Spring 2019

Maize and Bone: An Evaluation and Expansion of a Proposed Model for the Differential Diagnosis of Pellagra in Human Remains

Myra G. Miller
University of Southern Mississippi

MAIZE AND BONE: AN EVALUATION AND EXPANSION OF A PROPOSED MODEL FOR THE DIFFERENTIAL DIAGNOSIS OF PELLAGRA IN HUMAN REMAINS

by

Myra Gale Miller

A Thesis
Submitted to the Graduate School,
the College of Arts and Sciences
and the School of Social Science and Global Studies
at The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Master of Arts

Approved by:

Dr. Marie Danforth, Committee Chair
Dr. H. Edwin Jackson
Dr. B. Katherine Smith
Dr. Andrew P. Haley

Dr. Marie Danforth	Dr. Edward Sayre	Dr. Karen S. Coats
Committee Chair	Director of School	Dean of the Graduate School

May 2019

Published by the Graduate School

ABSTRACT

This study attempts to test and expand a previous study to establish a differential diagnosis of pellagra in human remains (Paine & Brenton, 2006a). Seven individuals with documented pellagra and nine individuals randomly selected for comparison from the Hamann-Todd Osteological Collection were evaluated for caries, alveolar bone loss, periostitis, osteoporosis, cribra orbitalia, and porotic hyperostosis. Results indicate that the pellagra sample had lower rates of caries and alveolar bone loss, and higher rates of periostitis of the tibia and fibula in relation to the comparison sample. No osteoporosis, cribra orbitalia, or porotic hyperostosis was found in the pellagra sample. No statistically significant difference was found between the groups for any pathology except for periostitis when combined with the findings of a previous study (Paine & Brenton, 2006a). Future study should attempt to identify additional remains of those known to have pellagra.

ACKNOWLEDGMENTS

I would like to thank Dr. Marie Danforth, Dr. Katie Smith, Dr. H. Edwin Jackson, and Dr. Andrew Haley for their time, dedication, support, and input in creating this thesis. I would also like to thank the Hamann-Todd Osteological Collection for allowing me access to their collection and the Paleopathology Association and Southern Foodways Alliance for allowing me to present the results of this study at their meetings.

DEDICATION

I would not have been able to complete this thesis without the support and encouragement of numerous individuals throughout my life. Thank you to Dr. Laura Vick for igniting my passion for anthropology and allowing a high school student to sit in on her classes while I visited my sister at William Peace University. I would also like to thank Dr. Charles Duncan of William Peace University for shaping and encouraging my writing and Dr. Bill Duncan of East Tennessee State University, for his advice and encouragement to pursue public health, which led to choosing my graduate program. A sincere thank you also to Dr. Marie Danforth for her instruction, advice, and patience in answering all of my emails.

I would also like to thank Matt Mercer and the cast of Critical Role for creating entertaining, funny, and touching stories that helped me make it through many long nights of writing.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

CHAPTER I - INTRODUCTION

The same sociopolitical forces that brought smallpox and enslaved Africans to the New World also brought maize and many other foods cultivated by Native Americans to the Old World, however, the process of nixtamalization (alkaline processing) was not taken with the maize. The faster and higher yield per acre of maize compared to other grains made it appealing to the peasants of Europe and maize took hold and became a staple of the foodways of many poor Italians. However, without nixtamalization, by the mid-eighteenth century, a mysterious disease began to emerge in Europe, especially Italy, and quickly spread to western Europe, Africa, and the United States (Hilliard, 1969; Nunn & Qian, 2010)

One hundred years later, still little would be known of its etiology although patterns had emerged among those afflicted. Once thought to be restricted by geography, it became clear the disease could strike anywhere, but particularly among the poor and maize-dependent. The disease became known as pellagra, Italian for "rough skin", because the most prominent symptom of the disease is dermatitis, the first of the four "D's" of pellagra. Diarrhea usually accompanies the skin inflammation and these symptoms often worsen as the third "D", dementia, sets in. The disease begins to follow a seasonal pattern that can last for years until the final "D", death, takes hold (Cazenave, Bulkley, Burgess, & Schedel, 1846).

Pellagra soon became a major cause of concern in public health. Its prevalence across America was tracked in quarterly public health reports and its presence in state asylums was noted often. Although the mysterious disease made sporadic appearances everywhere in the nation, southern states were those hardest hit, (Harris, 1910; King

1910; Lavinder, 1909a; 1909b; 1910; Lavinder, Williams, & Babcock, 1909; Mississippi State Board of Health, 1915), largely because of their dependence on a maize-based diet. In Mississippi in 1914, pellagra caused 5.6% of the deaths in the state, representing 1,201 individuals. Morbidity rates were much higher, however. From April until October, rates of pellagra would equal or exceed morbidity rates of tuberculosis and typhoid fever, and during the peak month of July, there would more cases of pellagra than tuberculosis and typhoid fever combined. African Americans were disproportionately affected, comprising nearly two-thirds of those afflicted and over three-quarters of those who perished. This means that 6.5% of whites with pellagra would die as compared to 13.5% of African Americans (Mississippi State Board of Health, 1915).

The etiology of pellagra baffled the medical community for decades before Joseph Goldberger's claims that it arose from a nutritionally imbalanced diet were accepted, and it was not until 1937 that Conrad Elvehjem and Carl Koehn isolated niacin as the specific nutrient involved (Roe, 1973). Part of Goldberger's quest to prove that pellagra was a nutritional deficiency included trials in asylums and penitentiaries. In an asylum of 4,000 patients in Georgia, Goldberger was able to cure the many patients committed for pellagra-induced madness by simply adding animal protein to their diets (Vaughan, 1918).

Despite the relatively recent prevalence of pellagra, the nutritional deficiency has received little recognition in paleopathology. Anthropology in the United States has historically relied upon the study of the remains of Native Americans and, with the advent of NAGPRA and the field's attempt to address its reliance on marginalized populations, there has been a shift towards the study of historic populations. This reliance

on prehistoric populations in the United States, as well as pellagra's relatively recent occurrence in the country, means that unlike other nutritional deficiencies such as scurvy, rickets, beriberi, and anemia (Ortner, 2012), pellagra has received little attention within bioarchaeology; instead most discussion concerning the condition has been limited to historical records. The first mention of pellagra within the paleopathological literature occurred in 2000; it was not the focus of a study per se, but rather a call for the field to recognize the disease as one that may be diagnosed using bioarchaeological markers (Brenton & Paine, 2000). By 2008, Brenton and Paine had evaluated some 25 known pellagrins (those who suffered from pellagra) in two research collections in South Africa and Washington, DC (Brenton, Tompkins, & Paine, 2008). Based on their observations of these individuals, they created a model for the effects of pellagra on the human skeleton. However, this remains the only work conducted to date in bioarchaeology investigating the condition, despite increasing numbers of studies evaluating historical populations. With the movement of the field towards research with historical populations, this is a major gap in the current literature.

The purpose of this study is to test the model created by Paine and Brenton (2006a) against individuals newly identified with pellagra listed as cause of death in the Hammond-Todd collection, housed at the Cleveland Museum of Natural History. This is one of the largest research collections in the nation and was established almost entirely during the height of the pellagra epidemic. Because the number of skeletal remains of known pellagrins is so small, expanding research to newly discovered, relevant remains may provide novel insights into the skeletal effects of pellagra. This study will attempt to strengthen the validity of the diagnosis model and possibly identify other markers which

were not discovered in the original research (Brenton & Paine, 2007; Brenton et al., 2008; Paine & Brenton, 2006a). Rates of pathologies will be compared between the sample of those with pellagra and a comparison sample of those without pellagra from the same collection. The patterns of lesions seen in individuals with pellagra in the study will also be compared to those with pellagra in the original research (Brenton et al., 2008; Brenton & Paine, 2007; Paine & Brenton, 2006a). Most specifically, this study will explore the possible effects of the dermatitis associated with pellagra on the sternum and clavicle.

Striving to find a singular pathological marker that is indicative of a singular clinical diagnosis has proven to be futile within bioarchaeology (Ortner, 2012). There are limited reactions to osseous tissue and multiple different stressors can cause the same pathology (Powell & Cook, 2012). It also cannot be presumed that any pathology found on the remains of a person diagnosed with pellagra was the result of the pellagra alone. However, finding a trend of pathologies that coincide among individuals known to have pellagra should bring the condition into the realm of consideration for future assessment of human remains, especially those from maize-dependent populations. If the findings of this study support the results of Brenton's and Paine's (2006b; 2008) studies – that pellagra has its own combination of pathologies that occur at different rates than those from general malnutrition – then the field of paleopathology should begin to recognize the possibility of identifying pellagra in future studies of historical populations, especially within the southern United States of America.

CHAPTER II- MAIZE NUTRITION, NIXTAMALIZATION, AND PELLAGRA IN THE PAST AND PRESENT

This chapter will explore the nutritional composition of maize, the process of nixtamalization, and the current known relationship between niacin and osseous tissue through three lenses - early medical literature, current anthropological studies, and current biomedical literature.

Nutrition and Nixtamalization of Maize

The basic physical, chemical, and nutritional composition of maize, as well as the changes to these properties affected by nixtamalization, is covered in this section.

Maize consists of large kernels with 4 main anatomical portions: the pericarp, tip cap, endosperm, and germ. The external pericarp protects the kernel as a semipermeable membrane but also hinders bioavailability of nutrients. The pericarp is high in fiber and non-bioavailable B vitamins and accounts for 5% of the kernel mass. The tip cap attaches the kernel to the cob and is the means by which all nutrients and moisture enter and leave the kernel. It is not covered by the pericarp and makes up 1% of the kernel mass. The endosperm makes up the majority of the kernel's mass (83%) and consists of starch and a protein matrix. The germ is the internal portion of the kernel that consists of 33% fat, B-complex and A vitamins, and enzymes that can produce a new maize plant. A dried, whole kernel is 74% starch, 12% water, 7-12% protein, 3.4% fat, and about 1 percent ash and fiber (Gwirtz, Garcia-Casal, 2014; Katz, Hediger, Valleroy, 1974).

Nixtamalization is the alkaline processing of maize kernels. Traditional nixtamalization is a long and labor-intensive process that involves the boiling of maize

kernels in water containing lime, ash, or lye. After boiling, the kernels are left to soak in the alkaline water for 12-16 hours. After soaking, the kernels are repeatedly rinsed with fresh water and the pericarp is removed either manually or through rinsing. In the Southern portion of the United States, the product at this stage is called hominy and can be eaten in its current state or dried and ground into a meal to make grits. However, traditional processing would often continue by grinding the maize in its current state using stone metates to create masa for tortillas or tamales, a process that can take six to eight hours for the grinding and upwards of three hours to form and cook tortillas (Beck, 2001; Katz, Hediger, Valleroy, 1974; Gwirtz, Garcia-Casal, 2014).

Maize that has undergone the nixtamalization process possesses different physical and nutritional properties than its raw state. Processing in an alkaline solution has an effect on the viscosity of the starch gels of the maize, depending on the concentration of the alkaline solution used. A 0.2% solution produces the most viscosity, with higher and lower concentrations producing less viscous starch gels (Mondragón et al., 2006).

Alkaline processing also affects the bioavailable nutrients in maize. Most significant to this study is the increase in bioavailable niacin and tryptophan — which can be metabolized into niacin — that occurs with alkaline processing. Tryptophan levels increase 129% with alkaline processing, however, the amino acid leucine also increases 116% and leucine inhibits the metabolism of tryptophan into niacin. This effect of leucine is negated by the amino acid isoleucine, however, whose levels rise 214%, therefore negating the rise in leucine (Katz, Hediger, Valleroy, 1974).

