant signs of osteoporotic degeneration as the vertebral bodies remained extremely dense throughout the process of disarticulation.

Figure 5: Photograph Left oblique anterior thoracic spine (A). Anterior lumbar and sacral spine showing "candle wax" ossification of five vertebrae consistent with diagnostic criteria (B). Left lateral lumbar and sacral spine (C). Right lateral lumbar and sacral view (D).
3.2 Radiographic Differential Diagnosis

Plain radiographs were obtained from Columbus Zoo allowing the documentation of DISH in life. Unfortunately, as this investigation commenced nearly six years postmortem, the clinical radiograph views are limited and were obtained for unrelated purposes. Lateral views were not obtained as per standards of practice due to difficulty in positioning the gorilla. However, anterior abdominal views allow for a clear view of the lower thoracic and lumbar spine. Fortunately, abdominal radiographs were taken earlier in life as well providing a temporal examination of disease progression. Lumbar views taken in 1993 (10 years prior to death) show initial stages of ligamentous ossification (see figure 6). In this posterior view, the bony excrescences are beginning to bilaterally affect L2-L4.
Figure 6: Posterior radiograph of gorilla specimen 10 years prior to death demonstrating the early stages of ectopic bone growth bridging the intervertebral disk spaces.

Radiographs obtained ten years later show the progression of the ectopic ossification.

Figure 7 demonstrates the extent of irregular and exuberant bony hyperostosis in the mid-lower thoracic spine and upper lumbar spine. Figure 7 also demonstrates the preservation of intervertebral disk spaces in the lumbar spine as well as the lack of sacroiliac involvement as is characteristic of ankylosing spondylitis.
Figure 7: Anterior view taken during year prior to gorilla's death demonstrating exuberant bony growths particularly, though not limited to, on the right side of the lower thoracic and lumbar spines (A). Posterior view taken during year prior to gorilla’s death demonstrating extent of hyperostosis in the lumbar spine (the most severely affected area) (B). Also, the lack of sacroiliac involvement and preservation of intervertebral disk spaces are present.

Three dimensional reconstruction of CT data demonstrates the “candle wax” bony growth in the lumbar spine and the less severe ossification in the thoracic spine (see Figure 8). Figure 8 demonstrates the right sided ossification in the thoracic spine; however, though less severe, the left side is also showing early signs of ossifications.

Though not consistent with Waldron’s (2009) operational diagnostic definition, this does not preclude identification of the spinal pathology as DISH. In the lumbar spine, bilateral irregular and thick bony growths are apparent (see Figure 8).
Figure 8: Mimics three dimensional CT reconstruction of thoracic spine (Right anterior Left) (A). Mimics three dimensional CT reconstruction of Lumbar and Sacral spine (Right anterior Left) (B).

In CT analysis of the transverse plane, the ossified ALL ligament is set apart from the vertebral column throughout the thoracic and lumbar spine congruent with expectations. However, there are instances particularly in the inferior lumbar spine where the separation is no longer apparent; the ossification has affected the vertebral body both anteriorly and bilaterally. Thoracic vertebrae show evidence of anterior ossifications beginning with T2 and descending inferiorly with clear separation and extension across
the disc space (see Figure 9). Evidence of Schmorl’s nodes is present in the lower thoracic spine from T9 to T12 (see Figure 10). Figure 10B also demonstrates right lateral ossification beginning at the midportion of the vertebral body and while descending into the intervertebral disc space, extending anteriorly and left laterally (consistent with descriptions of non-marginal syndesmophytes). Although some zygapophyseal changes appear on the CT that were not evident during macroscopic examination, there is no ankylosis involved even in the most severely affected vertebrae.

Figure 9: Transverse CT raw data of ALL ossification bridging intervertebral disk space between T5 and T6(A) and T7 into T8. Note location and severity of ossification. C demonstrates the “non-marginal” nature of ALL ossification; not limited to the intervertebral spaces.
Figure 10: Transverse CT raw data evidence of Schmorl's nodes in T9 (A) and T12 (B). Note the partial radiolucency between the ALL and vertebral body on right side T12. A sclerotic response in the vertebral body cortical bone subjacent to the ALL has begun.

The lumbar spine shows an ascending severity of ossification which continues into the thoracic spine; L3 and L4 showing the greatest lesion development. Schmorl’s nodes do not appear to affect any of the lumbar vertebral bodies. Inferiorly, L1 is characterized by bilateral ossification (yet more severe on the left antero-lateral surface) separated from the vertebral body (see Figure 11). Beginning “non marginally” and descending through L2, the severity of ossification increases and affects the vertebral body just prior to reaching the intervertebral disc space (see Figure 12). Superiorly, the vertebral body of L3 is being infiltrated by the ligamentous ossification (or causing a sclerotic response); the separation is still slightly visible right laterally but lost on the left
L3 appears to have less developed lesions around the midportion of the vertebral body compared to the superior and inferior areas extending across the intervertebral disc space (see Figure 13). Figure 14 demonstrates the general hypervascularity of the vertebral body extending into the ectopic bone. Superiorly, the lesion retains bilateral separation from L4 vertebral body (see Figure 15). The extent of the exuberant bone growth decreases more inferiorly in L4 (see Figure 15). Lastly, L5 demonstrates antero-lateral separation of the lesion from the vertebral body that closes as move bilaterally (see Figure 16).

