THE RELATIONSHIP BETWEEN ORAL INFECTION, SYSTEMIC DISEASE, MORTALITY, AND LIFE-HISTORY EVENTS

by

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DEDICATION

This is dedicated to my mom and dad.

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ABSTRACT

THE RELATIONSHIP BETWEEN ORAL INFECTION, SYSTEMIC DISEASE, MORTALITY, AND LIFE-HISTORY EVENTS

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This study explores the association between periodontal disease and periostosis in a sample of 874 individuals of known age at death originating from the Terry Collection, National Museum of Natural History. Because previous studies have found a potential hyper-inflammatory immunological reaction related to periodontal disease related to the dissemination of harmful bacteria it was expected that there would be a significant relationship between periodontal disease and periostosis independent of age. Log-linear analysis found a significant association between periodontal disease and periostosis when the two variables were considered without relation to age ($P < 0.008$). However, when age was included in the model, no significant association was found ($P < 0.390$). Instead, results indicate an age dependent association between periosteal lesions ($P \leq 0.0001$) and periodontal disease ($P \leq 0.0001$). The results suggest that both conditions become more common as individuals age, and that the association between the two variables was best

explained as chronic infection. Chronic infection has also been associated with mortality rates, therefore the other portion of this study evaluated survivorship in relation to carious lesion manifestation. Kaplan-Meir survival analysis was used to examine mortality between groups based on sex and carious lesion location on tooth surface (either crown or CEJ/root) because older individual have higher rates of periodontal disease and it was expected that these individual would have higher frequencies of CEJ/root carious lesions. Females with lesions had higher survivorship than females without lesions ($P \leq 0.0001$), males with lesions ($P \leq 0.0001$), and males without lesions ($P \leq 0.0001$). Females with CEJ/root lesions had significantly greater survivorship than males without carious lesions ($x^2 = 24.517$; $P \leq 0.0001$), males with only crown lesions ($x^2 = 19.591$; $P \leq 0.0001$), and males with CEJ/root lesions ($x^2 = 6.532$; $P \leq 0.011$). Females with crown lesions had lower survivorship than females with CEJ/root lesions ($x^2 = 18.310$; $P \leq 0.0001$) and males with CEJ/root lesions ($x^2 = 10.961$; $P \leq 0.001$). Differences in carious lesion expression within females appears around reproductive lifespan, while CEJ/root caries are found to increase in post-menopausal females. It is likely that these results represent a combination of dietary and life-history based parameters.

CHAPTER 1: IMMUNITY AND SYSTEMATIC DISEASE

Due to the highly mineralized composition of dental remains, teeth provide a durable record representing the dietary and health patterns within past populations (Oztunc et al., 2006; Larsen, 2015). Dental caries and periodontal diseases have been utilized as markers for oral health and, more recently, general health. The oral cavity is capable of hosting three hundred species of bacteria, with a single individual containing up to one hundred and fifty types (Pizzo et al., 2011). Even with the plethora of bacteria present within the oral cavity, only a few are associated with periodontal disease and dental caries, including species of *Lactobacillus, Viellonella*, and *Treponema* (Williams, 1990; Boyd and Madden, 2003). *A. actinomycetemcomitans* is one of the earliest bacteria to appear in a healthy mouth (Spahr et al., 2016). In 1891, W. Miler suggested oral microorganisms were capable of developing systemic diseases, influencing the overall health of the individual. Since then, numerous studies have examined the relationship between oral pathology and general health (Pizzo et al., 2011; DeWitte and Bekvalac, 2010; Ylostalo et al., 2006; Hujoel et al., 2000; Acs et al., 1999; DeStefano et al., 1993).

As mastication occurs, material is introduced to the oral cavity, allowing particles to adhere to the teeth. If the material is not removed, dental tissue can become irritated and inflamed, leading to increased gingivitis, alveolar bone loss, tooth mobility, and

carious lesion formation (Greene, 1963). This process is affected by type of food intake, oral hygiene, tobacco use, and genetics (Boyd and Madden, 2003; Sun et al., 2017; Siddiqui et al., 2017). For instance, fluoride and polyunsaturated fats can result in lower adhesion of harmful bacteria within the mouth, preventing irritation. Other food can contain sugars that increase periodontal disease, inflammation in the oral cavity, and cause gingival bleeding (Loskill et al., 2012; Najeeb et al., 2016).

On clean teeth, salivary glycoprotein film rapidly covers the enamel surface and a dental pellicle allows bacteria within the film to adhere to the tooth surface, gradually forming a highly structuralized mass of bacteria (Williams, 1990; Boyd and Madden, 2003; Jenkinson, 2013). Dental plaque is produced when the mass of bacteria becomes aged and mineralizes onto the tooth, forming a non-shedding surface (Papapanou, 2013). If this material is not removed, dental tissue can become irritated and inflamed, leading to increased gingivitis, alveolar bone loss, tooth mobility, and carious lesion formation (Greene, 1963). The inflammatory response to the biofilm can cause chronic infection in individuals not able to control transient bacteremia. This can result in systemic infection, altering tissues elsewhere in the body. Therefore, oral disease can lead to systemic disease through an identifiable mechanism *or* poor oral health and other disease conditions both are caused by other factors.

Periodontal Disease:

Periodontal disease is a chronic infection caused by an accumulation of bacteria within the oral biofilm; specifically, *gingivalis, Actinobacillus actinomycetemcomitans,*

Tannerella forsythensis, Bacteroids forsythus, and *Treponema denticola* (Li et al., 2000; Pihlstrom et al., 2005; Meyer et al., 2008; Connell et al., 2012; Larsen, 2015; Petersone-Gordina et al., 2018). This condition is characterized by inflammation, periodontium breakdown, alveolar bone destruction, and potential tooth loss (Williams, 1990; Strohm and Alt, 1998; Sasaki et al., 2008; DeWitte and Bekvalac, 2011; Gosman, 2012; Michaud et al., 2017). Periodontal disease is one of the most common infectious processes in current and past populations (Li et al., 2000; Bresolin et al., 2014). The condition currently affects 10-15% of people worldwide, with some populations having a prevalence rate as high as 90% (Meyer et al., 2008). Variances in periodontal disease pervasiveness may be associated with ecogeography and population structure (Strohm and Alt, 1998; Irfan et al., 2001; Loos, 2005; Meyer et al., 2008). Within the United States, two-thirds of the population between 18-70 years have some form of periodontal disease, with severe forms only affecting a small portion of the population (Hildebolt and Molnar, 1991; Kowolik et al., 2001; Yucel-Lindberg and Bage, 2013).

Periodontal disease is a term used for a variety of illnesses that affect the gingiva and alveolar bone within the mouth (Williams, 1990; Connell et al., 2012). This disease can originate due to traumatic, neoplastic, genetic, metabolic triggers including, broad-sense inflammation (Pihlstrom et al., 2005). Within living individuals, there are eight categories for classifying the severity of periodontal disease. Category 1 is the absence of disease, followed by gingivitis, and eventually aggressive bone loss at stage 3. The fourth category is when periodontitis becomes systemic, and the eighth stage relates to deformities of the body (Papapanou, 2013). While there are periods of quiescence,

periodontal disease is a progressive illness, that once initiated is irreversible and will continue to have detrimental impacts on the body (Hildebolt and Molnar, 1991; Irfan et al, 2001; Demmer and Desvarieux, 2006).

When gingiva, an oral mucous membrane that is pink and firmly attached in healthy oral cavities, becomes inflamed, it results in redness, swelling, or bleeding of the gingival margin (Williams, 1990; Hildebolt and Molnar, 1991; Boyd and Madden, 2003; Meyer et al., 2008; Mai et al., 2016). This is known as gingivitis and is a condition that is common among adults across the globe, affecting between 50-90% of adults. While a biofilm begins building on teeth within 24 hours of brushing, gingivitis only starts appearing between 10-21 days afterwards. Brushing and flossing are, therefore, essential to proper oral hygiene and breaking up biofilm, preventing gingivitis from developing (Streckfus et al., 1999; Pihlstrom et al., 2005; Bresolin et al., 2014).

Gingivitis is clinically evaluated through the examination of gum pocket depth (Irfan et al., 2001; Pihlstrom et al., 2005). Studies have shown that 26% of the United States' population have at least one tooth with a pocket depth of 4 millimeters or deeper (Hildebolt and Molnar, 1991). When examining plaque scores related to gingivitis, it was found that males had scores that were significantly higher than females (Kowolik et al., 2001). Since gingivitis only affects the gum tissue and not the alveolar bone, this immune response is not visible within the archaeological record (Larsen, 2015).