Along with a rise in niacin and tryptophan, nixtamalization increases other nutrients as well, most notable calcium and iron. Calcium is introduced to the maize via

the alkaline substance used, most often wood ash that contains high levels of the mineral. Iron levels are also increased, however, this increases only occurs if the maize is processed in stone implements (Greenhouse, 1981; Katz, Hediger, Valleroy, 1974).

Current Biomedical Research on the Skeletal Effects of Niacin Deficiency

Current studies about pellagra are as rare as the disease itself today, but there does exist a vast array of research about the physiological role of niacin in the human body. This research is vital for bioarcheological study in that, from a fundamental epistemological standpoint, it would be remiss to attempt to identify a disease within the skeleton if that disease has no effect upon the skeleton.

Niacin and Dental Health

Niacin deficiency (pellagra) causes a burning sensation in the mouth, swelling and redness of the tongue, the formation of a thick, gray pseudomembrane on the tongue, pain of the gingiva caused by dilation of capillaries, angular cheilitis (inflammation of the corners of the mouth), caries, and ulcers in the lingual margins (Tolkachjov & Bruce, 2017). Interestingly, excess niacin was found to cause gingival pain due to dilation of the capillaries in two case studies, although this is the only reported instance of this symptom (Leighton, Gordon, Small, Davis, & Ward, 1998).

There are several studies on the relationship between niacin and periodontal health. A study of eight cotton-top marmosets fed a niacin-free diet led to the development of stomatitis with necrotizing gingivitis and periodontitis (Dreizen, Levy, & Bernicki, 1977). A separate study in monkeys tested the effects of toothpastes with nicotinate (a form of vitamin B_3), chlorhexidine (an antibacterial substance), and a mix of

these two active ingredients against the control of the base paste. The nicotinate, chlorhexidine, and mixed pastes all reduced gingival crevicular fluid, inflammation, and bacterial colony forming units (Taguchi et al., 1989). These studies illustrate a relationship between niacin and periodontal health, supporting the use of alveolar bone loss in the model to identify pellagra in remains.

Niacin and Osteoporosis

There is limited evidence of loss of bone mass density due to niacin deficiency in biomedical literature despite the evidence in historic medical texts. However, the evidence that is present is compelling. A study of the relationship between osteoclast formation, calcium, and nicotinic acid adenine dinucleotide phosphate (NAADP, a byproduct of niacin) found a decrease in osteoclast formation and resorption at high NAADP concentration (100 and 500 μM), indicating a reduction of bone absorption (Cheng et al., 2015). This may mean that a reduction in NAADP (caused by niacin deficiency) could result in increased osteoclast formation and resorption.

The relationship between niacin and leukemia seems to be a well-tested one in the literature with the consensus that niacin supplementation can aid in the recovery of leukemia. This is because of the increase in cellular DNA damage in those with niacin deficiency, combined with a decrease in apoptosis, meaning an accrual of cells in the bone marrow with genetic damage (which are likely to become cancerous). Niacin supplementation in chemotherapy patients increased apoptosis of these damaged cells (Boyonoski et al., 2002; JC, JL, & JB, 2007).

Three observational studies of the relationship between bone density and niacin in Japanese, Korean, and Chinese populations found mixed results (Dai, Wang, Ang, Yuan,

& Koh, 2013; Park, Heo, & Park, 2011; Sasaki & Yanagibori, 2001). The cross-sectional study of post-menopausal women found a statistically significant correlation between increased consumption of niacin and increased bone mineral density (Sasaki & Yanagibori, 2001). However, the other studies did not find a statistically significant correlation between niacin consumption, bone mineral density, and hip fractures (Dai et al., 2013; Park et al., 2011).

Early Medical Literature on the Effects of Pellagra on Skeletal Tissue

Information about the effects of pellagra on skeletal tissue is severely limited. At the height of pellagra's prevalence in the late 1800s and early 1900s, very few of the numerous texts on the disease even included sections on the skeletal system. Those that did provided only cursory information and revealed that osteoporosis is the most common osseous sign of pellagra in early literature (Gillman & Gillman, 1951).

In 1909, the National Conference on Pellagra was held in South Carolina, and the country's leading researchers into the etiology and definition of the disease gathered. In the transcription of this meeting, the skeletal symptoms of pellagra are mentioned only twice, once to note that the "bones are often friable" (Harris, 1910, p. 90) and again during a description of an autopsy of a pellagrin in which the doctor was "struck with the fragility of the bones" of the vertebral column (King, 1910, p. 174). In his book, *Pellagra: An American Problem* (1912), George Niles also draws attention to the osteoporotic effects of pellagra. He states that this effect "is supposed to depend on the eccentric atrophy of the compact substance with hypertrophy of the medullary substances, and has been seemingly demonstrated by the microscope." (p.160)

Roberts (1914) included more in his text on pellagra about the disease's relationship with bones than did any of his contemporaries. His text includes the same wording as Niles about the "eccentric atrophy of the compact substance" (Niles, 1912, p. 160 as cited by Roberts, 1914, p. 193), but Roberts gives novel information about the bones of deceased pellagrins, gleaned from autopsies. He reports that a previous researcher, Strambio – one of the most prominent researchers of pellagra – noted that the sternum and ribs of these individuals to be softened and bright red in color. Strambio apparently found these similar to bones that had been affected by osteomalacia. Interestingly, Roberts attributed this to a nutritional deficiency in the body over a decade before Goldberger proved that pellagra is the result of niacin deficiency. Other than these vague comments, historical records of specific bony markers of pellagra are sparse.

Bioarchaeological Studies of the Effects of Pellagra on the Human Skeleton

Anthropological studies on the effects of pellagra on the human skeleton have, to date, only occurred in two collections in the world (Paine & Brenton, 2004; 2006b; Brenton & Paine, 2008). In 2000, Brenton and Paine drew attention to the possibility of identifying pellagra in a bioarchaeological setting. At the time, they had not evaluated any remains but encouraged the field of anthropology to consider pellagra when analyzing remains, especially those coming from maize-dependent populations (Brenton & Paine, 2000).

By 2006, Brenton and Paine had identified fourteen individuals with pellagra in the Raymond Dart Anatomical Collection in Johannesburg, South Africa. They also used a comparison sample of seventeen individuals who suffered from general malnutrition.

All the remains were inventoried for pathologies, specifically periostitis, cribra orbitalia, porotic hyperostosis, dental caries, and alveolar bone loss. Gross pathologies were evaluated according to Buikstra and Ubelaker (1994), and alveolar bone loss was assessed by direct measurement (Paine & Brenton, 2006a)

In a corollary study, Paine and Brenton (2006b) also assessed osteoporosis, the most common osseous sign of pellagra in the medical literature, via cortical bone loss of the ribs. The histological analysis was done using the Stout and Paine method (1994), which entails cutting cross-sections. These cross-sections were then embedded in epoxy and ground down to 75 µm in thickness so that the cortical area could be measured and secondary osteons could be counted. This separate investigation set out to test if Stout and Paine's method was applicable for individuals who suffered from malnutrition and indeed did conclude that malnutrition can influence age estimation using secondary osteon count. While the studies conducted by Paine and Brenton (2006a; 2006b) employed destructive microanalysis of the ribs, there is no evidence in the early medical literature that suggests the ribs are more affected by pellagra than any other bones, and instead their use of this element seems to be a choice stemming from personal research interest and possibly bone sample availability.

Paine and Brenton (2006a) found that some pathologies did occur at differing frequencies between the pellagra and general malnutrition samples. Periosteal lesions occurred in 71% of the individuals with pellagra while they were seen in only 50% of the general malnutrition sample. Dental caries actually occurred less frequently in the pellagra sample (35.7%) than the general malnutrition sample (58.8%). Alveolar bone loss was greatest in the pellagra sample with the average resorption being 0.50 cm, while

the average for the general malnutrition sample was 0.38 cm. These results were determined to be not statistically significant. However, Paine and Brenton do not report their method of measuring alveolar bone loss, other than to state that calipers were used. The rib cortical area of the pellagra sample was an average of 13.6 mm^2, and general malnutrition sample had a rib cortical area of 17.49 mm^2, a significant difference. Their analysis of the microstructure of the ribs in those with pellagra also found that 100% had large Haversian canals, 50% exhibited type II and double zonal secondary osteons, and 30% had Howship's lacunae.

A study comparing Paine and Brenton's findings in the Raymond Dart Anatomical Collection sample with eleven additional pellagrins identified in the Robert Terry Anatomical Collection, housed at the Smithsonian Institution, was presented at the 2008 meeting of the American Anthropological Association. Brenton and Paine were not able to identify a pellagra-specific pathology or pattern of pathologies with the addition of these new individuals, but periostitis of the lower limbs and higher rates of alveolar bone loss and dental caries were also present in the Robert Terry sample as in the Raymond Dart sample of pellagrins.

Current knowledge of pellagra's effect on skeletal tissue is limited by the cursory attention paid to it in the height of pellagra prevalence and research and the limited number of skeletal collections containing known pellagrins. While the early medical literature strongly suggests that most sufferers of pellagra also dealt with osteoporosis, these sources do not tell us much more (Gillman & Gillman, 1951; Harris, 1910; King, 1910; Niles, 1912; Roberts, 1914). Paine and Brenton's (2006b, 2008) study of twenty-five total individuals from collections around the world known to have pellagra has

yielded some promising patterns, and while no single pathology is indicative of the nutritional deficiency, they have provided substantial evidence that it does leave indications of its presence on the human skeleton.

There is an identifiable trend that skeletal pathologies of pellagra tend to correspond with areas affected dermally. Dermatitis associated with pellagra surfaces in warm weather and the sun exposure it brings. This leaves the face, neck, hands, and lower legs particularly vulnerable. This corresponds with the high rates of periostitis in the limbs, osteoporosis of the hands, and porotic hyperostosis and cribra orbitalia in the skull. One defining characteristic of pellagra dermatitis is Casal's Necklace, a skin lesion that can reach around the neck and usually extends down the chest over the clavicles and sternum (Roe, 1973). With this trend in mind, pathologies caused by pellagra may exist in the clavicle and sternum that have not yet been identified (Miller, 2015).

Several paleopathological studies of maize-dependent populations have yielded unusual rates of lesions on the clavicles and sternum argued to be caused by tuberculosis (Kelley & Eisenberg, 1987; Lambert, 2000). Brenton and Paine (2006) have called for a re-evaluation of lesions assigned to other nutritional deficiencies, but they do not address the confusion that may lie between pellagra and tuberculosis. Historically, pellagra has a high rate of co-morbidity with tuberculosis (Brenton & Paine, 2000; Roe, 1973). Modern clinical and case studies of tuberculosis have revealed that the disease only affects the sternum and clavicle in 1-2% of cases. The manubrium accounts for 35.7% of the cases in the sternum or a total of 0.35-0.71% of all cases of tuberculosis. (Agarwal & Maheshwari, 2014; Khan, Varshney, Hasan, Kumar, & Trikha, 2007). One study of 176 confirmed skeletal tuberculosis cases reported a prevalence rate of 7.9% of the sternum

and clavicle. However, ribs were also included in this group, and their contribution to this rate is not known (Miller, 2015; Nicholson, 1974).

Given this fact, it may be logical to not expect tuberculosis lesions of the clavicle and sternum frequently in archaeological remains. Current literature of maize-dependent populations with sternal and clavicle lesions attributed to tuberculosis yielded rates inconsistent with those expected. Kelley and Eisenberg (1987) attempted to develop a differential diagnosis for tuberculosis and blastomycosis between two populations at Mobridge, a 17th to 18th century site in South Dakota, and Averbuch, a 13th to 14th century site located in middle Tennessee. Archaeological analysis of floral remains revealed that Averbuch had a less varied diet, with only eight plants other than maize identified, while Mobridge had sixteen floral remains other than maize identified. Of the 47 individuals in the Averbuch sample, eight had identified sternal lesions and 7 had clavicle lesions, representing 17.02% and 14.89% of the sample respectively with a prevalence rate of 31.9% jointly. Lambert (2000) in a study of skeletal material from farming communities in North Carolina and Virginia noted osteolytic and osteoblastic changes to a manubrium as well as lesions to the sternal end of the clavicle in another individual (Miller, 2015).