Figure 11: Transverse CT raw data of bilateral ALL ossification in lumbar spine demonstrating clear separation between the ectopic growth and vertebral body. Note the zygapophyseal reactions.
Figure 12: Transverse CT raw data showing progression through L2 vertebral body from superior margin (A) through inferior margin entering the intervertebral disk space towards L3 (D). Notice the zygapophyseal involvement. The separation is lost anteriorly but retained laterally in C and D. B, C and D all show bony sclerosis reactions in the vertebral body subjacent to the ossified ligament.
Figure 13: Transverse CT raw data of superior L3 separation retained right laterally and obliterated left laterally. Note the potential (small) Schmorl’s node in B and C; these do not appear in any other lumbar vertebrae.

Figure 14: Transverse CT raw data. Note the extreme vascularization throughout the body and extending into the ALL ossification.
Figure 15: Transverse CT raw data of L4 (A) more severe bilateral ALL ossification with clear separation. Inferiorly, L4 ossification decreases in severity (B).
Figure 16: Transverse CT raw data of L5 showing bilateral ossification and the coexistence of obliterated and clearly present space between ALL and vertebral body.

3.3 Histological Description

Histological examination for descriptive purposes was done on two sections; a right lateral longitudinal oblique section through lesion affecting L2-L3 and a left lateral transverse section through the lesion affecting L3-L4. Macroscopically, these were determined to be the most severe based on size and thickness of the lesions. Figure 17 and 18 demonstrate the regions of interest and direction of sectioning.
Figure 17: Mimics three dimensional CT reconstruction Anterior L1 through superior L4. White boxes denote areas of interest for histological sectioning.
In both planes of sectioning, the primary focus was the lesion and the interface with the vertebral bodies. Therefore, each section contained both ligamentous ossification (lesion) and a portion of the vertebral body. Initial microscopic analysis was performed to identify features within the sections compared to normal non-pathological bone.
Polarized light was primarily used so as to visualize the lamellar pattern caused by birefringence resulting from the arrangement of collagen fibrils (Eriksen et al. 1994). Both lamellar bone and woven bone are present within the lesion. Vertebral body trabeculae show infilling or compaction, a term introduced by Enlow (1963) near its interface with the ectopic bone. The lesion appears to extend into the vertebral endplates. As evidenced in CT images, ligamentous ossification appears to be hypervascularized in both bright field light and polarized light. Haversian systems are present in both planes of sectioning though more prevalent in the transverse plane.

In the longitudinal oblique plane, all images are displayed with a magnification of 4x in order to provide context and a larger field of view. The sample includes the inferior portion of L3, the intervertebral lesion of bony growth and the superior portion of L3. Figure 19 demonstrates trabecular infilling near the vertebral endplate and at the interface of the ectopic ossification and vertebral body. Again, this may be representative of trabecular compaction or sclerosis (Enlow 1963). Figure 20 represents the area just lateral to figure 19 moving out into the lesion consisting of disorganized apparently woven bone. Figure 21 represents the area between the interface of the lesion and the trabeculae including the outermost and superior edge of the lesion which terminates at the midportion of the vertebral body. The Volkmann’s canals and high density of osteocyte lacuna are indicative of hypervascularity and consistent with woven bone. Figure 22 spans from the outermost periosteal edge of the lesion inwards and represents the
superior bridging region across the intervertebral disk space. Periosteal lamellar apposition is seen along the outermost edge while what appears to be woven bone persists more medially. Figure 23 shows the middle portion of the lesion that has bridged the intervertebral disk space. There are packets of organization surrounded by disorganized bone; however, these packets cannot be considered lamellar in nature as there is no distinct “plywood-like” pattern to the collagen fibrils. Nor do they appear characteristic of the highly organized fibrolamellar bone (Enlow 1968). There does not appear to be any dense periosteally deposited lamellar bone along the outer edge perhaps indicating a less developed/less mature stage. Figure 24 is approaching L4 and demonstrates what appear to be secondary osteons, possible resorption cavities and organized lamellar bone (similar to the corresponding region adjacent to L3 represented in Figure 22). The thickest portion of the lesion is located at the mid-vertebral disk space and appears to thin as it extends into the margin of the vertebral body. At these latter areas, there appears to be a higher ratio of organized periosteal lamellar bone to woven bone as opposed to the intervertebral bridging lesion.
Figure 19: Trabecular infilling or compaction with circumferential lamellar bone at the vertebral endplate.