Periodontitis can appear if gingivitis is longstanding, causing bony pocket formation and destruction of the periodontal ligaments (Costa, 1982; Clark et al., 1986; Strohm and Alt, 1998; Streckfus et al., 1999; Kowolik et al., 2001; DeWitte and

Bekvalac, 2011; Pizzo et al., 2011; Connell et al., 2012; Yucel-Lindberg and Bage, 2013). Periodontitis is an episodic disease that becomes aggravated by the buildup of plaque (Michaud et al., 2017; Petersone-Gordina et al., 2018). This plaque related condition is characterized by both soft tissue inflammation and destruction, as well as alveolar bone loss and potential tooth loss (Figure 1). Gum tissue can become inflamed, causing pain, bleeding, unpleasant tastes, gum recession, and degradation to the periodontal ligament, root cementum, and alveolar bone (Clark, 1990; Hildebolt and Molnar, 1991; LeResche and Dworkin, 2002). Each tooth is suspended within an alveolar socket by a periodontal ligament. The periodontal ligament consists of collagen fibers that are embedded into the alveolar bone and cementum of the tooth (Williams, 1990; Hildebolt and Molnar, 1991). An inflammatory response of the body can result in the detachment of the collagen fibers from the cementum and apical migration of junctional epithelium (Lundy, 2011). This can lead to the formation of pockets, measuring 1-4 millimeters deep, between the gum tissue and the root (Costa, 1982; Williams, 1990; Highfield, 2009; Papapanou, 2013; Mai et al., 2016; Michaud et al., 2017).

Dental crowding can intensify pocket formation resulting in bacteria proliferation and an increase of periodontitis (Guatelli-Steinberg, 2016). Periodontitis is more severe than gingivitis, leaving impacts on the skeleton, and can potentially lead to systemic illness. It should be noted, however, that not all gingivitis progresses into periodontitis. It is the result of persistent inflammation and not determined by the amount of bacteria present in the oral cavity (Borch et al., 2010). Therefore, while *P. gingivalis* or other

bacteria are often found within the oral cavity, the quantity is not always sufficient to result in periodontal disease (Sasaki et al., 2008).

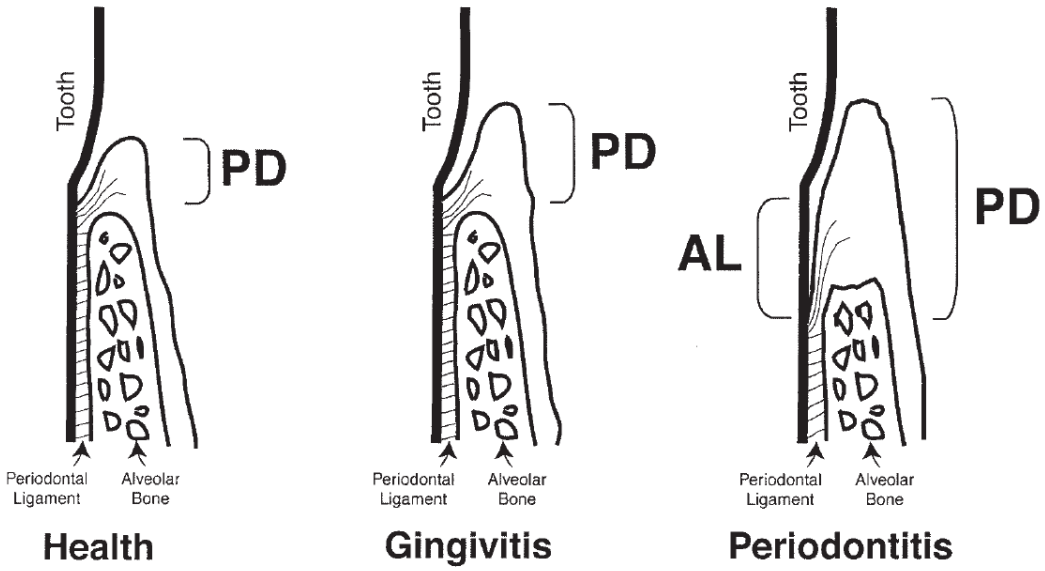

Figure 1: Periodontal tissue in healthy and diseased individuals. Shows differences between gingivitis and periodontitis. Overtime, the periodontal ligament becomes shortened, allowing more bacteria into the crevice. There is also observable alveolar bone resorption occurring within periodontitis (Papapanou, 2013).

In a healthy oral cavity, gingival crevicular fluid (GCF) prevents antigens from entering the cells of the mouth (Hajishengallis and Hajishengallis, 2013). The GCF is comprised of 70-80% granulocytes, 10-20% monocytes or macrophages, 5% mast cells, and 5% T-lymphocytes, providing a defense mechanism against foreign particles (Lundy, 2011). Antibacterial substances in saliva also protect the host (Breivik and Murison, 1996.). With adequate oral hygiene, the GCF and saliva are able to work effectively at

keeping bacteria from infecting the host. If an individual has inadequate oral hygiene, however, the biofilm is left undisturbed and begins to enter the gingival crevice. Since the subgingival biofilms consists of various antigens, such as *P. gingivalis, Treponema denticola,* and *Tannerella forsythia*, the host produces an inflammatory response to remove the pathogens, including an increased secretion of GCF. If persistent, this inflammatory response can lead to periodontitis (Trombone et al., 2009; Hajishengallis and Hajishengallis, 2013).

In an inflammatory response to oral pathogens, the body increases serum levels of CRP, hyper-fibrinogenemia, moderate leukocytosis, lymphotoxin, interlukin-1β (IL-1), and IL-6 (Williams, 1990; D'Aiuto et al., 2004). In periodontitis, IL-6, IL-1, and lymphotoxin become overexpressed, which activates osteoclasts for bone resorption, leading to an increase of RANKL, a membrane protein that controls bone remodeling, observed within diseased tissue (Kayal, 2013). This indicates a possible hyperinflammatory response to oral diseases with the body (DeWitte and Bekvalac, 2010; DeWitte and Bekvalac, 2011; Crespo et al., 2016).

Chronic inflammatory response of the oral cavity can result in destruction of the periodontal ligaments, bone loss, and even tooth loss. Because immune cells and inflammatory cytokines are important for bone turnover, bone homeostasis is influenced during immune response (Lundy, 2011; Crespo et al., 2016). Under the influence of inflammatory signals, T-cells within the periodontal tissues, increase the expression of RANKL. RANKL binds to a RANK receptor on osteoclasts, causing these cells to mature and activate (Page, 1991; Arron and Choi, 2000; Gosman, 2012; Klaus, 2014). Once

activated, osteoclasts are able to begin reabsorbing bone, which occurs during periodontitis.

In periodontitis, the activation of IFN-γ to fight oral pathogens might result in alveolar bone resorption as the host attempts to fight infection. Normally, interferon-γ (IFN-γ) blocks RANKL from activating RANK. In a study done on mice, mice with no IFN-γ will have less bone mass. As mentioned above, IFN-γ increases if the host is introduced to oral pathogens (Arron and Choi, 2000; Gosman, 2012). In humans, INF-γ production is different in individuals based on ethnicity, age, and stage of infection and can cause varying differences in level of destruction (Crespo et al., 2016).

These mechanisms allow periodontitis to identified within skeletal remains by the resorption of the alveolar bone, which exposes the underlying trabecular bone, producing porosity and potential tooth loss (Highfield, 2009). This bone destruction can be both vertical and horizontal (Strohm and Alt, 1998). As the alveolar crest recedes, relative to the cementoenamel junction, the tooth root is exposed, allowing periodontitis to be diagnosed. Periodontitis is typically noted within skeletal remains if the alveolar crest recession is at least two millimeters (DeWitte and Bekvalac, 2011). This resorption of the bone can result in tooth loss and is noted as the leading cause for tooth loss in individuals over 40 years (Hildebolt and Molnar, 1991; Strohm and Alt, 1998; Spahr et al., 2006).

Nevertheless, it should be cautioned that similar alveolar bone resorption appears with increasing age, especially within females, that has been determined to be independent from periodontal disease (Meyer et al., 2008; Liang et al., 2010). Alveolar resorption appears among 70.1% of individuals over the age of sixty-five (Abdellatif and

Burt, 1987; DeWitte and Bekvalac, 2011). Studies examining post-menopausal women receiving hormonal treatments found increased alveolar bone mass, potentially representing a relationship between decreases in sex-hormones have the ability to affect bone mineral density within the body (Hildebolt et al., 2002; Hildebolt et al., 2004). Furthermore, a study conducted on an Early Agricultural period sample from northwest Mexico found increasing antemortem tooth loss as individuals aged. Since alveolar resorption is associated with tooth loss, antemortem tooth loss might be related to age-related increases in periodontal disease and carious lesion formation along the CEJ/root (Watson et al., 2010).

While bacteria primarily affect periodontitis, other environmental factors exacerbate expression. Environmental factors that can contribute to periodontal disease include genetics, other chronic disease, host response, tobacco use, socioeconomic level, education level, frequency of dental visits, psychological stress, BMI, diabetes, and nutritional intake (Strohm and Alt, 1998; Boyd and Madden, 2003; Pihlstrom et al., 2005; Demmer and Desvarieux, 2006; Eshed et al., 2006; Meyer et al., 2008; Johansson and Ostberg, 2015; Hujoel and Lingstrom, 2017; Sun et al., 2017; Siddiqui et al., 2017; Petersone-Gordina et al., 2018).

Dental visits and daily oral hygiene are particularly important in moderating the severity of the disease. Individuals who do not practice adequate oral hygiene are 20.5 times more likely to develop periodontitis than people who do have adequate oral hygiene (Abdellatif and Burt, 1987; DeWitte and Bekvalac, 2011). Taking these factors into account, individuals who were more likely to exhibit severe periodontitis are older

non-white males who are uneducated, unmarried, and smoke (DeStefano et al., 1993; Pihlstrom et al., 2005).