Therefore, overall, there is no single condition that is diagnostic of pellagra, but it does appear that periostitis, alveolar bone loss, caries, and osteoporosis can point towards a diagnosis. There is also an additional potential marker, namely periostitis of the sternum and clavicle, that has yet to be explored but may be relevant to the identification of this disease in bioarchaeology.

Summary

The evidence of the effect of niacin deficiency on the human skeleton is sparse and inconclusive. However, there is evidence from historical medical texts, anthropological studies, and current biomedical research that suggests niacin affects both oral health and osseous tissue. The ability to identify pellagra in human remains would further the ability of anthropological studies to evaluate the foodways, socioeconomic status, and power dynamics of past peoples. The ability to do so, however, requires further study of historic remains and continued biomedical research of the physiological role of niacin in the human body.

CHAPTER III – MATERIALS AND METHODS

This chapter will discuss the methods used for data collection as well as describe the study series, the Hamann-Todd Collection. Methods based on previous studies will be explained and the relevance of the collection to the study of pellagra will also be discussed.

The Hamann-Todd Collection

The Hamann-Todd Collection began out of a desire to establish an anatomical teaching series at the Western Reserve Medical School. Creation of the collection began in earnest in 1912 when T. Wingate Todd became the Chair of Anatomy at Case Western Reserve and expanded the teaching series begun by Carl Hamann. The size of the series continued to grow for 26 years, adding the remains of over 3,000 individuals. These remains represented indigents from the county morgue, local hospitals, the Cleveland Workhouse, and sanatoria in Cleveland due to a law advocated by Hamann that required unclaimed bodies in the area be handed over to the Case Western Anatomy Department. The Hamann-Todd series is a wealth of data because of the collection procedure for new individuals. At the time of curation, vital statistics such as age, ethnicity, sex, and cause of death were all documented. More than 70 anthropometric measurements were also taken as well as stereoscopic pictures and radiographs, and the results of autopsies were archived (Kern, 2006).

Currently, the collection database available to the public contains the remains of 189 White females, 1,442 White males, 186 African-American females, 673 African-American males, three Asian males, two Asian females, and four males with a race of

"Other". It is important to note that the series was acquired during the height of pellagra prevalence in the country and that during this time Cleveland was experiencing a mass influx of African American migrants from the South. From 1910 to 1920 the city's African American population increased 308%, and from 1920 to 1930 increased another 100%, with nearly all migrants coming from states in the Deep South (Phillips, 1996). Although pellagra was a disease of the South, it was not absent in other parts of the United States (Lavinder, 1909b) and, undoubtedly, as individuals and families moved from the Deep South, they took their food and customs with them.

There currently are seven individuals in the Hamann-Todd Collection with pellagra listed as a cause of death (Lyman Jellema, personal communication, October 9, 2015). These seven individuals are four African-American males, one African-American female, one White male, and one White female. They range in age from 25 to 55 years. The discrepancy of prevalence between pellagra in this collection and known rates in the population at the height of the disease can be explained by the underrepresentation of females in the Hamann-Todd. Since the majority of individuals were unclaimed bodies, the overabundance of males within the collection has interesting implications about the social support available to men in Cleveland during the 1910s and 1920s. That aside, the fact that African-American males account for 24.48% of the collection and four of the seven cases of pellagra supports that African-Americans, as a whole, were more at risk of dying from pellagra than Whites, even outside the Southern states.

The role Prohibition played in pellagra rates has not been closely examined, even though the height of pellagra prevalence and Prohibition coincided. It is unlikely that Prohibition played a role in the increase of pellagra cases, specifically alcoholic or

secondary pellagra, as the consumption rate of alcohol dropped 30-40% during Prohibition (Miron & Zwiebel, 1991). However, individuals already struggling with alcoholism would have been in danger after Prohibition as any support for alcohol abuse such as self-help societies disappeared while the alcohol remained, just with more difficulty to obtain (Blocker, 2006). The absence of any notation of liver disease or alcoholism within the intake documentation of the seven individuals with pellagra also suggests that none of these individuals suffered from alcoholic pellagra.

The seven individuals with pellagra as a cause of death were compared to a sample of ten other individuals who were chosen by using a random number generator to select individual identification numbers. The comparison sample was to originally consist of individuals with general malnutrition given as a cause of death so as to closely adhere to Paine and Brenton's (2006a) methods and to strengthen the model of identification of pellagra separate from general malnutrition, but no such cause of death is used in the Hamann-Todd Collection. This comparison sample included four White males, four African-American males, and one African-American female. These individuals ranged in age from 26 to 61 years.

Table 1 *Pellagra Sample Demographics*

	Sex	*Ancestry*	*Age*
HTH-1459	Male	African-American	34
HTH-1549	Female	White	54
HTH-2387	Male	African-American	55
HTH-2512	Female	African-American	25
HTH-2519	Male	African-American	44
HTH-2552	Male	White	45
HTH-2678	Male	African-American	40

Table 2 *Comparison Sample Demographics*

	Sex	*Ancestry*	*Age*
HTH-395	Male	White	50
HTH-3308	Male	White	60
HTH-325	Male	White	40
HTH-3049	Male	African-American	27
HTH-2955	Male	White	45
HTH-2756	Male	African-American	61
HTH-2057	Female	African-American	33
HTH-1422	Male	African-American	50
HTH-1278	Male	African-American	26

Pathological Analysis

Methods for this study closely replicated those of Paine and Brenton (2006a) given the purpose was to test and possibly support their findings. Pathologies included in this study were alveolar bone absorption, caries, osteoporosis, periostitis, porotic hyperostosis, and cribra orbitalia as all were argued to be representative of pellagra.

Alveolar Bone Absorption

Alveolar bone absorption is a measure of the loss of alveolar bone relative to *in situ* teeth. Alveolar bone is lost due to periodontitis, a chronic inflammatory disease of the teeth and supporting tissues. Paine and Brenton (2006a) give no citation for their methodology in measuring alveolar bone absorption other than to say that calipers were used. Considering this, a linear method was used according to Liberman, Pilau, Orlandini, Gaio, & Rosing (2010). This method uses sliding calipers to measure the distance between the edge of the alveolar bone and the cemento-enamel junction. This measurement was taken ten times for each tooth and then the average was calculated to

account for intraobserver error. Digital sliding calipers were used as well to prevent errors in reading the results. The mandibular left first incisor was used for most individuals, except in those cases where this particular tooth was not *in situ*. For these individuals, the mandibular right canine was used, mainly because if the mandibular first incisor were missing, all four incisors were lost either ante- or post-mortem.

Caries

The frequency, severity, and location of caries were recorded according to *Standards for Data Collection of Human Skeletal Remains* (Buikstra & Ubelaker, 1994: p.54). Caries were recorded as either occurring either along the cemento-enamel junction, root, or on the occlusal, interproximal, or smooth surfaces of teeth. Antemortem lost teeth were counted as carious due to the likelihood that they were carious before loss. If teeth were lost post-mortem, but still present with the remains, then they were counted as present.

Osteoporosis

Paine and Brenton (2006a) evaluated osteoporosis via cortical bone loss of the ribs. This study, however, was limited to non-destructive methods and as such needed to find another way to measure the loss of bone density. Given the difficulty of assessing the cortical bone loss of ribs through radiography due to their curvature, the available radiography equipment at the Hamann-Todd Collection laboratory, and the radiography from Roberts' 1914 (p. 194-195) text illustrating osteoporosis in the phalanges of individuals with pellagra, this method was chosen to assess bone density. Mele et al. (1997) also established phalanx radiographs as statistically significant predictors of

osteoporotic breaks, adding to its validity as an alternate element to ribs. One medial and one distal phalanx were chosen at random from each individual. Radiographs were evaluated by Dr. Kamal Abouzaid of William Carey University College of Osteopathic Medicine. He marked osteoporosis as present with the observation of 30-50% of cortical bone mass. Other scoring options were not present or inconclusive.

Periostitis

Periosteal bone formation observations were also recorded according to Buikstra & Ubelaker (1994: p.118-9). The side, section, and aspect of each periosteal formation were noted as well as the percent of involvement on the affected bone. Paine & Brenton (2006a) limited these observations to the tibia; however, this study included the sternum (including sternal body and manubrium) as well as the clavicles in the assessment for periostitic lesions. This extension was done to determine if the pattern of skeletal involvement in pellagra corresponding with the dermal involvement also included the sternum and clavicles which would correspond with the classic pellagra dermatitis pattern known as Casal's Necklace.

Porotic Hyperostosis and Cribra Orbitalia

The methods for observation and recording of these pathologies were according to Buikstra & Ubelaker (1994: 120-21) as well. The frontal, occipital, and left and right parietal bones were examined for porotic hyperostosis while the orbits were examined for cribra orbitalia. The percentage of bone affected as well as the severity of the porosity was recorded on a three-point scale - indistinct, true, or coalescing pores.

Comparisons

The frequency of occurrence of periostitis, porotic hyperostosis/cribra orbitalia, and osteoporosis was compared between those with pellagra and the comparison sample using a Fisher's exact test. These frequencies were then combined with data reported by Paine and Brenton (2006a). The rate of caries was compared between the two samples of this study using the Mann-Whitney U test. Comparison between caries frequency in this study and that of Paine and Brenton (2006a) was not possible because this pathology was quantified for each individual in the present investigation, while it was reported as frequency among samples in Paine and Brenton (2006a).

The average alveolar bone loss for each group was then calculated and compared between groups and between the Paine and Brenton (2006a) groups. The average total alveolar bone loss among all pellagrins in both studies was then calculated and compared to the non-pellagrous group of this study and the general malnutrition group within Paine and Brenton's study using a Mann-Whitney U test. The average frequencies of osteoporosis, periostitis, and porotic hyperostosis/cribra orbitalia between the pellagrins of this study and Paine and Brenton's (2006a) was then calculated and again compared to the rates of non-pellagrous individuals within each study.

The individual hypotheses for this study are that:

- Periostitis will be present on the sternum and clavicles of the individuals within the pellagra sample.
- The pellagra sample will have a higher rate of alveolar bone absorption than the comparison sample.

- The pellagra sample will have a lower rate of caries than the comparison sample.
- The pellagra sample will exhibit more periosteal lesions on the tibia and fibula than the comparison sample.
- The pellagra sample will have more signs of cortical bone loss than the comparison sample.
- The pellagra sample will exhibit more signs of porotic hyperostosis and cribra orbitalia than the comparison sample.

The first hypothesis is unique to this study; however, all other hypotheses originate from previous studies conducted by Paine and Brenton (2006a, 2006b, 2007, 2008).

Summary

The attempt to define a differential diagnosis from skeletal remains while limited to non-destructive methods presents unique challenges. This chapter discussed the osteological collection the remains of this study originated from, the methodology used in the data collection, and comparative analysis of the data gathered from this study and a previous study (Paine & Brenton 2006a). While there is little data available for comparative analysis, this study will mark the third paleopathological analysis of the remains of individuals known to have pellagra.

CHAPTER IV - RESULTS

This chapter presents the results of the pathological analysis of two samples from the Hamann-Todd Collection. Findings are compared between the samples as well as with the results of previous studies looking at pellagra in other populations (Brenton and Paine 2006a).

Alveolar Bone Absorption

Given the effects of the high levels of sugar in a corn-based diet and findings of Brenton and Paine (2006a), it was expected that in this study the group with pellagra will have a higher rate of alveolar bone absorption, compared to the group without pellagra.