Figure 20: Interface between lesion, vertebral endplate and trabeculae. The upper portion of the slide is moving towards the trabeculae (note the secondary osteon); the right side of the image is toward the vertebral endplate; the bottom of the image is moving towards the lesion.
Figure 21: Hypervascularity (Volkmann’s canals) and dense population of osteocyte lacunae. Location near midportion of vertebral body. The bottom left portion of the image is towards the periosteum (or outer edge of the lesion) with evidence of periosteal apposition.
Figure 22: In both the top and bottom image, bottom left corner represents the periosteal edge of ossified ligament.
Figure 23: The middle of the bridging lesion with L2 to the right of the image and L3 to the left of the image. The periosteal edge is in the bottom right corner. Highly disorganized bone with random “packets” of more organized but not lamellar bone.
Figure 24: The top image is located just inferior to Figure 23 moving down into the lesion adjacent to L4. The bottom image represents the periosteal edge. Again, dense lamellar periosteal bone is present with less medially located woven bone or disorganized bone as descend towards the midportion of L4 vertebral body.
In the transverse lesion incorporating the inferior portion of L3, all images are presented at a magnification of 4x. Figure 25 represents a portion of the L3 vertebral trabeculae that does not appear to be affected by the hyperostosis. Figure 26 represents a compilation of slides representative of what appears to be the interface between the normal trabeculae and the ectopic bone growth. Identifiable features include Haversian systems either primary or secondary, as well as possible resorption cavities. There are areas of organized lamellar bone surrounding large cavities which were perhaps trabeculae experiencing varying stages of lamellar compaction (Enlow 1962). Figure 26 also shows a potential eccentric osteon dissected in an oblong plan. Grossly, there is a region of bone located midway through the lesion with highly consistent orientation which spans the entire section. Microscopically, the orientation is retained across the sample surrounded by Haversian systems. Located just medial to this macroscopically and microscopically distinct area, is a region of highly Haversionized bone with multiple secondary osteons and fragmentary osteons suggesting antiquity (see Figure 27).
Figure 25: “Normal trabeculae” in L3 vertebral body located medially away from the areas perceived to be affected by the lesion.
Figure 26: These images span the area that was macroscopically identified as the border between trabeculae of the vertebral body and lesion. A and B represent what appears to be sclerotic response in the trabecular bone at the interface.
Figure 26: Note the osteons and circumferential lamellar bone in C and the eccentric osteon in D.
3.4 Bioarchaeological Review

The bioarchaeological literature has been sparsely populated with documented cases of DISH. The presence of DISH in skeletal populations has frequently been linked to high status way of life (Waldron 1985; Arriaza 1993a, 1993b; Rogers and Waldron 2001; Jankauskas 2003). DISH as a skeletal lifestyle indicator can contribute to a more comprehensive understanding of ancient societies (Jankauskas 2003). Likely, a substantial link between DISH and social status exists, however, the presence of DISH
alone should not be considered indicative of elevated social status (Jankauskas 2003). A compilation of documented cases considering substantiating archaeological context has yet to be published. An organized, comprehensive and universal review of DISH was performed using multiple key-terms such as “skeletal hyperostosis,” “Forestier’s disease,” “senile ankylosing hyperostosis,” and “ligament ossification.” A reference of DISH cases in which behavioral implications have been inferred from published archaeological context is created in Table 2. Those marked with an asterisk did not include archaeological or burial context to support or refute social status or behaviors. The remaining cases appear to have substantiating evidence for higher status lives which would include increased sedentism and nutrient access.

Arriaza (1993a, 1993b) argues the existence of “ubiquitous” conditions with which to expect DISH cases to be found. These include sedentism and increased nutrient intake. The frequency of DISH in monastic cemetery populations has prompted some to assume the “monastic way of life” as a disease risk factor (Rogers and Waldron 2001; Verlaan et al. 2007). The “monastic” and high status ways of life are characterized by sedentism and diets high in saturated fats and alcohol but low in vegetables (Arriaza 1993a, 1993b; Rogers and Waldron 2001; Jankauskas 2003). Cases of DISH found in archaeologically and historically confirmed clergymen include the following: 40.4% of adults diagnosed with DISH in Abbey court in Maastricht, Netherlands dated from 275-1795 CE (Verlaan et al. 2007); 11.5% (6 of 52 male adults) prevalence in the Royal Mint.
medieval cemetery compared with a nearby rural lay cemetery (who were most likely farmers) prevalence of 0% (Rogers and Waldron 2001). In Lithuanian Iron Age, Medieval and Early Modern skeletal populations with archaeological context to substantiate status, 27.14% of high status individuals, 11.86% of urban individuals and 7.14% of rural individuals demonstrated vertebral or peripheral ossifications characteristic of DISH that increased with increasing age (Jankauskas 2003). Cosimo I (1519–1474 CE) and his son Ferdinand I (1549–1609 CE), both Grand Dukes of the Medici family from Renaissance era Florence, were diagnosed with DISH in correlation with an elite lifestyle (i.e. high caloric diet most likely contributing to obesity and type-II diabetes) (Canci et al. 2009). Table 2 demonstrates the antiquity and universality of DISH in human populations.
CHAPTER 4: DISCUSSION