Oral Health's Influence on Systemic Well-Being

Systemic Access for Bacteria

Early periodontal lesions begin with increased redness present in gum tissue and fibroblast breakdown that allows for leukocyte infiltration. Once the lesion is able to become established, lymphocytes and plasma cells increase, collagen continues to breakdown, and a loose epithelium pocket begins to deepen. The accumulation of gram-negative bacteria in a gingival crevice can result in destruction of the periodontal tissues and supporting bone because only an epithelial barrier resides between the biofilm and the underlying connective tissue (D'Aiuto et al., 2004). This overgrowth of bacteria leads to the pocket deepening, allowing more bacteria to fester in the wound. Deeper pockets, therefore, allows for the accumulation of bacteria and an exacerbation of gingivitis (Kayal, 2013). If left undisturbed, the dental plaque will accumulate, causing an inflammatory response (see figure 2) (Papapanou, 2013).

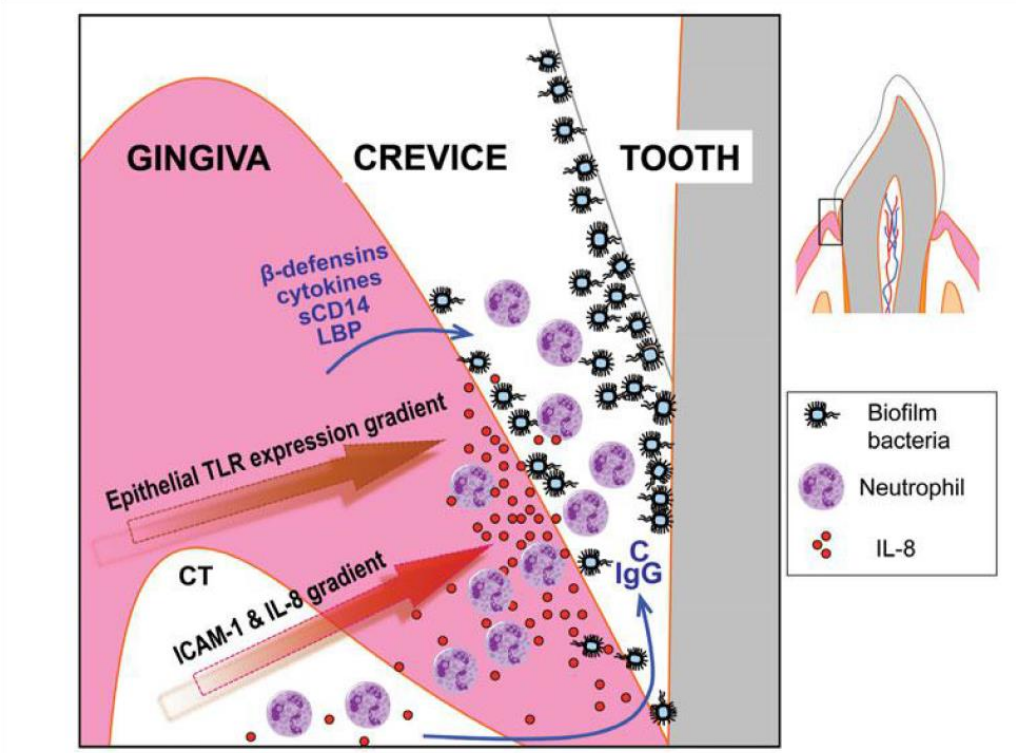

Figure 2: Immunology within the gingival crevice. Biofilm in the crevice initiates an immune response, which recruits neutrophils and cytokines.

The host initially responds by increasing vascular permeability, increased hydrostatic pressure in microcirculation, enlarges gaps between endothelial cells, and signals neutrophils and macrophages (Williams, 1990; Page, 1991; Kayal, 2013; Badran et al., 2015). This is essential for periodontal tissue defense because these mechanisms control the access pathogens have to tissues in the oral cavity. For example, neutrophils are vital to maintain oral health. If an individual is deficient, they have a higher susceptibility to periodontal disease (Boyd and Madden, 2003; Hajishengallis and Hajishengallis, 2013).

Neutrophils, nevertheless, can fail to control dental plaque bacteria, even though reasons are not understood at this time. If the biofilm persists, the adaptive immune response is triggered. Cytokines, antibodies, and lymphocytes are activated to respond, which can lead to increased aggregation in the blood vessels and damage elsewhere in the body. The transient bacteremia can affect the body systemically if the bacteria settles and colonizes (Li et al., 2000; DeWitte and Bekvalac, 2011). Macrophages, furthermore, can trigger an inflammatory response necessary at infection sites (North and Jung, 2004). While macrophages produce inflammatory mediators, these cells can be detrimental to the host as increased quantities result in collagen breakdown (Kayal, 2013).

A normal immune response begins locally, confined to local tissue or organ. Cytokines – such as TNF-α— and other immune cells, however, can increase due to a heightened inflammatory response, leading to a spillover effect that can become systemic. This can cause the activation of sensory nerves that report inflammation throughout the body and an increase of systemic levels of inflammatory mediators.

The persistent inflammation within periodontal disease allows bacteria in the oral biofilm are able to gain access to the bloodstream through the compromised gingival tissue due to a spillover effect (Li et al., 2000; DeWitte and Bekvalac, 2010; Hajishengallis and Hajishengallis, 2013). Bacteremia can occur during dental procedures (including extractions, fillings, and tooth repairs), mastication, and proper oral hygiene procedures (such as brushing and flossing), resulting in an intensified immune response. This can result in a hematogenous dissemination of diseases as the bacteria is able to travel throughout the bloodstream (Spahr et al., 2006). Once the bacteria enter the

bloodstream, the disease can become systemic, spreading to other organs of the body and initiating a hyperinflammatory state.

Lowering of Immunological Ability:

Periodontal disease has the potential to lower immunological ability, allowing for other pathogens to affect the body. The immune system must recognize the antigen appropriately, choosing the correct number and type of response to remove the foreign pathogen. If the wrong type or amount is implemented into the body, then the result can be detrimental to the fitness of the host in the form of autoimmune diseases and potentially trade-off effects (Graham et al., 2005).

The immune system is energetically costly to maintain and can involve trade-offs within the organism (McDade, 2003; Trotter et al., 2011). Trade-offs can emerge from nutritional, pathogenic, reproductive, and psychosocial factors (McDade, 2005). Malnutrition can lead to immunosuppression when T cells reduce in numbers; B lymphocytes remain normal. This can be due to deficiencies in Vitamins A, C, E and B, as well as iron, zinc, selenium, and copper (McDade, 2003). For example, a study examining Turkana Children from Kenya found that individuals with a low birth weight had higher risks for respiratory infection (McDade, 2005). Life-history events, such as growth and reproduction, also greatly affect immunity. When examining populations globally, there are adaptive challenges that each population is at risk from and has the ability to be altered by trade-off effects (McDade, 2003).

A study by Crespo et al. (2016), further, found a relationship between an increased cytokine production and individuals exposed to *Mycobacterium leprae, M.*

tuberculosis, and *P. gingivalis*. When exposed to *M. leprae* and *M. tuberculosis*, the expression of pro-inflammatory cytokines, such as TNF-α and IFN-γ, were increased slightly. When exposed to additional pathogens, such as *P. gingivalis*, TNF-α increased 14.5 times, and IFN-γ increased 13.2 times. This demonstrated a hyperinflammatory response when the body is confronted with additional pathogens and that periodontal disease is responsible for activating a host immune response that may be systemic due to lowered immunological ability.

This process is crucial for developing persistent inflammation and varies considerably between individuals based upon their immune competence (Holmstrup et al., 2003; McDade et al., 2010; Crespo and Lawrenz, 2016). If the host response is not sufficient, then this can result in chronic inflammation (Yucel-Lindberg and Bage, 2013). The inability to fight infection can promote a long-term inflammatory response that might indicate insufficiencies within the immune response of the body (Crespo et al., 2016). If the body has an impaired immune response, the infection can become systemic, leading to disease elsewhere in the body. This is especially relevant in immunocompromised individuals (Tolo, 1991; Shafer et al., 1991; Hollister and Weintraub, 1993; Johnson et al., 2006; Ichinohe et al., 2011).

Hyperinflammatory State within the Body

Inflammation of the oral cavity can result in a hyperinflammatory response due to the response mechanisms of the immune system (DeWitte and Bekvalac, 2010; DeWitte and Bekvalac, 2011). A hyperinflammatory trait creates elevated levels of cytokines within the body, which amplifies the inflammatory response necessary to remove the

harmful bacteria from the dental and gum tissue. Through oral infections, transient bacteremia can occur. If proper immune response does not eliminate the microorganisms, the bacteria might settle and colonize (Li et al., 2000).

This can result in a chronic infection because the impaired immune system is inadequately able to fight and control the bacteria, potentially leading to a hyperinflammatory response (Kornman et al., 1999; DeWitte and Bekvalac, 2011). In a hyperinflammatory state, the immune response has the potential to damage the host through immunopathology and can be life threatening due to energetic costs incurred by the host. Examples of immunopathology that can cause detrimental costs to the hose include, tuberculosis, malaria, and some influenzas.