The mean level of alveolar bone absorption of each individual in the study, both with and without pellagra, are shown in Table 2. This sample had an average of 4.275mm of loss associated with the canine tooth measured. The mean level of alveolar bone absorption among the sample without pellagra was 4.967 mm.

Table 3 *Mean Alveolar Bone Absorption of Pellagra and Comparison Samples*

	Individual	*Mean Alveolar Bone Absorption*
Pellagra Sample	HTH-1459	3.315 mm
	HTH-1549	2.84 mm
	HTH-2387	3.356 mm
	HTH-2512	3.726 mm
	HTH-2519	5.869 mm
	HTH-2552	5.12 mm
	HTH-2678	5.702 mm
Mean		4.275 mm

Table 3 (continued)

Comparison Sample	HTH-325	4.581 mm
	HTH-395	3.821 mm
	HTH-1278	4.521 mm
	HTH-1422	2.555 mm
	HTH-2057	6.624 mm
	HTH-2756	7.27 mm
	HTH-2955	5.995 mm
	HTH-3049	2.89 mm
	HTH-3308	6.445 mm
Mean		4.967 mm

Table 4 *Comparison of Average Alveolar Bone Absorption between Study Samples*

	Avg. Alveolar Bone Absorption (mm)	*Sample Size*
Current Study Pellagra	4.275	7
Current Study Comparison	4.967	9
Paine Brenton (2006a) Pellagra	5.0	14
Paine Brenton (2006a) Comparison	3.8	17
Total Pellagra	4.758	21
Total Comparison	4.204	26

The rate of bone loss among those with pellagra was less, which was the opposite of expectations. The rates of alveolar bone loss were compared between the two groups in this study using a two-tailed Mann-Whitney U test. This test had a p-value of 0.1970 at the 95% confidence interval with a U-value of 22 and a critical value of 15 and was therefore found to not be statistically significantly different at alpha-level 0.10.

The lack of significance between these averages may be due to the small sample size. Brenton and Paine's (2006a) samples were twice as large as these, and therefore, according to the Central Limit Theorem, are closer to the true mean for these populations. The total averages of these two groups, when taking both studies into consideration, reveals that Brenton and Paine's findings, and the expectations of this study, still hold true that the pellagrous population has a higher rate of alveolar bone absorption. Ideally, the groups compiled from data from both studies would also be tested statistically, but without the raw data of the Brenton and Paine study, this is not possible.

While age is very closely related to alveolar bone loss (Ruquet et al., 2015), it is unlikely that age is a contributing factor in the difference of alveolar bone loss between the pellagra and comparison samples. There is not a significant difference in the distribution of the samples as the pellagra sample has an average age of 42.4 years and the comparison sample 43.6 years. HTH-2756 (male, 61) is the oldest individual in either samples and

Dental Caries

It was expected that the rate of caries among those with pellagra would be higher compared to the rate of caries among those without pellagra. This is again related to the findings of Brenton and Paine (2006a).

As may be seen in Table 3, individuals with pellagra in this sample have an average of 6 caries and an average of 8 antemortem lost teeth. The pellagra group has more maxillary caries with an average of 3.7, and an average of 2.3 mandibular caries. Antemortem lost teeth were counted as carious due to the likelihood that they were

carious before loss. Their inclusion brings the mean number of caries among those with pellagra to 14.

Individuals without pellagra were found to have an average of 6.67 caries and 8.67 antemortem missing teeth. The comparison sample has more mandibular caries with an average of 3.78 and 3.11 maxillary caries. The comparison sample has a higher rate of total caries with a combined mean of 15.33 caries and antemortem missing teeth.

Table 5 *Caries in Pellagra and Comparison Samples*

	Individual	*# Max. Caries*	*# Mand. Caries*	*Total # Caries*	*# AMTL*	*Total Caries & AMTL*
Pellagra Sample	HTH-1459	4	2	6	8	14
	HTH-1549	3	1	4	10	14
	HTH-2387	3	3	6	6	12
	HTH-2512	4	3	7	0	7
	HTH-2519	3	2	5	17	22
	HTH-2552	5	2	7	10	17
	HTH-2678	4	3	7	5	12
	Average	3.71	2.29	6	8	14
Comparison Sample	HTH-2955	2	3	5	6	11
	HTH-325	3	5	8	12	20
	HTH-395	2	1	3	5	8
	HTH-3049	1	1	2	2	4
	HTH-3308	2	3	5	15	20
	HTH-2756	4	9	13	18	31
	HTH-1422	5	6	11	5	16
	HTH-2057	4	5	9	8	17
	HTH-1278	5	1	4	7	11
	Average	3.11	3.78	6.67	8.67	15.33

In this comparison, the expected pattern of pellagrins having more caries due to the high carbohydrate diet related to the condition was not seen. A Mann-Whitney U test of these groups with alpha level 0.1 and two-tailed resulted in a U-value of 30.5. The

critical value of U at $p < 0.1$ is 15 and therefore these groups were found to not be statistically significantly different.

Periostitis

It was expected that the sample of those remains with pellagra would exhibit more periostitic lesions than those without pellagra. As will be seen in the discussion below, periostitic lesions were present on the remains of six of the seven individuals (85.7%) with pellagra. The only individual in this sample without lesions on any bone was HTH-2552 (white male, age 45 years).

HTH-1459 (34, male)

Among those with lesions, HTH-1459 has periostitic nodes with plaque present on both the right and left fibula (Figure 1).

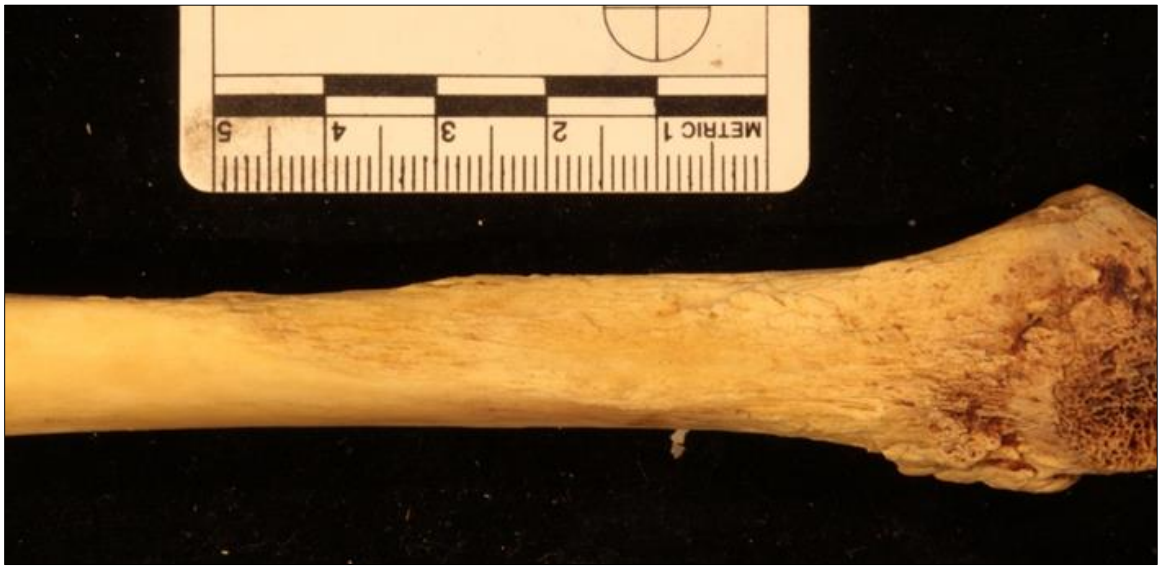

Figure 1. HTH-1459 Right Fibula with Periosteal Lesions

This individual also has plaque-like formations on the medial anterior portion of the right tibia. Other formations are also present on the right fibula along the mid-diaphysis and distal epiphysis (Figure 2).

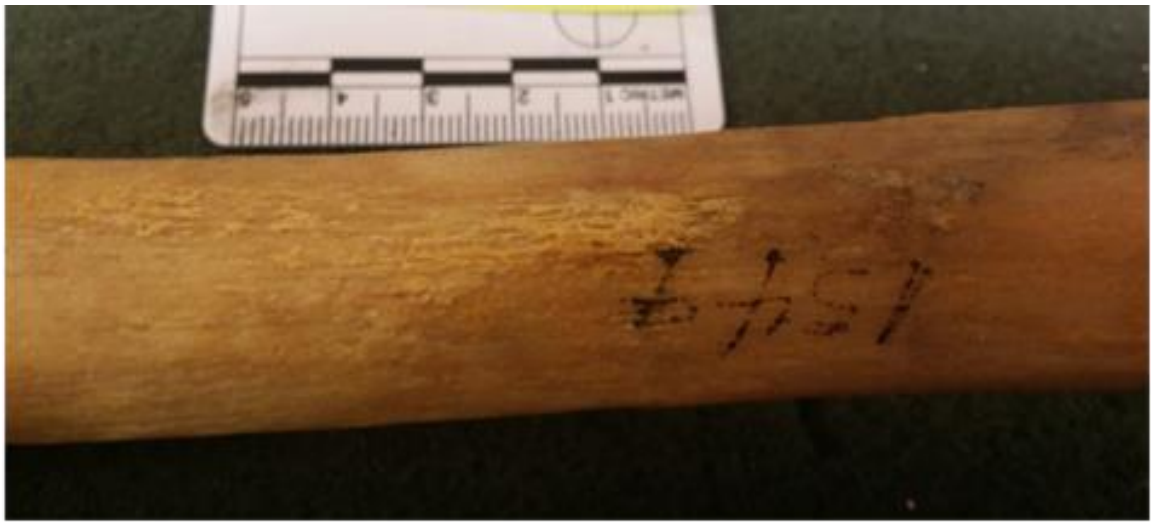

Figure 2. HTH-1549 Right Tibia with Periosteal Lesions

HTH-2387 (55, male)

HTH-2387 has rugose nodes with slight changes along the posterior edge of the left and right fibulae. Plaque formation is also present along the middle third of the left tibia (Figure 3).

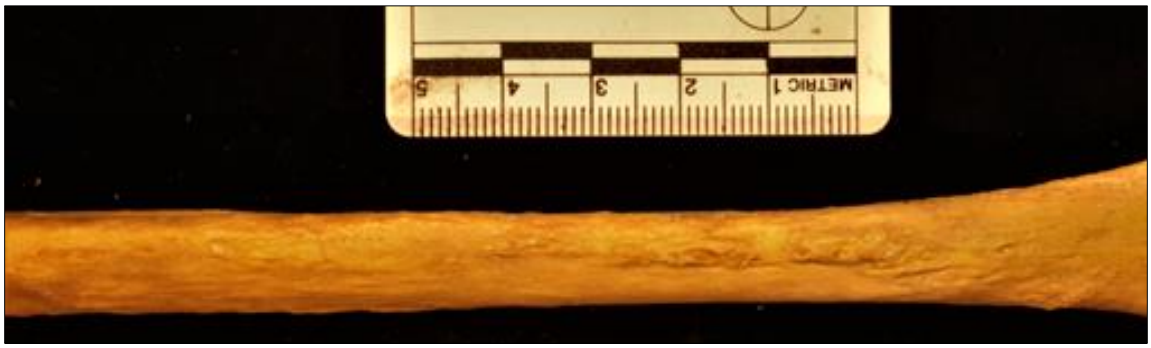

Figure 3. HTH-2387 Left Fibula with Periosteal Lesions

HTH-2512 (25, female)

HTH-2512 has periosteal formations along the medial and lateral aspects of the distal epiphyses on both tibiae (Figure 4). There are also sclerotic formations on the left fibula along the lateral aspect of the diaphysis and on the right fibula there are formations of woven bone with visible lamellae along the entire diaphysis.