4.1 Macroscopic Diagnosis

Using macroscopic differential diagnosis criteria, the gorilla specimen was determined to have been afflicted with DISH. The specimen was treated with the consideration of, or as a proxy for, a bioarchaeological situation. As the first step in identifying the skeletal manifestations of a condition in skeletal remains, a qualitative examination revealed diagnostic attributes consistent with DISH. The most frequent confounding condition in the clinical literature is ankylosing spondylitis (AS). Thus, throughout the differential diagnostic process, characteristics of both DISH and AS were considered. The classic “candle-wax” ossification was present particularly in the lower thoracic and lumbar spine ankylosing at least four vertebrae as per Resnick and Niwayama (1976) and Waldron (2009). The hyperostosis appeared irregular and exuberant in contrast to the “fine, thin” syndesmophytes and “bamboo” spine characteristic of ankylosing spondylitis (see table 1) (Hannallah et al. 2007). Intervertebral disc space was retained despite bridging across these spaces. In contrast to diagnostic criteria, the stage of thoracic bony growth appears to be less advanced than the lumbar region. This patterning of affected vertebrae more resembles ankylosing spondylitis; however, lack of sacroiliac involvement, zygapophyseal ankylosis, and the preservation of disk space is not congruent with AS. Nevertheless, the sacroiliac joint
may be affected in DISH cases further complicating differential diagnosis (Olivieri et al. 2009). The upper third of the sacroiliac joint may show narrowing, sclerosis and even ankylosis resembling sacroiliitis which is pathognomonic of AS (Olivieri et al. 2009). AS typically shows an ascending pattern throughout the vertebral column. However, Resnick and Niwayama (1976) cite L3 as the most affected lumbar vertebral body in DISH cases. In accordance, El Miedany et al. (2000) noticed the lumbar lesions were symmetrical (bilateral) and more severe inferiorly than superiorly. The thoracic spine involvement of the specimen shows more severe lesions likely in the earlier stages of formation than the lumbar lesions. Though classically more severe on the right side than the left due to the pulsation of the aorta overlaying the left lateral thoracic spine, this does not preclude the presence of ossifications on this side (Olivieri et al. 2009).

Macroscopically, the specimen does demonstrate a more advanced set of ectopic bony growths right laterally. Further investigation radiographically was needed to confidently diagnose DISH in the specimen.

4.2 Radiographic Diagnosis

The importance of radiographic diagnosis in clinical populations has created a multitude of clinical literature and diagnostic criteria based on this understanding. Radiographic changes are difficult to recognize in early stages of any spinal condition (Olivieri et al. 2009). The temporal span of ten years between figure 11 and figures 12 and 13 demonstrates the amount of hyperostosis that occurred in a decade. It has been
estimated that at least 10 years is needed for the pathologic process to become characteristically DISH (Mader and Lavi 2008). The plain radiographs of the gorilla taken antemortem were limited in comparative diagnosis as the medical literature discusses mainly lateral view characteristics. It is recognized that since the ALL covers both anterior and lateral aspects of the vertebral bodies, an anterior and/or posterior view of the spine would result in the ossification appearing bilaterally (Olivieri et al. 2009). This is evidenced in figures 11-13. If a lateral view was present, a radiolucent line should be visible between the ossified ALL and the vertebral body (Hannallah et al. 2007). However, in more advanced stages of the disease, this space may become obliterated through “focal bony ankylosis” (Resnick and Niwayama 1976:564). Radiographically, AS results in the “squaring” of the vertebral bodies beneath the ossification (Olivieri et al. 2009) which is not present in the macroscopic nor radiographic examination of the gorilla specimen.

The syndesmophytes associated with DISH are considered “nonmarginal” in comparison with the “marginal” syndesmophytes of both AS and osteoarthritis (Hannallah et al. 2007, Olivieri et al. 2009). “Non-marginal” ossifications are not limited to the margins of the disk space (Hannallah et al. 2007, Olivieri et al. 2009). Thus, it is expected that the ligamentous ossification would not only bridge the intervertebral disk space, but also extend to cover the anterior and/or lateral aspects of the vertebral bodies as well. This is evidenced in the plain radiographs, CT data as well as histological
sections (to be discussed later). Plain radiographs are limited in their power for
differential diagnosis; fortunately, in dealing with skeletal remains in an archaeological
context, researchers have access to other avenues of diagnosis. Mazieres and Rovensky
(2000) present a more in depth and recent radiological criteria for the differential
diagnosis of DISH from other hyperostosis inducing conditions including AS and
osteoarthritic changes (see table 3). These radiographic criteria must then be translated
into the appropriate avenue or avenues with which the bioarchaeologist will be
diagnosing the remains.