Immunopathology occurs when the host activates the wrong mechanism to remove antigens or the response is too strong (Huynh et al., 2011; Straub, 2011). For instance, TNF-α is a highly productive cytokine that is critical for immune response and eliminating harmful antigens, but long-term production can also cause damage to the host. Individuals with a heightened TNF-α can result in symptoms including higher internal body temperature, loss of appetite, and lethargy (Strieter et al., 1993). There have also been changes observed within the heart, lungs, central nervous system, kidneys, and skeletal system when there are increases in TNF-α levels (Strieter et al., 1993; Graham et al., 2005; Liang et al., 2010; Crespo et al., 2016). In combination with IL-1, TNF-α has been found in elevated concentrations in individuals exhibiting periodontal disease (Borch et al., 2010; Yucel-Lindberg and Bage, 2013). The host might respond in this manner for a few reasons, including limited time to react to the antigen, or the precise

immunological control is more expensive than a hyperinflammatory response (Graham et al., 2005).

These hyperinflammatory responses are robust and have the ability to alter other systems within the body. Infections in the oral cavity have, specifically, been associated with numerous other diseases, such as cardiovascular diseases, respiratory infections, cancer, Alzheimer's disease, obesity, diabetes, renal disease, osteoporosis, pneumonia, and rheumatoid arthritis (Garcia et al., 1993; Kornman et al., 1999; Van Winkelhoff and Slots, 2000; Scannapieco et al., 2003; Beck and Offenbacher, 2005; Beck et al., 2005; Demmer and Desvarieux, 2006; DeStefano et al., 2007; Kamer et al., 2008; Amabile et al., 2008; Williams et al. 2008; Ozcaka et al., 2014; Engstrom et al., 2014; Siddiqui et al., 2017). Cancers such as lung, kidney, pancreatic, oral, esophageal, upper gastrointestinal, gastric, and kidney are also attributed to oral infection (Meyer et al., 2008; Pizzo et al., 2011; Mai et al., 2016; Michaud et al., 2017). Oral infection has also been associated with increased preterm birth, low birth weight, and stillbirths (Goepfert et al., 2004; Boggess, 2005; Boggess et al. 2006; Mobeen et al., 2008). Since periodontal disease and dental caries are the most common oral pathological conditions worldwide, recent studies have examined the relationship between these infectious diseases and overall health (Li et al., 2000; Holmstrup et al., 2003; D'Aiuto et al., 2004; Pihlstrom et al., 2005; Meyer et al., 2008; DeWitte and Bekvalac, 2010; DeWitte and Bekvalac, 2011; Pizzo et al., 2011).

The majority of studies examining the systemic effects of oral disease have focused on soft tissue illnesses. While no clinical studies have examined a systemic link between periodontal disease and the skeleton, a bioarchaeological study has found a

possible association (DeWitte and Belvalac, 2011). The study examined periodontal disease in association to periosteal lesions. Periostosis is a non-specific indicator of chronic disease and has been linked to injury, infection, as well as nutritional deficiencies; therefore, the prevalence of this condition has been used to examine health, biological stress, and immunocompetence (Connell et al., 2012; DeWitte, 2014a; Klaus, 2014; Weston, 2008; Mensforth et al., 1978). Differential diagnosis of lesion distribution helps differentiate conditions associated with chronic infection. For example, bilateral distribution of lesions is more frequently associated with chronic systemic disease, while those found on a single bone are more likely associated with traumatic injury (DeWitte, 2014a; Ortner, 2003; Mensforth et al., 1978).

The basic mechanisms behind the hyperinflammatory response with periodontal disease begins when active periodontal disease allows bacteria systemic passageway into the body, once in the circulatory system the bacteria is able to settle in injured periosteal due to the inflammation. The bacteria are then able to colonize and infiltrate the periosteum with similar pathways exhibited in periodontal disease.

More specifically, periosteal lesions and periodontal disease both have infectious etiologies, which can be connected through an impaired immune system. It has been postulated that bacteria associated with periodontal disease would able to gain systemic access through the circulatory system and is able to negatively impact bone elsewhere in the body with the same mechanisms utilized in breaking down alveolar bone. The body responds to infection, such as periodontal disease, with increased IL-1β, TNF-α and TNF-

β. These cytokines are known to have systemic effects, as well as the ability to stimulate osteoblastic activity and production of bone matrix.

Periosteal lesions form when the periosteum is stretched or compromised. Once perturbed, pus can build up, causing pressure between the bone and periosteum. This can result in a hematoma and decreased oxygen to the bone (Mensforth et al., 1978; DeWitte, 2014a; Larsen, 2015). If the blood supply is reduced for a sufficient duration, the periosteal bone dies off. When hypoxia occurs, osteoblasts are stimulated and new bone is laid down on the underlying cortex (Klaus, 2014; Connell et al., 2012; Weston, 2008). This manifests as new layers of bone that are smooth and irregular, forming a periosteal lesion. The new bone begins as a small mass of woven bone before forming a hard callused bone, and ultimately remodeling in healthy individuals (Walton and Rothwell, 1983; Lange et al., 2010; Van den Bossche et al., 1993; Mensforth et al., 1978).

Damaged periosteum can then trigger an inflammatory response in which the damaged areas would allow bacteria to adhere to the bone. Once the bacteria adhere to the bone, similar mechanisms related to bone remodeling in periodontal disease would be able to occur. IL-1β, TNF-α and TNF-β, originally triggered in response to periodontal disease, would respond to the inflammation by producing sclerotic bone (Demmer and Desvarieux, 2006; DeWitte, 2014a).

A study found an association between periodontal disease and periostosis (DeWitte and Bekvalac). This study, additionally, used age as a covariate to determine that the relationship observed between periodontal disease and periosteal lesions was not associated with age. These results might suggest a link between reduced

immunocompetence and periodontal disease, bacteria access to internal organs, or a potential hyperinflammatory response.

Other factors could have influenced these results, such as malnutrition or genetic factors. Malnutrition can reduce the ability of the host to mount an effective inflammatory response to fight illness (Boyd and Madden, 2003). Nevertheless, these results are informative for bioarcheological studies examining oral health. Oral disease does not have straightforward effects on the body as earlier studies had proposed. This study also demonstrated a relationship between oral infection and survivorship, adding additional dynamics to studies examining periodontal disease.

Conclusions:

Periodontal disease has been utilized in the study of oral health; however, they might serve as a proxy in identifying general health and mortality patterns in past populations (DeWitte and Bekvalac, 2010; DeWitte and Bekvalac, 2011). Inadequate oral health allows bacteria from the oral biofilm to enter into the gingival crevice. This results in an inflammatory response where the host recruits cytokines to remove harmful antigens, causing destruction to the gingival tissue (Gomez et al., 2009; Lundy, 2011; Papapanou, 2013; Michaud et al., 2017). If this process is long-term, cytokines, such as INF-γ, might activate osteoclasts that reabsorb bone tissue (Crespo et al., 2016). It is important for bioarchaeologists to understand these molecular responses to disease and the resulting observable impacts on the skeletal remains (Klaus, 2014).

Several studies have demonstrated a potential hyperinflammatory response to oral infection that has systemic consequences to health. These results could, additionally, indicate inadequacies within the immune response. Damaged gingival tissue allows for the dissemination of oral bacteria to other parts of the body. This results in hyperinflammatory response that worsens other diseases, such as cardiovascular disease (Beck and Offenbacher, 2005; Beck et al., 2005; Amabile et al., 2008; Huynh et al., 2011; Pizzo et al., 2011; Siddiqui et al., 2017). This relationship could be bi-directional (Johnson et al., 2006).

Furthermore, previous studies indicate that hyperinflammatory responses might be observable within skeletal remains (DeWitte and Bekvalac, 2011). It is possible, therefore, to postulate that an inflammatory response to oral pathogens will increase levels of IFN-γ elsewhere in the body, resulting in bone destruction in other anatomical regions than just the alveolar bone (Crespo et al., 2016). This has broader implications for the relationship between oral health and systemic diseases that are observable within the archaeological record (Larsen, 2018). These possibilities have been examined in a study of periodontitis and periostosis, but further research is necessary in this area (DeWitte and Bekvalac, 2011). A study of the relationship between oral disease and periostosis might also show a correlation of mortality since hyper-inflammatory responses are energetically costly to the body.

In the examination of periodontal disease in relation to general health, other factors could be affecting immune competence. Other factors include smoking, diabetes, nutritional intake, and social environment (Sun et al., 2017). For example, one study

found minorities were more affected by periodontal disease (Siddiqui et al., 2017). While in theory it would be ideal to incorporate all variables, it is not always plausible. A study examining more than one marker for systemic disease, however, might glean insight on the relationship between oral disease and general health of a population. The evaluation of periodontal disease should be able to infer stronger relationships between oral health and general health. In this study, periodontal disease should have a positive associated with periostosis that is independent of age. This will demonstrate a systemic interaction between oral health and general health within skeletal remains. Furthermore, periodontal disease will be associated with higher mortality.