Figure 4. HTH-2512 Right Fibula with Periosteal Lesions

HTH-2519 (44, male)

The remains of HTH-2519 were unusual compared to the other remains in this collection in their waxy texture (Figure 5). This may have contributed to the visible lamellae of the right tibia.

Figure 5. HTH-2519 Right Tibia with Periosteal Lesions

HTH-2519 also has possible healed periostitic lesions of nodes with plaque along the lateral aspect of the left fibula diaphysis (Figure 6).

Figure 6. HTH-2519 Left Fibula with Periosteal Lesions

HTH-2552 (45, male)

HTH-2552 has plaque-like formations and fine striations along both diaphysis of the right and left tibiae (Figure 7).

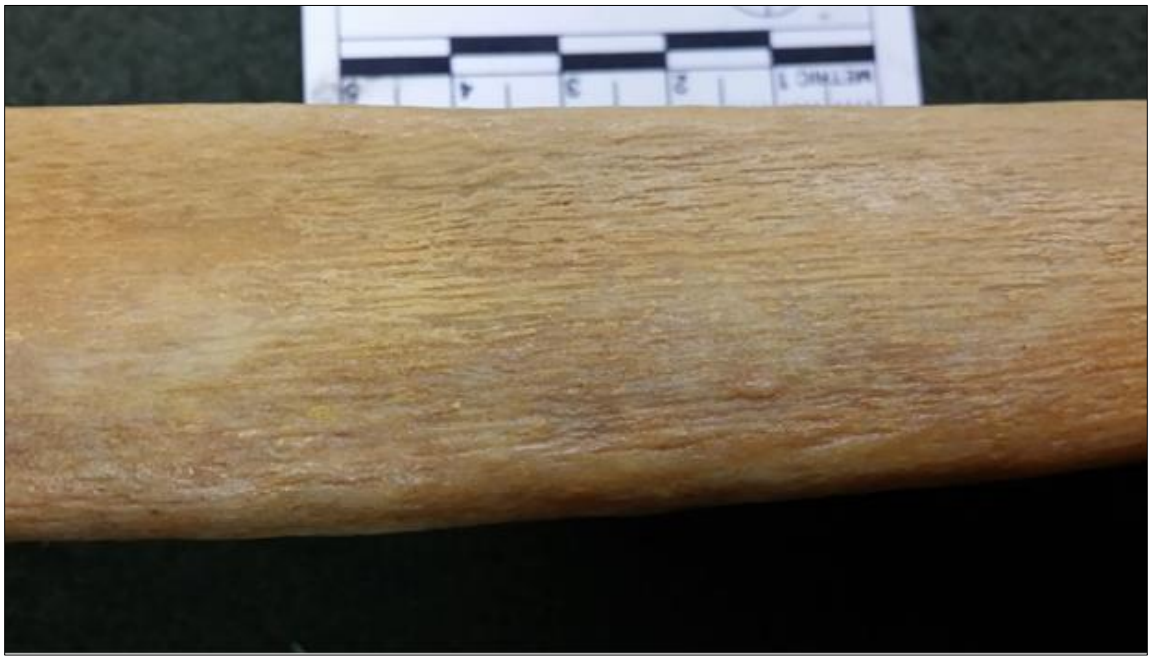

Figure 7. HTH-2552 Right Tibia with Periosteal Lesions

HTH-2552 also has coarsely striated expansions along the diaphysis of the left and right fibulae (Figure 8).

Figure 8. HTH-2552 Left Fibula with Periosteal Lesions

HTH- 2678 (40, male)

HTH- 2678 has plaque formations with fine striations along the diaphysis of both tibiae (Figure 9).

Figure 9. HTH-2678 Left Tibia with Periosteal Lesions

Periostitic formations were also present on five of the nine individuals (55.6%) without pellagra. HTH-325, HTH-1278, HTH-1422, HTH-2057, HTH-2756, and HTH-2955 all had lesions on the tibiae or fibulae. It is important to note that HTH-2057 and HTH-1278 both have pulmonary tuberculosis listed as their cause of death, which could contribute to their periostitis.

A Fisher's exact test comparing the presence of periostitis in these two samples yielded a p-value of 0.3077, which is not statistically significant at $p<0.10$. A second test, combining the data from this study and Brenton and Paine (2006b), resulted in a p-value of 0.0796, which is significant at $p<0.10$. The general trend in both studies of higher rates of periostitis among those with pellagra, and the significant decrease in the p-value when combining study samples conforms to expectations, which may suggest that the study of not-yet-identified remains of individuals with pellagra in other osteological collections might yield more statistically significant results.

Porotic Hyperostosis and Cribra Orbitalia

It was expected that those remains with pellagra would be more likely to exhibit signs of anemia as expressed through porotic hyperostosis and cribra orbitalia than those without pellagra.

In the observation of cribra orbitalia, HTH-325 (male, 40) who did not have pellagra is the only individual from either sample to exhibit cribra orbitalia. It is present in both orbits in this individual but only as a minor porosity (Figure 10).

Figure 10. HTH-325 Right Orbit with Minor Cribra Orbitalia

Porotic hyperostosis is not present in any individual with pellagra, but is present in three individuals without the disease – HTH-395 (male, 50), HTH-1422 (male, 50), and HTH-1278 (male,). HTH-1422 and HTH-1278 exhibit minor healed porosity of the parietals (Figures 11 and 12, respectively), while HTH-395 has more extensive involvement of the parietals, frontal, and occipital (Figure 13).

Figure 11. HTH-1422 Cranium with Porotic Hyperostosis

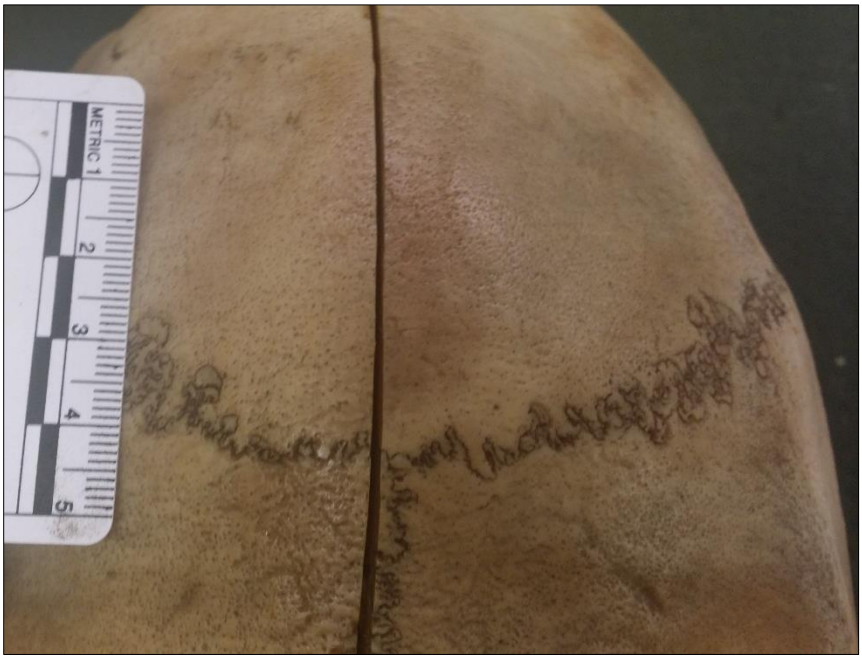

Figure 12. HTH-1278 Cranium with Porotic Hyperostosis

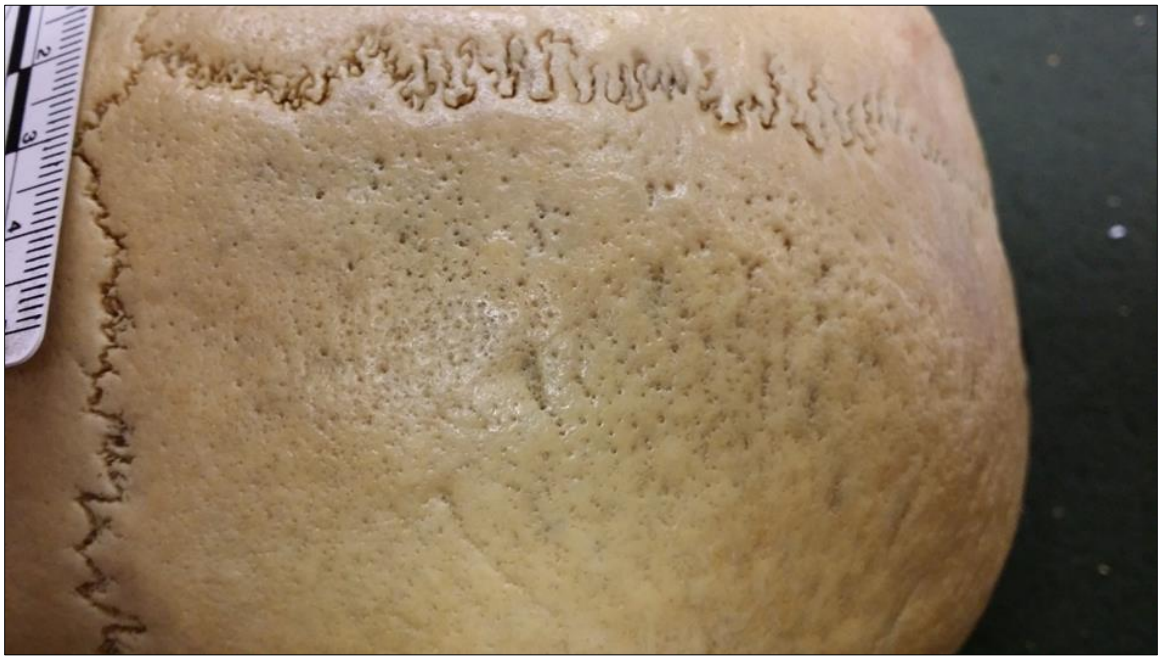

Figure 13. HTH-1422 Cranium with Porotic Hyperostosis

A Fisher's exact test between both samples for the presence of cribra orbitalia or porotic hyperostosis yielded a p-value of 0.0885, which was statistically significant at $p<0.10$. A second test combining the data from this study and the Brenton and Paine (2006a) study produced a p-value of 0.2047, which was not statistically significant and actually moved findings further away from expected results. The lack of significance of this pathology is not unexpected given the results of past studies (Brenton & Paine 2006a). However, the complete absence of both cribra orbitalia and porotic hyperostosis among those with pellagra is unexpected give Brenton & Paine's observations in the South African sample (2006b).

Osteoporosis

It was expected that the radiographs of phalanges would show greater loss of bone density among those with pellagra than those without pellagra. Osteoporosis was marked as present, not present, or inconclusive with a loss of 30-50% of cortical bone mass loss as the threshold for osteoporosis to be present.

Table 6 *Osteoporosis Results*

	Individual	*Osteoporosis Present*
Pellagra Sample	HTH-1459	Negative
	HTH-1549	Negative
	HTH-2387	Negative
	HTH-2512	Inconclusive
	HTH-2519	Negative
	HTH-2678	Negative
Comparison Sample	HTH-2955	Inconclusive but leaning toward osteoporosis due to clear evidence of cortical thinning
	HTH-325	Inconclusive but leaning toward osteoporosis - some thinning of cortex
	HTH-395	Inconclusive but leaning towards osteoporosis
	HTH-3049	Negative
	HTH-3308	Inconclusive- slightly thinner cortex
	HTH-2756	Negative
	HTH-1422	Negative

All individuals with pellagra were determined to not have osteoporosis present, except for HTH-2512 for whom was determined to be inconclusive. In contrast, there was more evidence of cortical thinning among those without pellagra, although no individuals in either sample could be conclusively determined to have present osteoporosis.