<table>
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<th>Spondylosis (osteoarthritis of the spine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebral body</td>
<td>Thick overbridging ossifications (enthesophytes)</td>
<td>Thin syndesmophytes and squaring of the vertebral body</td>
<td>Osteophytes with sclerosis of the subchondral plates</td>
</tr>
<tr>
<td>Vertebral disc</td>
<td>Normal</td>
<td>Normal, with possible appendicular ossification</td>
<td>Narrowed, with possible vacuum phenomena</td>
</tr>
<tr>
<td>Zygosphophysemal joints</td>
<td>Preserved or sclerotic with ossifications on the non-articular surface (mainly at the lumbar level)</td>
<td>Erosions, sclerosis, ankylosis</td>
<td>Sclerosis, osteophytes</td>
</tr>
<tr>
<td>Sacroiliac joints</td>
<td>Preserved, without erosions; ossification of the iliosacral ligament in the anterior and superior parts of the joint</td>
<td>Erosions, widening of the joint space, then ankylosis</td>
<td>Appropriate to age, sclerosis, small osteophytes, vacuum phenomena sometimes observed</td>
</tr>
</tbody>
</table>

Table 3: From Mazieres and Rovensky (2000): Differential diagnosis of DISH, AS and Osteoarthritis
CT analysis allows for an extensive look at the anatomical aspects of hyperostosis and vertebral column involvement. In both the thoracic and lumbar transverse sections, there is a clear separation between the ossified ALL and the vertebral body. However, particularly in the older and more advanced lesions of the lumbar spine, evidence of vertebral body ankylosis and obliteration of the space between the ALL and the body are present. Resnick and Niwayama (1976) provide a radiographic example of this as seen in Figure 28. Although many in the rheumatology field use the separation or clear radiolucency between the ossified ligament and the vertebral body as a differential diagnostic criteria of DISH, this may not be the case in the presence of more severe hyperostosis. Mazieres and Rovensky (2000) and Cammissa et al. (1998) provide comparative transverse CT images of the thoracic spine (see Figure 29). In terms of the nature of the hyperostosis, generally the spondyloarthopathies (including AS) are characterized by linear and slender ossifications without thickening opposite the vertebral body (Mazieres and Rovensky 2000). These criteria are not met in the gorilla sample as evidenced by CT data in both the thoracic and lumbar vertebrae. A number of Schmorl’s nodes are present indicative of some degenerative changes. El Miedany et al. (2000) noted Schmorl’s nodes in their study coexisting with DISH. The invasion of the vertebral body by disk matter does not necessitate disk space collapse.
Figure 28: Obliteration of space between ALL and vertebral body in the lumbar spine. From Resnick and Niwayama (1976)

Figure 29: (A) Transverse CT raw data showing right antero-lateral ossification and separation from the vertebral body. From Mazieres and Rovensky (2000). (B) Transverse CT raw data showing similar conditions along with vertebral body sclerosis under the ossified ligament and zygapophyseal joint involvement. From Cammissa et al. (1998).
4.3 Observational Histological Description

Histological descriptions of spinal ligament ossification are difficult to find in the clinical literature and, in the scope of this researcher, not present in the histopaleopathological literature. As such, basic observational descriptive analysis can significantly contribute to the established body of knowledge on DISH. The ossification process is believed to begin as endochondral ossification (EO) with areas of metaplastic cartilage in the ligament contributing to the commencement of the process (Resnick and Niwayama 1976). For EO to begin there must be a cartilaginous template formed in the ALL. Ono et al. (1999) published a pathological study of the ossification of the posterior longitudinal ligament (PLL) and the ligamentum flavum (LF) of the spine. Unfortunately, the authors do not provide images of the pathological sections, only descriptions. It is noted that the nature of ligamentous ossification in the PLL and LF could be translated to the ALL in cases of DISH as well (Ono et al. 1999). Some argue that PLL ossification is a separate disease entity from DISH; others believe PLL or LF ossification can be another manifestation of DISH (Ono et al. 1999). The mature lesions of ossified ligament would be composed of lamellar bone and well developed Haversian systems (Ono et al. 1999). The immature lesions would be characterized by woven bone (Ono et al. 1999). These concepts are in accordance with fundamental principles of bone formation and remodeling: woven bone is younger and more rapidly formed whereas, lamellar bone and any indications of remodeling is in later stages of development (Enlow
1963; Stout and Simmons 1979). Haversian systems function as “replacement” units (Enlow 1963); woven bone is gradually replaced by lamellar bone and remodeled by osteons (Stout and Simmons 1979). Limited by skeletonized material, the examination of the gorilla specimen as a proxy for a bioarchaeological examination of human skeletal remains precludes the inclusion of the soft tissue changes discussed in the literature. As such, those will not be considered here.