CHAPTER 2: CARIOUS LESIONS AND LIFE-HISTORY EVENTS

Dental caries is a process associated with localized enamel demineralization due to erosion by weak organic acids (Larsen et al., 1991; DeWitte and Bekvalac, 2010; Selwitz et al., 2007; DeWitte and Bekvalac, 2011). Organic acids are the byproduct of dietary carbohydrate fermentation by oral bacteria (Hujoel and Lingstrom, 2017). These bacteria live within the oral biofilm, which can lead to carious lesion formation if the plaque remains on the tooth surface for an extended time, affecting the enamel, cementum, and dentin of the tooth. Bacteria commonly associated with dental caries include *Streptococus mutans*, *Streptococcus sanguis*, *Staphyloccus albus* and species of *Lactobacilli*, while lesions forming at the cementum enamel junction are more often associated with *Actinomyces viscosus* and *Actinomyces naeslundi* (Caselitz, 1998; Zukanovic, 2013). The evaluation of lesions produced by these bacteria have the potential to provide information regarding life-history events.

The destruction produced by the organic acid ranges from small pinprick lesions in the enamel to the total obliteration of the crown (Larsen et al., 1991; Selwitz et al., 2007; DeWitte and Bekvalac, 2010). Dental caries is caused by essential and modifying factors, both of which contribute to an increased presence of oral bacterial flora, resulting in plaque residing on the tooth surface (Larsen, 2015). Essential factors affecting frequency of lesion formations are tooth surface exposure to oral environment, oral

bacterial flora, and diet. Modifying factors are, conversely, site location and speed of lesion formation, tooth crown morphology and size, enamel defects, occlusal surface attrition, food texture, rate of food consumption, oral pH, and heredity (Larsen et al., 1991; Larsen, 2015). For example, the crenulations on the occlusal surface of posterior dentition trap food particles easier than anterior teeth. This causes more bacteria to adhere to the posterior teeth, resulting in higher prevalence of lesion formation (Watson et al., 2010). Increased attrition, on the other hand, leads to fewer carious lesions as the fissures are smoothed over, preventing particles from sticking to teeth surfaces. Several of these factors are influenced by changes in carbohydrate load; thus, dental caries prevalence has typically been used as a proxy to reconstruct past diets and oral hygiene (Hildebolt and Molnar, 1991; Larsen, 2015).

Agriculturalists are often cited as having higher dental caries frequencies than hunter-gatherer groups (Bentley et al., 1993). This is due to increased carbohydrate intake and adhesiveness of food particles found within domesticated cereal crops. The high sucrose content found within carbohydrates is easier digested by bacteria, producing more acid than low carbohydrate type food (Nicklisch et al., 2016). Furthermore, domestic crops are often assumed to be stickier than food consumed by hunter-gatherers, resulting in slower clearance rates. Slower clearance allows bacteria more time to breakdown food particles, causing an increase in fermentation and destruction of enamel (Humphrey et al., 2014). For these reasons, agriculturalists are associated with increased carious lesion frequencies (Turner, 1979). Carious lesion frequencies among

agriculturalist groups ranges from 2.2-48.1%, while hunter-gatherer groups usually range between 0-14.3% (Humphrey et al., 2014).

With perceived differences in lesion rate, anthropologists have utilized lesion frequency to determine health changes associated with the advent of agriculture. Increased reliance on agriculture has been associated with several indicators of declining health, including dental caries, when compared to hunter-gatherer economies and lifeways. Numerous studies have been conducted that utilize carious lesion frequencies to determine when populations began consuming domestic crops. Dental caries has also been utilized to examine dietary shifts during the industrial revolution when sugar became widely accessible (Caselitz, 1998; Guatelli-Steinberg, 2016; Eshed et al., 2006; Lanfranco and Eggers, 2010). For instance, industrial countries have a carious lesion frequency of 60-80% due to the high amount of sugars being consumed (Petersone-Gordina et al., 2018).

A study completed on the Basketmaker and post-Basketmaker populations, for instance, argued that the lesion frequencies, 12.3% and 11.1% respectfully, were representative of agricultural subsistence. The authors argued that these frequencies were outside of the typical range for mixed subsistence groups. The rates did not change drastically between these periods, indicating that reliance on domesticants did not increase; however, there might have been differences in processing techniques that resulted in stickier food (Schollmeyer and Turner, 2004).

The examination of dental caries frequencies among the pre-Hispanic population from Gran Canaria similarly found high rates of dental caries (Delgado-Darias et al.,

2005). Approximately 65.2% of the individuals studied has at least one carious lesion. The authors argued this was closer to agriculturalists than either mixed or foraging groups.

The Jomon foragers in Japan, further, have been found to have lower dental caries frequencies when compared to the Yayoi period farmers (Temple and Larsen, 2007). This was supported with pervious evidence of greater social complexity through possible ranked families or clans. The Jomon, based on dental caries rates, were determined to have consumed 30-50% of their annual caloric intake through wet rice. This study argued that these differences demonstrated variability in dietary choices.

A study completed on Jomon hunter-gatherers examined carious lesion frequencies for dietary reconstruction between East Asian groups and the Jomon (Turner, 1979). This study found that the Jomon possessed higher carious lesion frequency than observed within hunter-gatherer groups. Frequencies were comparable rates to agriculturalists such as the Atayal and An-yang Chinese. Therefore, it was argued that the Jomon consumed a domesticated crop. While millet was the best-established cultigen during Jomon times, the Jomon were not consuming it. Millet was the primary cereal consumed by the An-yang and differences in carious lesions presence between the An-yang and Jomon indicated the Jomon carious lesions were caused by a different cultigen. Instead, it was postulated that Jomon were consuming taro, a tuber-like food that results in a high prevalence of caries and appeared in Southeast Asia approximately 14,000 years ago. Taro was, therefore, capable of reaching Japan by the Middle Jomon period. This

study, however, did not account for seeds, nuts, and fruits consumed by hunter-gatherers that are highly cariogenic.

Recent studies have demonstrated that groups of hunter-gatherers can have high carious lesion frequency when consuming acorns and pine nuts (Humphrey et al., 2014). Among hunter-gatherers found at Grotte des Pigeons in Morocco, dating to the Middle and Later Stone age, 51.2% of the teeth observed contained carious lesions. This study argued that acorns from the Holm Oak and pine nuts from the Maritime Pines were responsible for the high frequencies of carious lesions. This hunter-gatherer sample demonstrated that frequency of dental caries is not a direct indication of subsistence strategy. These studies demonstrated that dental caries should not be taken alone as an indicator of diet, but should be combined with other cultural information. Furthermore, these methods are beneficial when isotopic analysis is not possible in reconstructing diets (Karsten et al., 2019).

Dental caries has also been utilized in determining dietary differences between males and females. Sexual divisions in labor, easier access to stored foods, and eating more frequently throughout the day have caused higher carious lesion frequencies among females when compared to males (Temple and Larsen, 2007; Lukacs 2008; Nicklisch et al., 2016). There are studies that have been hypothesized to account for the observed rate differences between males and females. Females were observed to have a higher dental caries rate in a study of the Neolithic and Early Bronze Age. This was potentially due to higher intake of carbohydrates and less protein than males were consuming. Protein acts as an inhibitor to bacteria adhesion to enamel, resulting in lower carious lesion rates. This

difference in diet consumed was postulated to be the reason for sex differences in dental caries rates (Nicklisch et al., 2016).

Dental caries has, furthermore, been associated with lifestyle and increased mortality risk. Dental caries is the most common chronic illness found amongst children, which has been associated with suboptimal nutrition and negative impacts on growth. Toothaches, associated with lesion formation, can affect nutritional intake (Acs et al., 1999).

A relationship was found between carious lesion presence and selective mortality (DeWitte and Bekvalac, 2010). Individuals with carious lesion and periodontal disease had an increased risk of dying when compared to those without oral pathological conditions. Without proper nutrition, trade-offs can occur within the body, resulting in lower immunocompetence (McDade, 2005). This could lead to higher mortality and might be related to systemic diseases within the body or an underlying problem with the immune system (DeWitte and Bekvalac, 2011). A hyperinflammatory state may also be associated with frailty because inflammation from the lesion can spread from the tooth to surrounding bone (Caselitz, 1998).

Infectious Disease and Mortality

The quality of life and survivorship within a population is often evaluated based on the prevalence of skeletal and dental lesions (Larsen, 2015). Critical explorations of bioarchaeological research do, however, suggest that the straightforward use of lesion frequency in the evaluation of health may be problematic (Wood et al., 1992). This work

argued that hidden heterogeneity and selective mortality are equally important confounders to interpretations of death assemblages. Hidden heterogeneity are all of the contributing factors to mortality that are not observable within the skeleton. This can be linked to genetic, socioeconomic, and temporal trends. Selective mortality is when there is an increased frailty due to a particular condition, which can appear in earlier years of life and are not always observable within the skeletal record. These ideas urged bioarchaeologists to adopt methods that help explain risk of death in relation to disease indicators in order to gain an improved perspective on the role of skeletal and dental lesions as appropriate indicators of morality.