Statistical analysis was done using Fischer's Exact Test. For the purpose of the test, individuals determined to be inconclusive of osteoporosis were counted as positive.

The results of the test at $p < 0.10$ were not significant at 0.2657. These results were surprising given the historical evidence of osteoporosis of the phalanges among those with pellagra (Roberts 1914), histological evidence of the loss of bone density (Paine & Brenton 2006b), and biomedical evidence of the effect of niacin on bone density (Cheng et al., 2015; Sasaki & Yanagibori, 2001).

In summary, analysis of gross paleopathologies suggests that niacin deficiency does have an effect on osseous tissue. Individuals with pellagra exhibited a high rate of caries, periosteal lesions, and alveolar bone loss. However, these pathologies did not occur at a statistically significant different rate than the comparison sample from the same population. The complete absence of evidence of porotic hyperostosis, cribra orbitalia, and osteoporosis was surprising given the strong evidence that these pathologies are related to niacin deficiency (Paine & Brenton 2006a). The considerably small samples of this study and others (Brenton & Paine 2008, Paine & Brenton 2006a) may be skewing the results. However, the more significant results gleaned from combining individuals with pellagra from different collections strongly suggests that with further study significant and distinctive patterns may emerge.

CHAPTER V– DISCUSSION AND CONCLUSIONS

The ability to recognize individual diseases and nutritional deficiencies within a population through the analysis of human remains is a valuable tool for bioarchaeologists as they attempt to understand past cultures. The ability to identify pellagra, specifically, would expand this toolset in historic populations the world over. While past studies have attempted to define a differential diagnostic model for pellagra (Paine & Brenton 2006a, Brenton, Tompkins, & Paine 2008), these studies were sparse with limited data sets. The work presented here sought to test and expand upon one of these past studies with the analysis of seven individuals with pellagra as a cause of death within the Hamann-Todd Osteological Collection. The identification of these individuals has expanded the number of individuals used to construct this model from twenty-five to thirty-two. These individuals were evaluated for periostitis, caries, alveolar bone absorption, cribra orbitalia, porotic hyperostosis, and osteoporosis. The sample of pellagrins was compared to a randomly selected sample of ten individuals from the same collection.

Discussion of Results

The analysis of the pathologies assessed provided valuable data for the proposed differential diagnostic model of those with pellagra.

Periostitis

Given the high rate of periosteal lesions in other studies (Brenton & Paine 2008, Paine & Brenton 2006a), it was expected that the pellagra sample in this study would exhibit a higher rate of periosteal lesions. Those with pellagra were found to have higher rates of periostitis than those without pellagra. These results echoed those of Brenton and

Paine (2006a). Although they were found to not be statistically significant, the drastic drop in the p-value to .07 when combining data from this study and Brenton and Paine (2006a) suggests that a larger sample size may yield a significant result.

Alveolar Bone Absorption

Based on previous studies (Brenton & Paine 2008, Paine & Brenton 2006a) and the biomedical evidence of the resorptive effect of niacin deficiency (Bernicki 1977; Taguchi et al. 1989), it was expected that those with pellagra would exhibit higher rates of alveolar bone absorption. However, those with pellagra were found to have lower rates of alveolar bone absorption. This discrepancy may be explained by the small sample size. Statistical analysis combining the data from this and other studies was not possible, but the combined averages of the samples (4.758 mm) did result in a higher rate of alveolar bone absorption than the comparison samples (4.204 mm). The results of this study should not discount the utility of this pathology in a differential diagnostic model, especially considering the biomedical research that strongly indicates that niacin deficiency influences periodontal health (Dreizen, Levy, & Bernicki 1977, Taguchi et al. 1989).

Dental Caries

While the Paine & Brenton study (2006a) found a lower rate of caries among those with pellagra compared to those without, these results are unexpected given the documented role maize has played in increasing caries in populations (Vega Lizama & Cucina, 2014). This study also found a lower rate of caries among those with pellagra (mean = 14) among those without (mean = 15.33). However, these results were also not

statistically significant. The combined rates of caries between the two studies may yield statistically significant results, but was not possible due to a lack of access to data concerning individual rate of caries in the Paine & Brenton (2006a) study needed to perform statistical tests.

Porotic Hyperostosis and Cribra Orbitalia

The complete absence of porotic hyperostosis and cribra orbitalia in the pellagrins sample was quite unexpected given the high frequency reported by Paine & Brenton (2006a) and the co-occurrence of vitamins, B3, B12, and iron in most food sources (Linus Pauling Institute 2019). Walker et al (2009) also strongly argue that diarrhea caused by parasites can exacerbate vitamin B12 and iron deficiencies, greatly increasing the likelihood of developing megaloblastic anemia that can cause of porotic hyperostosis and cribra orbitalia. This large disparity may indicate that Paine & Brenton's sample came from a population also suffering from a parasitic infection that the pellagrins of this study were not experiencing. This possible relationship between parasites and PH/CO is significant for the development of the differential diagnosis of pellagra, especially in the American South given the historic large rate of co-morbidity of pellagra and hookworms (Roe, 1973). Discrepancies such as this emphasize the need to increase the number of remains with pellagra studied. Without further data, the reason for this difference is not easily identified.

Osteoporosis

The rate of osteoporosis among those with pellagra between the two studies is also unexpected. The established relationship between phalanx radiographs indicating

loss of bone mass and osteoporotic breaks also indicates that this element is suitable for diagnosing osteoporosis. The complete lack of evidence of osteoporosis among those with pellagra in this study may be due to the choice of element to radiograph. Vertebrae may have been a more ideal element to assess bone loss due to their susceptibility to stress factors due to osteoporosis (Ruquet et al. 2015).

The relationship between caries and alveolar bone absorption among those with pellagra may be more significant than either pathology on its own. It is generally accepted that indicators of oral health deteriorate in tandem; however, these pathologies seem to have an inverse relationship among those with pellagra. This may be due to the physiological role of niacin and the nature of the maize consumed by those with pellagra. Bioarchaeological studies that indicate poor oral health in relation to maize consumption have focused on cultures that treated maize through nixtamalization. This process may result in maize that is more prone to adhere to the dental surface and contribute to caries that maize that has not been altered due to the increased viscoelasticity of maize that has undergone nixtamalization (Mondragon et al., 2006). The relationship between these pathologies among those with pellagra may indicate that a deficiency of niacin has a more significant and faster impact on oral health than the consumption of maize.

The conclusions of this study are as follows:

- Periostitis was not present on the sternum and clavicles of the individuals within the pellagra sample.
- The pellagra sample has a lower rate of alveolar bone absorption than the comparison sample.

- The pellagra sample has a lower rate of caries than the comparison sample.
- The pellagra sample has a higher rate of periosteal lesions on the tibia and fibula than the comparison sample.
- The pellagra sample did not exhibit more signs of cortical bone loss than the comparison sample.
- The pellagra sample exhibited fewer signs of porotic hyperostosis and cribra orbitalia than the comparison sample.

Those with pellagra were found to have higher rates of periostitis and lower rates of alveolar bone loss, caries, and porotic hyperostosis than the comparison sample. However, caries, alveolar bone loss, periostitis, cribra orbitalia, porotic hyperostosis, and osteoporosis were all found to not occur at statistically significant rates between the sample of pellagrins and the comparison sample. Additionally, the hypothesis that proposed the dermatitis associated with the skin followed a similar pattern of periostitis in the skeleton, and would therefore present with periostitis of the clavicles or sternum, was not supported. None of the individuals studied showed lesions on these elements.

Limitations of Study

This study to test and expand upon a proposed differential diagnosis of pellagra in human remains was subject to a few weaknesses. The lack of access to the raw data collected in previous similar studies (Brenton & Paine 2008; Paine & Brenton 2006a) limited the statistical analyses available and was the most significant limitation of the

study. Had this data been available, more equivalent comparisons of all known pellagra remains would have been possible.

HTH-2756 (male, 61) may have affected the outcome of some statistical tests. This individual is the oldest in either sample and has values for alveolar bone loss and caries that far exceed other individuals within the comparison sample.

Other limitations were the small sample size and the choice of element to radiograph for osteoporosis. The small sample size was unavoidable and not unusual in bioarcheological studies. Other research collections containing the remains of individuals with pellagra may exist in Europe, especially Italy. However, the lack of funding for the study limited research to collections within the United States, where the disease had a shorter presence than other areas of the world.

Contributions of Findings and Recommendations for Future Study

Although none of the statistical analyses in this study yielded statistically significant results, there is now more evidence that vitamin B3 deficiency does leave its mark on the human skeleton at the macro level. To further strengthen the known patterns, other collections with known pellagrins must be identified and studied. Unfortunately, there are not many collections available in the United States of known individuals from the period pellagra was most rampant in the country. Brenton and Paine (2007, 2008) found known pellagrins in South Africa, but the search should also be turned towards European collections (especially those in Italy). International collections were not feasible due to budgetary limitations of this study so there was no attempt to identify any possible collections outside of the United States of America; however, this is a further

avenue of research that should be addressed. Future study should include a complete reassessment of each individual with pellagra in the Raymond Dart, Robert Terry, and Hammond-Todd Collections to ensure consistency in methods.

With the increase in the study of historic populations in bioarchaeology, the need for a clear differential diagnostic model for pellagra increases as well. It may be remiss to attempt to apply this model to collections in an attempt to identify unknown pellagrins at this stage, but one day it may be a possibility. This possibility is what should be strived for.

Pellagra occupies a unique position in the collective consciousness of anthropological research in that it has been largely overlooked for decades compared to other nutritional deficiencies such as beriberi, rickets, anemia, and scurvy. This unintentional dismissal of this deficiency can be partly attributed to its recent historical and relatively short-lived prevalence in the United States. However, the impact of pellagra had significant geographical and temporal reach, existing for centuries in Europe and Africa. There is also the strong possibility that although first recognized in the United States at the beginning of the twentieth century, pellagra was likely present long before this. The ability to identify this deficiency would provide valuable insight into the nutritional status, health, and socioeconomic status of marginalized individuals across the world.

APPENDIX A– Hamann-Todd Osteological Collection Research Request

CLEVELAND MUSEUM OF NATURAL HISTORY
Department of Physical Anthropology
1 Wade Oval Drive, University Circle
Cleveland OH, 44106
(216) 231-4600

RESEARCH REQUEST FORM

Note: This application form has 3 pages. Please read all pages carefully as fees may apply to your research request. Inquiries regarding this form should be forwarded to the Curator of Physical Anthropology (<yhailese@cmnh.org>).

A. General Information

1. Name of Researcher: Myra Miller
   E-mail: myra.miller@eagles.usm.edu
   Position and Title: Graduate student
2. Faculty Advisor's Name (if student): Dr. Marie Danforth
   Position and Title: Professor of Anthropology
   E-mail: m.danforth@usm.edu
   Telephone: Home _____ Office: 601-266-5629
3. Name of Institution: University of Southern Mississippi
   Address: _____
   _____
   Telephone: 601-266-1000

B. Research Information

1. Title of proposed research: Application of a proposed model of the skeletal effects of pellagra on an additional population
2. Manner in which research will be utilized: (Ph.D. thesis, Publication, etc.)*
   Master's thesis
3. Proposed dates for utilizing CMNH collections: March 14-18

* Should any research conducted on the Hamann-Todd Osteological Collection results in any form of publication, The Cleveland Museum of Natural History should be properly acknowledged and PDF copies of such publications provided to the museum.

4. Brief synopses of the extent and nature of proposed research. Include proposed materials and methods (110-115 words): Attach additional pages, if necessary.