Resnick and Niwayama (1976) discuss the vertebral body sclerosis associated with the bony excrescences at the superior and inferior margins of the body. This is further elucidated by Fornasier (1983) as sclerosis of the subjacent vertebral spongiosa. This can be seen on both the longitudinal and transverse sections at the interface of the lesion with the trabeculae (or spongiosa). The transverse section contains features that may be consistent with this description. The ALL ossified through the process of EO: the images from this section contain secondary Haversian systems suggesting their antiquity. The “border” of bone that appears to be organized but not in a traditional lamellar pattern spanning the entire section may have once been the space between the ossified ALL and the vertebral body (see Figure 30). This bone pattern without any secondary osteons suggests it’s younger age than the ossified ALL. Just medial to this region is evidence of Haversian systems consistent with Resnick and Niwayama’s (1979) and Fornasier’s (1983) suggestions of vertebral body sclerosis. The vertebral cortex seems to be exaggerated in width evidenced by trabecular compaction or infilling. As to the
chronological order of these processes, the only measurement here is the amount of Haversian systems present (in accordance with Ono et al. 1999). Determining the exact order of processes may not be possible. However, these features seem to be consistent with the overall process of increasing severity of hyperostosis.

The presence of identifiable Haversian systems (secondary osteons) in both planes of sectioning indicates inconsistent orientation. These are thought to be secondary osteons in most cases; however, the presence of a reversal line was not identified for each supposed osteon. Therefore, it is possible some should be classified as primary. The majority of secondary osteons is seen in the transverse section suggesting their orientation to be longitudinal. However, the presence of the probable eccentric osteon in Figure 26 and those found in the longitudinal section suggest a transverse or oblique orientation. Some of this may be a product of sectioning plane, particularly the eccentric osteon. The mechanical forces present on the vertebral column and ectopic bone growth are not simply compressive (in which the osteons would retain a consistent orientation parallel to the force). These features of remodeling occurring both in the ossified ligament and the vertebral body sclerotic lesions make histological differentiation between them complicated. The presence of highly vascularized and dense osteocyte lacunae populations in woven bone (consistent with Ono et al. 1999 description of immature lesions of ossified ligaments) allows for some differentiation and identification of ectopic bone growth. However, as in the transverse plane examples of remodeled
ossified ALL, features of the pathological bone resemble features found in “normal” bone.
Figure 30: Merged image (4x) of a representative sample of the transverse section depicting vertebral body (far left) interface with ectopic bone out to the periosteum (far right). Note the consistently organized bone through the center of the image surrounded by evidence of remodeling both medially (towards the vertebral body) and laterally (towards the periosteum).
The discussion of EO as the primary and initial process associated with DISH (Resnick and Niwayama 1976; Rothschild and Martin 1993) does not explain what happens after the ligament is ossified. If it was merely the EO of the ligament, the size of the ossification would be limited to the original size and thickness of the ligament (Ono et al. 1999). However, this would not produce the “candle wax” or irregular, bulky, “flowing” pattern characteristic of DISH. The longitudinal sections in Figures 22 and 24 display periosteally deposited dense lamellar bone with perpendicularly oriented vascular canals. The literature does not address the process of periosteal apposition in regards to spinal ligament ossification. Ono et al. 1999 suggest a “growth plate” that exists between the ossified ligament and the vertebral body where fibrocartilaginous cells proliferate and essentially “push” the ALL outward. However, in this specimen, there is evidence of periosteal apposition contributing to the size and thickness of the lesion. In the dense lamellar bone found in Figures 22 and 24, the orientation of the vascular supply seem to be headed into the less organized woven bone located closer to the vertebral body. There is no evidence of remodeling occurring in this area (i.e. visible secondary osteons); however, it is possible these are Haversian canals oriented longitudinally for which the reversal line is not clear in this plane. The clearly organized periosteal lamellar bone here continues inferiorly across the intervertebral disk space. Interestingly, the lamellar bone located near the middle of disk space lesion is less clearly organized and the vascular channels appear to be running longitudinally. This bone may be “younger” than
the bone located opposite the vertebral bodies consistent with the concept that the
gs begin around the midportion of the vertebral body and extend across the disc
pace to meet with the ossifications from above or below. Figure 23 may demonstrate the
immaturity of the midportion of the bridging lesion; highly disorganized bone with little
to no periosteal lamellar depositions. Figure 24 located just inferiorly to figure 23 shows
imilar features to figure 22; the suggested maturity of these areas of bone and their
atomical location at the midportion and margin of the vertebral body supports the
viously suggested pattern of ossification.

The clinical literature contains sparse histological descriptions of DISH with few
published images. Those that are available are typically cadaver samples with
companying soft tissues contributing to the understanding of stages of the disease
cess. However, in bioarchaeological situations, researchers are limited to skeletal
ains. Differentially diagnosing DISH histologically must be founded in what little
ical pathological literature present; however, it is suggested here that perhaps there
re more processes occurring than thus far discussed in the field. Using and describing
multiple lines of diagnostic evidence has confidently pointed to the presence of DISH in
sample. However, it is difficult to say much as to the variation seen in the specimen
pared to “classic” diagnostic criteria such as the predilection of the lumbar spine over
the thoracic spine for ossification, slight involvement of the zygapophyseal joints, etc.
All possibilities are within the realm of variation for DISH, in so far as can be determined

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4.4 Behavioral Contributions to the Etiology of DISH