Mortality and chronic infection was examined through the analysis of periosteal lesion formation in a sample of 538 individuals from East Smithfield, Guildhall Yard, St. Mary Graces cemetery, and St. Mary Spital (DeWitte, 2014a). Tibiae were examined for evidence of periosteal lesions, which were scored as absent, healed, active, or mixed based on expression. Changes in periosteal infection over the course of an individual's life were found, with active lesions observed in younger individuals and healed lesions found among older individuals. Individuals with healed lesions had an increased chance of survival when compared to individuals with active lesions or without any lesion present. These observed differences in survivorship could be related to several factors, including differences in immune competence or different etiologies causing the lesions. This study showed that there is a complexity in the skeletal expression of chronic infectious diseases over the life span. Individuals capable of surviving the illness causing

the active periosteal infection then the risk of death goes down. It would be these healed individuals who are viewed as healthier, rather than those actively sick.

Similar mortality pathways may be operating in cases of oral infection. For example, 190 individuals from St. Mary Graces cemetery in London to determine if there was a link between risk of death and oral pathological conditions, specifically dental caries and periodontal disease (DeWitte and Bekvalac, 2010). The work found that dental caries and periodontal disease were associated with increased risk of death. Such findings might be related to oral pathological conditions causing systemic disease in other tissues throughout the body. The immune system might be compromised and not able to carry out an effective immune response, ultimately resulting in death (DeWitte and Bekvalac, 2010). The authors also posit that the oral lesions are associated with poor nutritional intake following the onset of lesions.

While this study demonstrated greater risk of death among individuals with dental caries, the work only focused on lesion presence and absence infection. Progression of oral infection would, however, provide more information on potential life-history parameters that accentuate or inhibit risk of lesion formation. Numerous studies have indicate that life-history events impact carious lesion formation and the presence of periodontal disease, especially within women.

Saliva Changes during Hormonal Shifts

Divisions of labor between males and females has been cited for differences in carious lesion frequency observed between the sexes (Cucina et al., 2011; Temple and

Larsen, 2007; Lukacs, 1996; Larsen, 1983). Lukacs (2008) and Lukacs and Largaespada (2006) have, however, examined the link between female reproductive ecology and dental caries frequencies in agricultural populations. These studies argued that dental caries is the result of sexual development rather than behavioral differences in food consumption. Sex hormones have the ability to result in differences in the biochemical composition of saliva, food cravings or aversions during pregnancy, suppressed immune system during pregnancy, and lower saliva rate. Increased levels of estrogen—including estradiol, estrone, and estriol—have been linked to higher frequencies of carious lesions. This is due to in composition and flow rate of saliva. Androgens—such as testosterone and dihydrotestosterone— are not linked to changes in saliva. The advent of agriculture resulted in an increased fertility and pregnancy rate that changed hormone levels and other physiological factors more often than in hunter-gatherers, potentially causing females to express higher frequencies of carious lesions than males.

Saliva is an essential part of the oral cavity. Each person has three salivary glands that produce different types of saliva, which contain buffering agents, antibacterial properties, and agents for tooth mineralization. An alteration in these properties due to hormones can have a detrimental effect on the individual. Throughout pregnancy, the placenta causes estrogen levels to increase 100-fold. This has been linked to severity of periodontal disease and, potentially, carious lesion formation as periodontal pockets provide ideal nutrient environments for oral bacteria to proliferate (Lukacs and Largaespada, 2006; Laine, 2002).

Pregnancy, additionally, changes the composition of saliva. Saliva decreases in pH, leading to demineralization, while there is a decrease in mineralization due to reductions in calcium and phosphate levels. Together, these increase the levels of *S. mutans* in late pregnancy, allowing for the potential increase in carious lesion formation (Laine, 2002). While these changes might only occur in females during brief moments of their lives, increased reliance on agriculture allowed for higher fertility rates and decreases in inter-birth intervals (due to high rates of infant mortality) and could have led to increases in carious lesions (Bentley et al., 1993). Changes in sex hormones has the ability to alter physiological factors enough between males and females to result in changes in dental caries frequency (Lukacs and Largaespada, 2006; Lukacs, 2008). Saliva composition and flow rate has, therefore, been observed to be influenced by life-history parameters; however, cultural and environmental influences must be taken into account (Temple, 2015). For example, in a study done on late-pre-Hispanic and colonial-period Mochina individuals from Peru found that there was an increased frequency of dental caries but that this was associated with decreases in fertility within this population. (Klaus and Tam, 2010). Fertility was, therefore, not associated with increases in dental caries as suggested by Lukacs and Largaespada (2006) and Lukacs (2008).

Life-Histories and Periodontal Disease

Hormonal shifts during pregnancy and menopause can also produce inflammation within the gingival tissue and reduce bone mineral density, both leading to periodontitis. Several studies have examined the relationship between child-rearing and either

periodontal disease or antemortem tooth loss in females. There has been a saying that states “a woman loses a tooth for each child”. Therefore, a longitudinal study on Danish twins examined tooth loss in association to the number of children a woman produced (Christensen et al., 1998). Results indicated that there was a negative correlation between the number of children and tooth loss, with approximately one tooth per child in lower socioeconomic classes. Twins that had more children typically had fewer teeth. These results were not observed within male twins who had children, indicating changes in antemortem tooth loss was potentially related to sex hormones rather than other factors brought but by child rearing.

Similar results were found in a study examining the relationship between pregnancy and periodontal disease (Russell et al., 2008). Results suggest that periodontitis was exacerbated during pregnancy.

Gingival changes have also been observed in post-menopausal women. A study conducted on post-menopausal women with good oral health and hygiene examined the reason for increased gingival attachment loss and alveolar bone resorption (Pilgram et al., 1999). The study found changes in alveolar bone height were age-related rather than a response to periodontal disease. This is potentially related to hormonal changes in post reproductive years. These correlations were weak and might be due to time delays between periodontal attachment loss and alveolar bone loss.

A study was done that hypothesized that post-menopausal women would experience a decrease in cranial bone mass that was concomitant with age-dependent postcranial bone loss (Hildebolt et al., 2002). Post-menopausal women who had minimal

signs of periodontal disease were followed over a three-year period. The women received hormonal treatments that ultimately lead to increased bone mass. It is likely that the hormonal treatment suppressed cytokine production, stimulating bone production. These results were, however, generalized and not site specific. Follow-up studies found that post-menopausal receiving estrogen hormone therapy, calcium, and vitamin D, resulted in increased mandibular bone mass (Hildebolt et al., 2004). Taken as a whole, this body of research demonstrates that alveolar bone loss decreases in bone mineral density similarly to postcranial bone loss. In this sense, changes in hormone, vitamin, and mineral availability may exacerbate alveolar bone loss and periodontal disease in post-reproductive females.

Studies examining the relationship between bone mineral density and sex hormone levels in males is rare; however, low testosterone levels have been associated with bone mineral density decreases in the radius, spine, and hip (Kenny et al., 2000). Some studies suggest these rates are lower than found within post-menopausal women. This might have more to do with endogenous estrogen in bone turnover in males and females rather than testosterone levels (Greendale et al., 2009).

A study examining carious lesions and antemortem tooth loss was completed on an Early Agricultural Period (1600 BC- AD 200) sample from northwest Mexico (Watson et al., 2010). While there were no age-related increases in carious lesion frequencies, the study found that there was age-related antemortem tooth loss among the La Playa individuals. Antemortem tooth loss first began appearing in individuals 25-34 years of age, and increased by age. There were also sex-based differences among females

when antemortem tooth loss was examined. Post-menopausal women lost three times more teeth than males of the same age. Furthermore, the authors postulated that CEJ/root carious lesions were associated with horizontal loss of alveolar bone and periodontal disease. Differences in lesion location on the tooth were found among females in the post-reproductive group. These changes were not observed among males of the same age, indicating these changes could be the result of sex hormone variation due to life-history events that include loss of alveolar bone associated with post-menopausal lifespan.

Conclusions

Taken as a whole, a wide variety of studies demonstrate that carious lesion formation is associated primarily with dietary intake. However, these lesions also appear to have relationships with mortality, and when lesion location is considered, life history factors. As such, research addressing survivorship in association with carious lesion formation as well as the interaction between carious lesion formation, periodontal disease, age, and sex is need to further clarify these associations.

This study aims to examine lesion manifestation, in terms of chronicity and tooth surface. Due to sex hormone changes throughout life, there should be differences in lesion location between males and females. Estrogen fluctuations during pregnancy and menopause results in changes to saliva flow and composition, as well as alveolar bone resorption.

During reproductive years, females should have increased carious lesion frequency as gingival crevice fluid increases and *Streptococcus mutans* become more

prevalent. There should also be a difference in lesion location as females reach post-menopausal years and there are sex hormone changes. This would result in resorption of the alveolar bone, leaving the tooth exposed. Carious lesion, therefore, should provide information regarding life-history events and should differ between males and females and by age.