This study seeks to create a model for identification of pellagra in skeletal remains. Some preliminary research has been done to determine the skeletal effects of pellagra. This investigation will apply past findings to seven individuals known to have had pellagra at the time of death in the Hamann-Todd collection. The model will then be tested on an additional 100 African individuals selected for signs of general malnutrition to ascertain that these possible pellagra indicators do differentiate from general malnutrition. The majority of analysis will comprise of gross evaluation of the remains to assess periostitic lesions and any other pathologies observed on the sternum and clavicles. Caries and alveolar bone loss will be scored along with porotic hyperostosis and cribra orbitalia as markers of general malnutrition following Buikstra and Ubelaker. Phalanges will also be x-rayed to assess osteoporosis and ribs will be x-rayed to assess cortical thickness.

5. Is this research to be used for commercial purposes? If yes, please describe in detail (75 words): Attach additional pages, if necessary.

No.

COMMERCIAL USE OF THE CLEVELAND MUSEUM OF NATURAL HISTORY'S PHYSICAL ANTHROPOLOGY COLLECTIONS

The Department of physical Anthropology may allow the utilization of its collections for commercial purposes, but strictly impose a fee for such use. Individuals who wish to utilize the collection(s) for commercial purposes must specify this, in writing and in detail, prior to initiating any work. All such fees must be clearly understood in advance and are to be specified in the written agreement between The Cleveland Museum of Natural History, Case Western Reserve University, and the individual(s) wishing access to the collection(s) for commercial purposes. Certain conditions, including those related to copyrights, patents and royalties may be imposed when deemed appropriate. The Head of the Department of Physical Anthropology and the Museum Director, in consultation with Case Western Reserve University, will jointly establish guidelines for assessing fees for commercial use of the collection on a case-by-case basis. Note that any agreement is a one-time agreement as specified by the study proposed in this application form. Additional research, even on the same dataset, requires new agreement.

Researcher's Signature*

Student Advisor's Signature*

* Read the conditions on page 3 before signing this application form.

Conditions that apply to the use of the Hamann-Todd Osteological Collection (H-TOC)

1. All images (photographs, laser scans, x-rays, CT scan, MRIs) of any material in the H-TOC are the property of the Cleveland Museum of Natural History (CMNH).

2. Images generated from the H-TOC can be used in the public domain, (scientific papers, theses, monographs, books, lectures) without permission from the CMNH, as long as the source of the image is acknowledged. If images are presented in any other way, written permission from the CMNH will be required and such permission will not be unreasonably withheld. Apply for permission to:

   The Curator of Physical Anthropology
   Cleveland Museum of Natural History
   1 Wade Oval Drive, University Circle
   Cleveland, Ohio 44106-1767

3. Images from the H-TOC generated by students, scientists, commercial entities and their agents, cannot be sold without written permission from the CMNH. Permission will not be unreasonably withheld and a fee or royalty will be due the CMNH.

4. If images from the H-TOC are used to create or modify a commercial product, a fee or royalty will be due the CMNH.

5. The H-TOC is accessible, free of charge, to all undergraduate and graduate students and professionals who wish to utilize the collection for non-commercial, academic research. However, bench fees may apply in some circumstances, especially when the collection is used for commercial purposes. Bench Fees and royalties from commercial entities and their agents will be determined after their research applications are reviewed, approved, and an agreement is reached between the applicants, the Cleveland Museum of Natural History, and Case Western Reserve University.

6. All data and images generated during research on the H-TOC, must be downloaded onto the CMNH's confidential database at the conclusion of a visit to the H-TOC. It is hoped that research on the H-TOC will allow the researchers who conduct the research and others to create knowledge about human osteology and human skeletal variation. Upon request, data collected by researcher(s) can be withheld from use by others for two years. This time might be extended for another year upon the researcher's written request.

Please acknowledge agreement to all the conditions listed above by signing your name, and entering the date, below. Applications will NOT be reviewed without valid name and signature on this page.

Name Myra Miller

Signature _____ Date 11-12-15

APPENDIX B – Radiographs of Phalanges

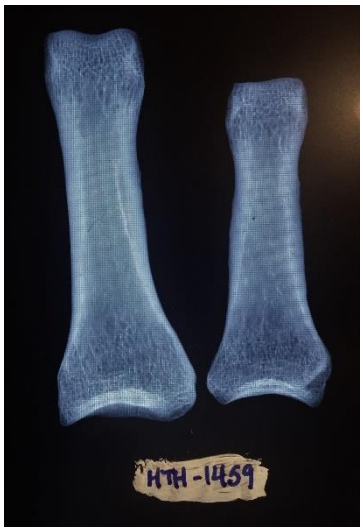

Figure A1. HTH-1459 Phalanges Radiograph

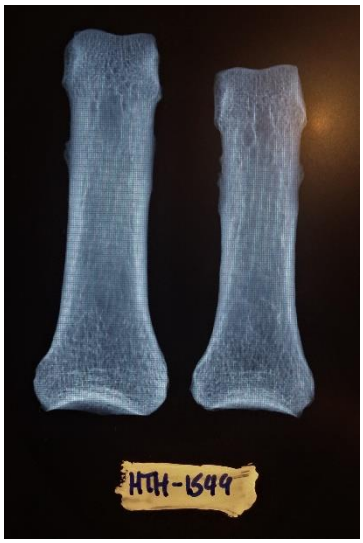

Figure A2. HTH-1549 Phalanges Radiograph

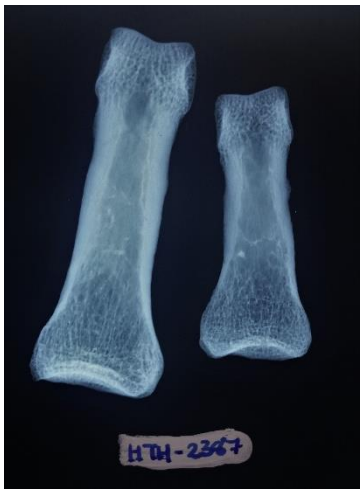

Figure A3. HTH-2387 Phalanges Radiograph

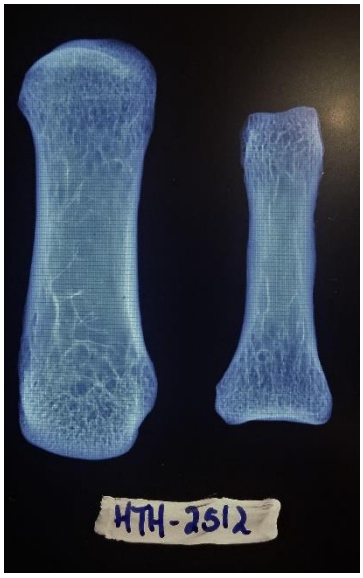

Figure A4. HTH-2512 Phalanges Radiograph

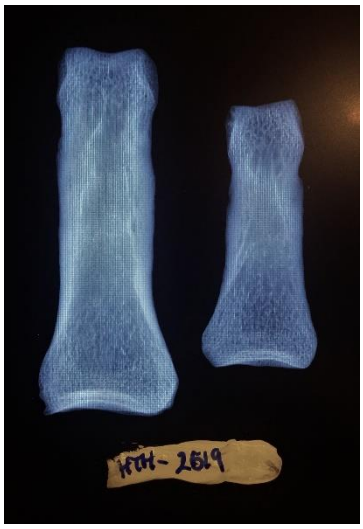

Figure A5. HTH-2519 Phalanges Radiograph

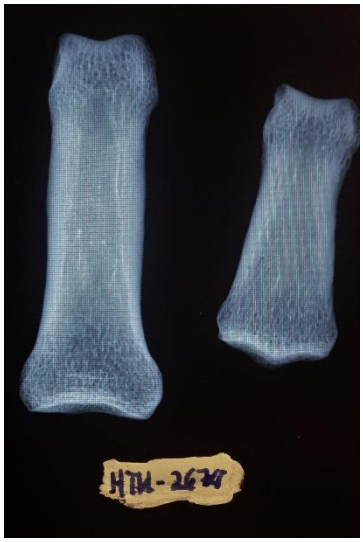

Figure A6. HTH-2678 Phalanges Radiograph

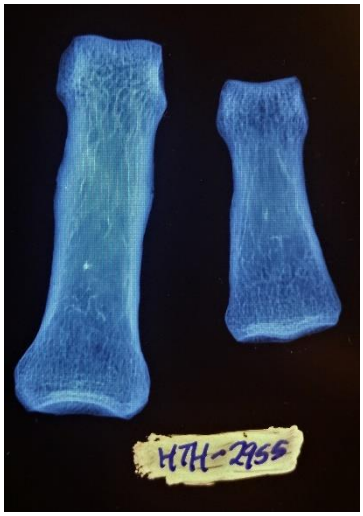

Figure A7. HTH-2955 Phalanges Radiograph

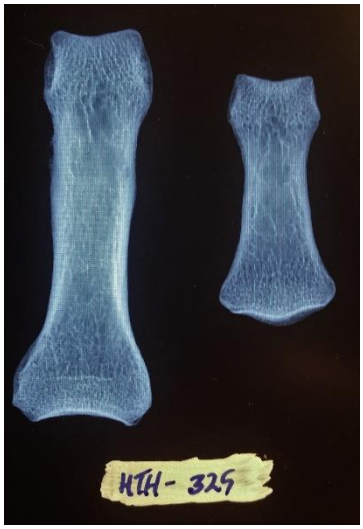

Figure A8. HTH-325 Phalanges Radiograph

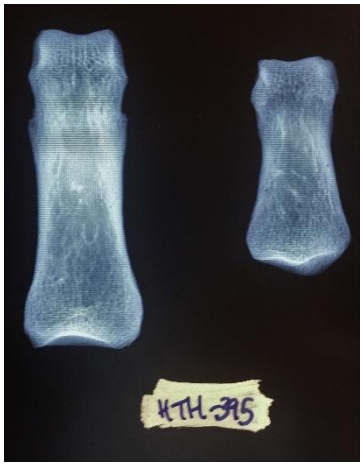

Figure A9. HTH-395 Phalanges Radiograph

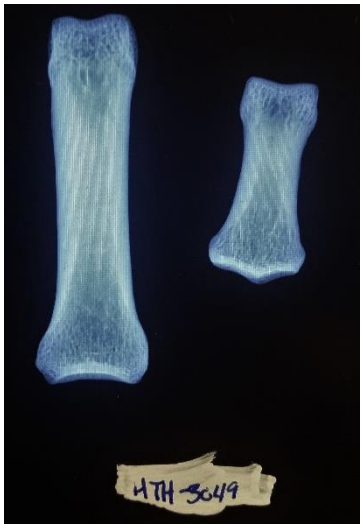

Figure A10. HTH-3049 Phalanges Radiograph

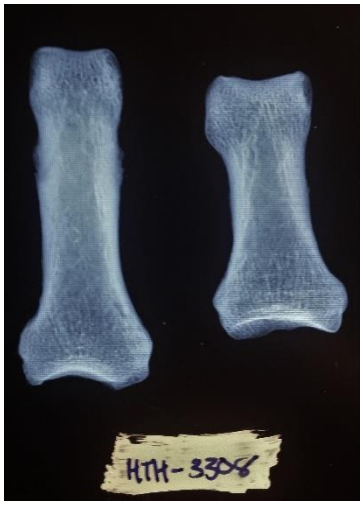

Figure A11. HTH-3308 Phalanges Radiograph

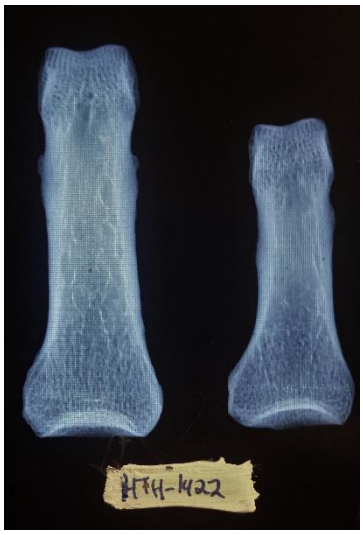

Figure A12. HTH-1422 Phalanges Radiograph

REFERENCES

Agarwal, A., & Maheshwari, R. (2014). Tubercular osteomyelitis of the clavicle: a case report. *Journal of Orthpaedic Case Reports*, *4*(4), 51–53.