As previously discussed, the etiology of DISH is unknown and likely includes a combination of genetic, environmental, behavioral, endocrinologic and metabolic factors. Though much recent work has focused on the genetic factors contributing to hyperostosis, here the behavioral links will be emphasized. This research focuses on the role of sedentism and excessive food intake, as would be expected in higher status individuals and/or monastic individuals, resulting in promotion of the MS and subsequent increased serum levels of insulin and insulin-like growth factor (IGF-1). However, conflicting reports on prevalence of DM in patients with DISH suggests population dependent results. Sencan et al. (2005) found no difference in serum insulin or IGF-1 between a Turkish population with DISH and a control group with type II diabetes mellitus prompting the suggestion of further investigation into the connection between DISH and DM. Denko and Malmud (2006) found DISH patients with a BMI greater than 28 kg/m2 had higher serum insulin levels but no differences in IGF-1 levels. Arguably, clinical studies with patients treating their DM and/or hyperinsulinemia as was the case with Sencan et al. (2005), cannot be projected on past populations who probably did not undergo similar treatment. Assuming clinical correlations with metabolic syndromes in individuals with DISH are applicable to past populations can allow for behavioral
inferences based upon social inequality as well as differential access to nutritional resources. The frequency of DISH in monastic cemetery populations has prompted some to assume the “monastic way of life” as a disease risk factor (Rogers and Waldron 2001; Verlaan et al. 2007). This does not suggest a genetic predisposition for the disease associated with monastic populations, rather it suggests a series of behavioral and nutritional factors associated with this way of life contributing to metabolic dysfunction (MS) and increased disease risk for DISH (Rogers and Waldron 2001). Monastic diets high in saturated fats and alcohol but low in vegetables coupled with sedentism characterize not only the “monastic way of life” but also high status lifestyles (Arriaza 1993; Rogers and Waldron 2001; Jankauskas 2003).

Arriaza’s (1993a, 1993b) “ubiquitous” behavioral conditions under which DISH is found have been heavily supported in the clinical and bioarchaeological record as evidenced in Table 2. Yet, Rogers and Waldron (2001) caution the direct assumption that individuals possessing skeletal manifestations consistent with diagnostic criteria for DISH should be designated high status or to have lead a monastic lifestyle. The presence of DISH in two individuals thought to be sea mammal hunters from the Late Jomon period in Hokkaido, Japan demonstrates the variation in behavioral risk factors for the disease (Oxenham et al. 2006). This anomaly coupled with the presence of the disease in rural individuals from Jankauskas (2003) indicates the critical role archaeological context must assume in further investigation into variation among DISH cases, social
stratification and associated behavioral and lifestyle risk factors. Using historical data and burial location, especially in Christian burial practices, can provide the archaeological context for determining the social status of the interred individuals. Unfortunately, in some reported cases of DISH, archaeological context has not been provided limiting our understanding of past behaviors (indicated by asterisks in Table 2). In the presence of anomalous behaviors indicated by the burial context, DISH as a lifestyle indicator of elite status still cannot be firmly established. Behavioral variation must continue to be considered in any investigation of past population.

Confounding the identification of DISH in the prehistoric archaeological record is the direct relationship with disease prevalence and age. Thus far, DISH has rarely to appear independent of indications of social stratification; however, this could potentially be an artifact of the increasing longevity associated with social complexity. As previously mentioned, the onset of pathological changes associated with DISH may be as early as the second decade of life though skeletal manifestations require decades to mature into characteristic features of DISH (Hannallah et al. 2007). Therefore, individuals may not have been living long enough for DISH to become a significant factor in quality of life or for bioarchaeological identification until the advent of social complexity. The amount of time required for development of hyperostosis to a level of severity recognized as DISH may cause misdiagnosis of the condition in individuals at earlier developmental stages if careful and meticulous diagnostic criteria is not applied.
4.5 Implications of DISH in a *Gorilla gorilla gorilla* Specimen

Although the clinical literature documenting the patterning, behavioral correlates, and metabolic dysfunction associations in humans is abundant, the literature on DISH in mammals and particularly non-human primates is sparse. The documented case of DISH in a deceased captive 42 year old male Bornean Orangutan (*Pongo pygmaeus pygmaeus*) is among the first in non-human primates (Klaver and Kompanje 1996). Implementing the current clinical diagnostic criteria, the gorilla specimen was diagnosed with DISH. However, variations in vertebral patterning were present. The predilection of the lumbar spine over the thoracic spine in a quadruped in comparison to a biped where the thoracic spine is most often afflicted first could be due to mechanical differences associated with locomotion. The gorilla was not diagnosed during life despite the presence of hyperostosis on antemortem radiographs. The “classic” right antero-lateral thoracic spine predilection was not necessarily the case here potentially precluding an initial diagnosis of DISH. Again, a sample size of one individual does not dictate the need for a reevaluation in diagnostic criteria; however, it is suggested that further research on diagnosing spinal pathologies in non-human primates is needed to develop a more applicable criteria.