CHAPTER 3: MATERIAL AND METHODS

Materials

This study examined 874 individuals of known sex, race, and age from the Terry Collection, National Museum of Natural History, Smithsonian Institute. The sample collected includes 372 black males, 231 black females, 186 white males, and 85 white females (Table 1). Age ranged from 14 to 91, with a mean age of 45 years. Number of anterior, premolars, and molar teeth are listed in Table 2. Based on 32 teeth expected for 874 individuals, there should have been 27,968 teeth present. Teeth not represented here were due to antemortem tooth loss, postmortem tooth loss, or were unable to receive a score due to dental crown caps, being to worn, were unerupted or impacted, or were recorded as not present.

Table 1: Number of individuals by race and sex.

	N INDIVIDUALS OBSERVED
BLACK MALES	372
BLACK FEMALES	231
WHITE MALES	186
WHITE FEMALES	85
TOTAL	874

Table 2: Number of anterior, premolars, and molar teeth by race and sex.

	ANTERIOR	PREMOLARS	MOLARS
BLACK FEMALES	1,797	1,376	1,638
BLACK MALES	2,942	2,416	2,990
WHITE FEMALES	498	390	352
WHITE MALES	1,210	1,026	1,110
TOTAL	6,447	5,208	6,090

The Terry Collection was created through the efforts of Robert J. Terry and Mildred Trotter. Influenced by Huntington, Terry began collecting cadavers in 1898 to use for anatomical dissection in his anatomy classes at Washington University, St. Louis. After two failed attempts, he was successful in the creation of the current collection. Individuals in the collection were primarily unclaimed bodies of lower socioeconomic status from St. Louis hospitals and morgues after the 1920s (de la Cova, 2019). Many of these initial individuals were people who had died during the Great Depression. After an economic boom around World War II and legislation change, however, more individuals donated their bodies to science, which influenced the demographic structure of the collection (Hunt and Albanese, 2006; Hunt, 2003). The unclaimed individuals were not representative of the whole population, but that the additional bodies willed to science created a collection that attempted to illustrated actual demographics of the area (Ericksen, 1982). While efforts were made to create a more demographically representative sample of the region, this sample was never characteristic of the St. Louis population. For instance, around half of the sample consists of higher percentages of blacks—roughly half of the cadavers— than was in the actual population. Furthermore,

the age distributions and average age at death were inaccurate. The Terry Collection has most of the sample consisting of individuals over the age of 50 years, this is inconsistent with the average life expectancy of 20-40 years (de la Cova, 2010).

When Terry retired, Trotter and Mr. Rhoades continued collecting human remains to the Terry Collection. Trotter attempted to balance the demographic composition of the sample, focusing on adding more females and younger individuals. Ultimately, the sample was comprised of 1728 documented skeletons of individuals born between 1822-1943. Each specimen had names, sex, age, race, cause of death, date of death, institute, and pathological conditions recorded. Within the collection there are there are 461 white males, 546 black males, 323 white females, 392 black females, five Asian Males, and one Unknown. This results in a sex ratio of 1.4 males to every 1 female. Age at death for the sample range of 14-102 years, with a high percentage of individuals over the age of 45 years. Trotter did, however, acknowledged that the sample was deficient in white females under 27 years (Hunt and Albanese, 2006; Hunt, 2003; Trotter, 1981).

Many of the individuals represent in this sample were non-white, older males. Based on previous research, this demographic has higher prevelances of oral infection (DeStefano et al., 1993; Pihlstrom et al., 2005). Furthermore, relevant to this study, individual in the collection exhibited evidence of fillings and tooth repairs. This can result in bacteremia occurring and systemic spreading of oral bacteria (Spahr et al., 2006)

Terry and Trotter had a specific way in which to prepare the bodies for use in the collection. The bodies were macerated to strip them of soft tissue by soaking them in hot water for 72 hours. The remains were then degreased by exposure to hot benzine fumes,

but care was taken so not to void the bones of fat. Terry believed that fat would allow for more durable specimens (Hunt and Albanese, 2006; Hunt, 2003; Trotter, 1981; Tobias, 1991). Due to the manner in which the collection was dissected and cleaned, the Terry Collection remains relatively well preserved. Thus, with the written records of each individual, it has been used extensively for research that requires known demographic information and medical history (Hunt and Albanese, 2006).

Methods

Age, Sex, and Race

As noted above, the Terry Collection has demographic information for each specimen recorded; therefore, information on age, sex, and race was based on this documentation. Specimen with discrepancies in age, sex, or race were not examined.

Dental Caries

All erupted permanent teeth were examined macroscopically for the presence of carious lesions. Lesions were identified as any distinctive necrotic pit that penetrated the enamel surface (based on recommendations from Caselitz, 1998; Moore and Corbett, 1971; Watson et al., 2010; Souza et al., 2013; Novak et al., 2012). In cases where etiology was uncertain, a dental probe and magnifier (10x) were utilized. Lesions were then classified based on standardized locations on the teeth as suggested by Buikstra and Ubelaker (1994), which were modified from Moore and Corbett (1971). Each tooth was

given a score between 0-8, with teeth possessing more than one lesion receiving multiple scores.

The following definitions are provided for each score: 0) no lesion present; 1) occlusal carious lesion; 2) lesions on the interproximal contact facets; 3) lesions on either buccal or lingual smooth surfaces; 4) lesions originated at the CEJ on either the buccal or lingual regions; 5) root carious lesions; 6) large lesions that had destroyed much of the tooth; 7) non-carious pulp exposure. Noncarious pulp exposure is often caused by extreme wear or damage to the tooth (Lanfranco and Eggers, 2010; Clark, 1990). These scores are similar to methods completed by Lanfranco and Eggers (2010) and Souza et al. (2013). A supplementary score of 8 was added to this analysis to indicate lesions that formed specifically at the CEJ within the interproximal regions. Teeth that possessed more than one carious lesion were given multiple scores to represent each carious lesion. These scores were later lumped together for analysis purposes.

Periodontal Disease

Measuring between the CEJ and AC is ideal for preventing subjective analysis and for comparing individuals, but it does not incorporate any anatomical, developmental, and pathological factors that could result in an increased distance between the CEJ and AC (Oztunc et al., 2006). Furcation, for example, is a disease that affects the pulp chambers of the molars. This can result in an increased distance between CEJ and AC that is not the result of periodontal disease (Clark, 1990; Hildebolt and Molnar, 1991). Furthermore, as individuals increase in age, teeth continuously erupt to

compensate for attrition (Oztunc et al., 2006; Clark et al., 1986; Clark, 1990). Individuals with severe wear might exhibit greater distances between the CEJ and AC without being affected by periodontal disease; thus, relying on only amount of recession might not be the most accurate way to determine presence of the disease. Instead, changes in alveolar bone architecture and texture should be examined in conjunction with the measurement.

Each alveolus should be examined for widening of the foramina and changes to the cortical bone surface surrounding each tooth. Bone that is porous, contains pitting, or changes to a shelf-like margin, instead of a healthy knife-edged shape, indicates alveolar bone resorption (Oztunc et al., 2006; Strohm and Alt, 1998; Clark et al., 1986; Clark, 1990; Larsen, 2015; Hildebolt and Molnar, 1991). As bone resorbs, it loses the smooth surface and takes on a ragged texture. This begins with small foramina and grooves but escalades to an irregular porous structure as periodontal disease becomes more severe (Kerr, 1998).

Currently there is no standard way to measure and identify periodontal disease within dry bones (Strohm and Alt, 1998). Therefore, for this study, periodontal disease was recorded based on a combination of techniques to develop a form of best practice. Since periodontal disease is not evenly distributed around the mouth, each tooth and socket were evaluated for indicators of disease (following Eke et al., 2012). Individuals with a recession of 2 millimeters or more between the CEJ and AC, as well as marked morphological changes to the alveolar bone were determined to have periodontal disease (as suggested by Clark, 1990). Recession was determined with a dental probe. Scores were given to each socket as either periodontal disease being absent (0) or present (1) if

moth methods were consistent with periodontal disease. Degree of severity was not measured.

Antemortem Tooth Loss

Antemortem tooth loss can occur due to trauma, periodontal infection, or exposure to bacterial infections in the pulp chamber, which can be the result of carious lesions or heavy attrition (Watson et al., 2010; Moore and Corbett, 1971; Lanfranco and Eggers, 2010; Badran et al., 2015; Streckfus et al., 1999; Guatelli-Steinberg, 2016; Clark et al., 1986; Larsen, 2015). Tooth loss in older adults is more likely attributed to periodontal disease while in younger individuals it might be the result of extensive carious lesions; for these reasons antemortem tooth loss was also recorded for each specimen. Antemortem tooth loss was recorded present (1) if there was partial or complete absorption was observed. If the tooth was present or the alveolus did not show evidence of absorption, antemortem tooth loss was recorded as 0.

Periostosis

Woven, or active, lesions are present at time of death and were identified by the porous and loosely organized characteristics of the patch. These patches are also recognizable from sharp edges that sit on top of the cortical bone (DeWitte, 2014a; Larsen, 2015; Mensforth et al., 1978). Woven bone formation might take on a pinkish, grey, or darker color than surrounding bone (Weston, 2008). Sclerotic lesions are those that healed prior to death. Sclerotic lesions have patches of bone that are more rounded,

with remodeled edges that are incorporated into the surrounding cortical bone. Sclerotic patches are also more organized than woven bone and are the same color as the surrounding cortical bone (DeWitte, 2014; Larsen, 2015; Weston, 2008; Mensforth et al., 1978).