Beck, M. (2001). Archaeological Signatures of Corn Preparation in the New World. Kiva, 67(2), 187–218. Retrieved from https://www.jstor.org/stable/30246390

Blocker, J. S., & Jr. (2006). Did prohibition really work? Alcohol prohibition as a public health innovation. American Journal of Public Health, 96(2), 233–243. https://doi.org/10.2105/AJPH.2005.065409

Brenton, B. P., & Paine, R. R. (2000). Pellagra and paleonutrition: assessing the diet and health of maize horticulturists through skeletal biology. *Nutritional Anthropology*, *23*(1), 2–9. http://doi.org/10.1525/nua.2000.23.1.2

Brenton, B. P., & Paine, R. R. (2007). Reevaluating the health and nutritional status of maize-dependent populations: evidence for the impact of pellagra on human skeletons from South Africa. *Ecology of Food and Nutrition*, *46*(5-6), 345–360. http://doi.org/10.1080/03670240701486545

Brenton, B. P., Tompkins, D., & Paine, R. R. (2008). Skeletal pathologies associated with pellagra mortality: a comparative analysis of pellagrins from the Raymond Dart and Robert Terry anatomical skeletal collections. *American Journal of Physical Anthropology 46*, 72 (abstract).

Buikstra, J. E., & Ubelaker, D. H. (1994). *Standards for Data Collection from Human Skeletal Remains: Proceedings of a Seminar at the Field Museum of Natural History*. Arkansas Archeological Survey Research Series No. 45. Fayetteville, AR: Arkansas Archeological Survey No. 44.

Cazenave, P. L. A., Bulkley, H. D., Burgess, T. H., & Schedel, H. É. (1846). *Manual of Diseases of the Skin*. New York: Langley. Retrieved from https://books.google.com/books?id=4x5AAAAAYAAJ

Cheng, X., Hookway, E. S., Kashima, T., Oppermann, U., Galione, A., & Athanasou, N. A. (2015). The Role of Calcium and Nicotinic Acid Adenine Dinucleotide Phosphate (NAADP) in Human Osteoclast Formation and Resorption. Calcified Tissue International, 96(1), 73–79. https://doi.org/10.1007/s00223-014-9939-3

Gillman, J., & Gillman, T. (1951). *Perspectives in Human Malnutrition: A Contribution to the Biology of Disease from a Clinical and Pathological Study of Chronic Malnutrition and Pellagra in the African*. New York: Grune & Stratton.

Greenhouse, R. (1981). Preparation effects on iron and calcium in traditional Pima foods. Ecology of Food and Nutrition, 10(4), 221–225. https://doi.org/10.1080/03670244.1981.9990642

Gwirtz, J. A., & Garcia-Casal, M. N. (2014). Processing maize flour and corn meal food products. Annals of the New York Academy of Sciences, 1312(1), 66–75.

https://doi.org/10.1111/nyas.12299

Harris, H. F. (1910). Pathology of pellagra. In *Proceedings from The National Conference on Pellagra, Held at Columbia, S.C. November 3 and 4, 1909*, (pp. 83-86). Columbia, S.C.: State Co. Printers. https://archive.org/details/transactionsofna00nati/page/86

Hilliard, S. (1969). Hog Meat and Cornpone: Food Habits in the Ante-Bellum South on JSTOR. *Proceedings of the American Philosophical Society*, 113(1), 1–13. Retrieved from http://www.jstor.org/stable/986013

Katz, S. H., Hediger, M. L., & Valleroy, L. A. (1974). Traditional Maize Processing Techniques in the New World. *Science*, 184(4138), 765–773. Retrieved from https://www.jstor.org/stable/1738647

Kelley, M., & Eisenberg, L. (1987). Blastomycosis and tuberculosis in early American Indians: a biocultural view. *Midcontinental Journal of Archaeology*, *12*(1), 89–116.

Kern, K. (2006). T. Wingate Todd: pioneer of modern American physical anthropology. *Kirtlandia*, 55, 1-42

Khan, S., Varshney, M., Hasan, A., Kumar, A., & Trikha, V. (2007). Tuberculosis of the sternum. *Journal of Bone & Joint Surgery*, *87*, 817–820.

King, J. M. (1910). Report of pellagra at Nashville, Tenn. In *Proceedings from The National Conference on Pellagra, Held at Columbia, S.C. November 3 and 4, 1909*, (pp. 171-178). Columbia, S.C.: State Co. Printers. https://archive.org/details/transactionsofna00nati/page/170

Lambert, P. M. (2000). Life on the periphery: health in farming communities in interior North Carolina and Virginia. In *Bioarchaeological Studies of Life in the Age of Agriculture: A View from the Southeast* (pp. 168–194). Tuscaloosa, AL: Univeristy of Alabama Press.

Lavinder, C.H. (1909a) Pellagra in the State Hospital for the Insane at Peoria, Ill. *Public Health Reports (1896-1970) 24*(38), 1362.

Lavinder, C. H. (1909b). The National Conference on Pellagra, Held at Columbia, S. C., November 3 and 4, 1909. *Public Health Reports (1896-1970)*, *24*(46), 1697–1702. http://doi.org/10.2307/4564077

Lavinder, C. H. (1910). The theory of the parasitic origin of pellagra. *Public Health Reports (1896-1970)*, *25*(22), 735–737. http://doi.org/10.2307/4564870

Lavinder, C. H., Williams, C. F., & Babcock, J. W. (1909). The Prevalence of Pellagra in the United States. A Statistical and Geographical Note, with Bibliography. *Public Health Reports (1896-1970)*, *24*(25), 849–852. http://doi.org/10.2307/4563179

Liberman, D. N., Pilau, R. M., Orlandini, L. F., Gaio, E. J., & Rösing, C. K. (2010). Comparison of two methods for alveolar bone loss measurement in an experimental periodontal disease model in rats. *Brazilian Oral Research*, *25*(1), 80–84. Retrieved

from http://www.ncbi.nlm.nih.gov/pubmed/21271178

Linus Pauling Institute. (2019) Micronutrients in Health. Retrieved from https://lpi.oregonstate.edu/publications/micronutrients-health

Miller, M. (2015). Tracking the adoption of maize through America. Unpublished manuscript on file, Department of Anthropology and Sociology, University of Southern Mississippi, Hattiesburg.

Miron, J. A., & Zwiebel, J. (1991). Alcohol Consumption during Prohibition. American Economic Review, 81(2), 242–247. Retrieved from https://ideas.repec.org/a/aea/aecrev/v81y1991i2p242-47.html

Mississippi State Board of Health. (1915). *A Statistical Report of Pellagra in Mississippi and Suggestions to the Legislature Relative to Its Prevention and Cure*. Jackson, MS:

Mondragón A, M., Mendoza-Martínez, A. M., Bello-Pérez, L. A., & Peñ, J. L. (2006). Viscoelastic behavior of nixtamalized maize starch gels. Carbohydrate Polymers, 65, 314–320. https://doi.org/10.1016/j.carbpol.2006.01.011

Nicholson, R. (1974). Twenty years of **B**one and joint tuberculosis in Bradford. *Journal of Bone & Joint Surgery*, *56-B*(4), 760–765.

Niles, G. M. (1912). *Pellagra: An American Problem*. Philadelphia, PA: W. B. Saunders. Retrieved from https://books.google.com/books?id=gC8pAAAAYAAJ&pgis=1

Nunn, N., & Qian, N. (2010). The Columbian Exchange: A History of Disease, Food, and Ideas. Journal of Economic Perspectives, 24(2), 163–188. https://doi.org/10.1257/jep.24.2.163

Ortner, D. J. (2012). *Differential diagnosis and issues in disease classification*. In A. L. Grauer (Ed.)., *A Companion to Paleopathology* (pp. 250-267). Malden, MA: Wiley-Blackwell.

Paine, R., & Brenton, B. (2006a). The paleopathology of pellagra: investigating the impact of prehistoric and historical dietary transitions to maize. *Journal of Anthropological Science, 84*, 125–135.

Paine, R., & Brenton, B. (2006b). Dietary health does affect histological age assessment: an evaluation of the Stout and Paine (1992) age estimation equation using secondary osteons from the rib. *Journal of Forensic Sciences*, *51*(3), 489–492. http://doi.org/10.1111/j.1556-4029.2006.00118.x

Phillips, K. L. (1996). “But it is a fine place to make money”: migration and African-American families in Cleveland, 1915-1929. *Journal of Social History*, *30*(2), 393–413. Retrieved from http://www.jstor.org/stable/3789386

Ruquet, M., Saliba-Serre, B., Tardivo, D., & Foti, B. (2015). Estimation of Age Using Alveolar Bone Loss: Forensic and Anthropological Applications. Journal of Forensic Sciences, 60(5), 1305–1309. https://doi.org/10.1111/1556-4029.12827

Powell, M. L., & Cook, D. C. (2012). *How does the history of paleopathology predict its future?* In A. L. Grauer (Ed.), *A Companion to Paleopathology* (pp. 214-224). Malden, MA: Wiley-Blackwell.

Roberts, S. R. (1914). *Pellagra; History, Distribution, Diagnosis, Prognosis, Treatment, Etiology*. St. Louis, MO: Mosby. Retrieved from https://books.google.com/books?id=ExA1AQAAMAAJ&pgis=1

Roe, D. A. (1973). *A Plague of Corn: The Social History of Pellagra*. Ithaca, NY: Cornell University Press. Retrieved from https://books.google.com/books/about/A_plague_of_corn.html?id=rKt8AAAAIAAJ&pgis=1

Ruquet, M., Saliba-Serre, B., Tardivo, D., & Foti, B. (2015). Estimation of Age Using Alveolar Bone Loss: Forensic and Anthropological Applications. Journal of Forensic Sciences, 60(5), 1305–1309. https://doi.org/10.1111/1556-4029.12827

Taguchi, S., Wada, T., Kijima, S., Yoshie, H., Hara, K., Tonomura, M., & Tsujita, S. (1989). Effects of nicotinate ethyl ester treatment on gingival blood circulation of experimental gingivitis in monkeys. Nihon Shishubyo Gakkai Kaishi, 31(1), 184–199. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/2517791

Tolkachjov, S. N., & Bruce, A. J. (2017). Oral manifestations of nutritional disorders. Clinics in Dermatology, 35(5), 441–452. https://doi.org/10.1016/j.clindermatol.2017.06.009

Vaughan, V. C. (1918). Abstract of discussion on papers of Drs. McCollum, Hess, Goldberger, Wheeler, Sydenstricker, Murlin and Roth. *Journal of the American Medical Association*, *71*(1), 954–956. Retrieved from https://books.google.com/books?id=TsAhAQAAMAAJ&pgis=1

Vega Lizama, E. M., & Cucina, A. (2014). Maize dependence or market integration? Caries prevalence among indigenous Maya communities with maize-based versus globalized economies. American Journal of Physical Anthropology, 153(2), 190–202. https://doi.org/10.1002/ajpa.22418

Walker, P. L., Bathurst, R. R., Richman, R., Gjerdrum, T., & Andrushko, V. A. (2009). The causes of porotic hyperostosis and cribra orbitalia: A reappraisal of the iron-deficiency-anemia hypothesis. *American Journal of Physical Anthropology*, *139*(2), 109–125. https://doi.org/10.1002/ajpa.21031