A lifestyle in captivity may have contributed to the progression of the disease. Gorillas in their natural habitat experience intra-annual variation in climate and food resources (Watts 1998). Ecological variables such as rain fall, vegetation growth, and
access to nutrients do not factor into a captive lifestyle where resources are provided rather than procured. Remis et al. (2001) found Western lowland gorillas are not as strictly folivorous as previously thought; exploitation of seasonally and yearly variable fruit resources was a vital portion of subsistence at Bai Hokou in Central African Republic. An oscillating pattern of fruit abundance tied to rainfall amounts influenced the amount of foliage consumed by gorillas (Remis et al. 2001). Nishihara (1995) states the basic diet for a Western lowland gorilla consists of the fibrous parts of plants, terrestrial herbaceous vegetation and aquatic herbs high in protein. Dietary adaptations in wild, natural environments vary compared to the consistently provided dietary foods in a captive setting. The following items were available daily for this gorilla: biscuits, primate diet mix, parrot seed mix, popcorn, apples, bananas, broccoli, carrots, celery, and kale. Additional food resources were provided on a rotating basis throughout the week such as: rice, bread, and other fruits including grapes, oranges, sweet potatoes, and grapefruits. An abundance of nutrients provided without simulation of inter-annual variability in addition to a somewhat sedentary or reduced activity patterns in comparison with behaviors in natural habitats could predispose captive gorillas to metabolic disease and DISH manifestations.

As per zoo records, this female gorilla was considered overweight at time of death weighing 276 pounds with her ideal weight at 245 pounds. The only medical records available were from her last year of life; there is no indication of MS other than her
weight. However, serum levels of insulin or IGF-1 were not provided. It is possible the prevalence of DISH in captive non-human primates experiencing similar conditions to higher status individuals such as continuously rich diets and semi-sedentary/sedentary lifestyles may increase as this diagnosed case increases awareness of DISH. As held throughout this research, the etiology of DISH is complicated, and there is no reason to suggest this would not be the case in a non-human primate. Knowledge and awareness of DISH in settings in which captive non-human primates are cared can potentially increase quality of life.
CHAPTER 5: CONCLUSION

Using multiple steps to differentially diagnose the spinal pathology in a skeletonized Gorilla gorilla gorilla specimen has elucidated possibilities for bioarchaeologists encountering a similar situation in past populations. Focus was placed on the vertebral column as this is universally affected in DISH, potentially mis-diagnosed, and less subject to taphonomic destruction than peripheral manifestations. Standardization of bioarchaeological diagnostic criteria will increase the accuracy and comparability of paleopathological diagnoses across populations and species. Diagnosis began at the macroscopic level using criteria delineated in both the medical literature as well as paleopathological literature, including Waldron (2009) and Ortner (2003). Non-destructive radiological techniques were then used to further investigate the extent, location, and patterning of ossification. The ligamentous ossification exhibited characteristics consistent with a diagnosis of DISH. Should destructive analysis be available as part of a bioarchaeological diagnostic toolkit, histological descriptions were provided. The features identified through histological analysis seem to be consistent with descriptions of other ossified spinal ligaments. Suggestions as to the processes occurring can only be validated through further research. Taking serial sections through both the longitudinal and transverse sections and using concepts of “mature” lamellar bone and “immature” woven bone to retain a temporal context is planned for future research.
Comparison should be done with a human sample of DISH to determine similarities or differences between species. It is suggested here that diagnostic criteria for DISH in humans can be applied to non-human primates with the amount of flexibility exercised in human diagnosis.

The bioarchaeological review revealed, with a few exceptions which lacked appropriate burial context, consistency between DISH and individuals thought to have been high status. Correlates between high status individual lifestyles and captive lifestyles of non-human primates are made in terms of activity and nutrient access. The result of such behaviors in metabolic disturbances, particularly insulin dysregulation, has been suggested as the link between behavior and hyperostosis. However, investigation into this relationship has resulted in conflicting results. As such, the etiology and effects of behavioral patterns remains ambiguous. Behavioral inferences may be made in terms of care taking and accommodations for individuals with severe cases of DISH (Oxenham et al. 2006). Individuals with advanced cases of DISH experience joint and vertebral pain as well as spinal immobility and dysphagia (Oxenham et al. 2006; Rogers and Waldron 2001).

This research presents evidence for the first identification of DISH in a female Western lowland gorilla. The descriptions of skeletal manifestations consistent with DISH and skeletal biology can speak to processes occurring in humans as much as non-human primates as they are frequently used for models of osteoporosis and other skeletal
pathologies. Histological examination within the individual specimen into the nature of the thoracic ossifications in comparison with the lumbar ALL ossifications could also potentially flesh out the processes taking place in a temporal context. Samples from human skeletal remains should also be taken in the future. Cadaveric samples with known medical histories would be ideal for investigating not only the bone involvement but the soft tissue involvement as well (particularly the early developments in the ALL). Immunohistochemical staining could be a potential avenue for delineating direction of growth and collagen fibers as well. The possible avenues for future research are cross-disciplinary and can inform not only on the field of bioarchaeology but the clinical field as well.
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