Periosteal lesions most often form postcranially on the shafts of the tibia, humerus, and femur (Mensforth et al., 1978). The tibia is the least vascularized area of the body that is poorly protected anteriorly, is surrounded by limited soft tissue, has a low circulatory rate, is slow to trigger an immune response, and it preserves well, making the tibia ideal for analyzing periostosis frequency (Larsen, 2015; Klaus, 2014). The anterior diaphysis of the tibia, in particular, was examined because it does not have muscle attachments that might skew results (DeWitte, 2014a). This study required that both right and left tibiae of each individual be present. The presence/absence of lesions on the anterior diaphysis of each tibia were then scored according to the following criteria: 0) no lesion formation; 1) presence of sclerotic lesion; 20 presence of an active lesions; and 3) presence of both sclerotic and woven lesions.

Statistical Analysis

Log-linear analysis. To analyze the association between oral infection (antemortem tooth loss, periodontal disease, and carious lesions), periostosis, and age, a log-linear test was applied using SPSS version 24. This allowed for a three-way interaction between the variables to be tested and to help explain if associations between tibial periostosis, periodontal disease, and antemortem tooth loss, and carious lesions

occur independent of age. Backwards elimination was used to hierarchically remove interactions that lacked statistical significance. With the ability to test three variables, it is possible to determine if there is an association between oral infections and periostosis when accounting for age. If there is a significant interaction between oral infection and periostosis, then log-linear can test if this relationship is dependent upon age. Tests were also completed to examine the relationship between periosteal lesions, periodontal disease, and age, when accounting for sex and race. It should be noted here that race does not mean the genetic diversity between humans, but rather is based on the cultural construction of race. There are biological consequences defined through sociocultural constructions of race, which have been observed to have an effect on the health of various groups (Gravlee, 2009).

In addition, log-linear analysis was used to evaluate the interaction between age, sex, periodontal disease presence, and carious lesion type following the survival analysis. The goal here is to understand if the differences found between each group could be attributed to a particular association between variables.

For the purposes of log-linear analysis, periodontal disease was coded as present/absent. Carious lesion type were listed according to standards derived from previous research (i.e., Watson et al., 2010) as absent, crown carious lesion, and root/CEJ carious lesion. Here, dental caries score was simplified from the recorded data based on Buikstra and Ubelaker (1994) standards. Sex was listed as male/female. Age was divided according to notional reproductive (19-49 years) and post-reproductive (50+ years)

groups for both males and females. These ages are associated with average age-at-first-birth as well as average menopausal age in contemporary and traditional populations.

Survival analysis. The effects of carious lesions formation on survivorship was tested using the Kaplan-Meier survival analysis. The survival analysis was used to analyze survival differences between males and females with differences in carious lesion expression. This test uses age as a time series variable with sex and carious lesions—presence/absence and expression type—as covariates.

Multivariate four-way ANOVA test. To evaluate the interactions between crown and CEJ/root lesions, sex, periodontal disease, and age as interaction variables, a multivariate four-way ANOVA test was completed. This test provides information on significant differences between the mean number of teeth with carious lesions dependent on age, sex, and periodontal disease status.

CHAPTER 4: RESULTS

The frequencies for carious lesions, periosteal lesions, and periodontal disease are shown in Table 3, Table 4, and Table 5. There are 88 (10.1%) individuals without carious lesions, 224 (25.6%) with only crown carious lesions, and 562 (64.3%) individuals with at least one CEJ/root lesion. Periodontal disease is present in 799 (91.4%) individuals and periosteal lesions were observed in 465 (53.2%) individuals.

Carious lesion frequencies by age is listed in Table 6. Among the youngest cohort, 14-19 years of age, there are 15 (75%) individuals with carious lesions present; whereas, there are 143 (88%) individuals in the 60+ year cohort that exhibit one or more carious lesion. When examining periodontal disease frequency by age (Table 7), there are 9 (45%) individuals in the youngest cohort to exhibit periodontitis, while 161 (99%) individuals over 60 years showed signs of periodontal disease. Individuals of reproductive age with periodontal disease are more likely to exhibit carious lesion at the CEJ/root than crown lesions. Similar results appear in post reproductive males, who are twice as likely to have carious lesions located at the CEJ/root if they exhibited periodontal disease (15.4% of individuals) when compared to crown lesions (5.3% of individuals). Post-reproductive females with periodontal disease are nearly six times more likely to have carious lesions located at the CEJ/root (10.9% of individuals) than on the crown (2.1% of individuals).

Table 8 lists frequency of antemortem tooth loss by age. The youngest cohort has 4 (20%) individuals with at least one tooth lost antemortem, while 159 (98%) individuals over 60 years had one or more antemortem teeth lost. When examining periosteal lesion frequency by age (Table 9), 8 (40%) individuals from 14-19 years show presence of lesion formation, whereas, 111 (69%) individuals 60 years or over exhibit periosteal lesions.

Table 3: Frequency of carious lesion type.

	# WITH LESION	% AFFECTED
NO CARIOUS LESION	88	10.1
CROWN CARIOUS LESIONS ONLY	224	25.6
CEJ/ROOT CARIOUS LESIONS	562	64.3

Table 4: Frequency of periodontal disease.

	N	% AFFECTED
PERIODONTAL DISEASE NOT PRESENT	75	8.6
PERIODONTAL DISEASE PRESENT	799	91.4

Table 5: Frequency of tibial periosteal lesions.

	# WITH LESION	% AFFECTED
PERIOSTEAL LESIONS NOT PRESENT	409	46.8
PERIOSTEAL LESIONS PRESENT	465	53.2

Table 6: Frequency of carious lesions by age.

AGE	N	# WITH LESIONS	% WITH LESIONS
14-19	20	15	75
20-29	135	110	81
30-39	185	153	83
40-49	213	176	83
50-59	159	138	87
60+	162	143	88
TOTAL	874	735	84

Table 7: Frequency of periodontal disease by age.

AGE	N	# WITH LESIONS	% WITH LESIONS
14-19	20	9	45
20-29	135	100	74
30-39	185	172	93
40-49	213	202	95
50-59	159	155	97
60+	162	161	99
TOTAL	874	799	91

Table 8: Frequency of antemortem tooth loss by age.

AGE	N	# WITH LESIONS	% WITH LESIONS
14-19	20	4	20
20-29	135	86	64
30-39	185	152	82
40-49	213	179	84
50-59	159	151	95
60+	162	159	98
TOTAL	874	731	84

Table 9: Frequency of periosteal lesions by age.

AGE	N	# WITH LESIONS	% WITH LESIONS
14-19	20	8	40
20-29	135	59	44
30-39	185	83	45
40-49	213	106	50
50-59	159	98	62
60+	162	111	69
TOTAL	874	465	53

Log-linear Analysis

Frequencies of periosteal lesions and periodontal disease by age group is listed in Table 10. The results of the log-linear analysis are reported in Table 11 and Table 12. Log-linear analysis was also completed on dental caries, however results did not vary from periodontal disease and was not the relationship examined in this study.

Table 10: Contingency table for periodontal disease and periosteal lesions.

AGE		PERIODONTAL DISEASE	NO PERIODONTAL DISEASE
14-19	Periosteal lesions	5	6
	No Periosteal lesions	6	3
20-49	Periosteal lesions	223	25
	No Periosteal lesions	251	34
50+	Periosteal lesions	206	3
	No Periosteal lesions	110	2

Table 11: Results of log-linear analysis of the interaction of periodontal disease, periosteal lesions, and age.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X PERIODONTAL DISEASE X PERIOSTEAL LESIONS	1.885 (2)	0.390
AGE X PERIODONTAL DISEASE	38.642 (2)	0.0001
AGE X PERIOSTEAL LESIONS	34.005 (2)	0.0001
PERIODONTAL DISEASE X PERIOSTEAL LESIONS	7.094 (1)	0.008

Table 12: Results of log-linear analysis of the interaction of antemortem tooth loss, periosteal lesions, and age.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X AMTL X PERIOSTEAL LESIONS	3.091 (2)	0.213
AGE X AMTL	58.062 (2)	0.0001
AGE X PERIOSTEAL LESIONS	39.594 (2)	0.0001
AMTL X PERIOSTEAL LESIONS	10.452 (1)	0.001

Among males and females, no significant association between periodontal disease and periosteal lesions was observed ($P \leq 0.651$; $P \leq 0.372$) (Tables 13 and 14). When examining the results between blacks and whites, the results were also not significant ($P \leq 0.602$; $P \leq 0.891$) (Tables 15 and 16).

Results further indicate there is no significant relationship between antemortem tooth loss, periosteal lesions, and age among males and blacks ($P \leq 0.973$; $P \leq 0.991$) (Tables 17 and 20). There is, however, a marginally insignificant relationship between

these variables when individuals are either female or whites ($P \leq 0.068$; $P \leq 0.082$) (Tables 18 and 19). Among whites, there is a significant relationship between age and antemortem tooth loss ($P \leq 0.0001$), as well as between age and periosteal lesions ($P \leq 0.002$). Similar results were found in females, with significant relationship between age and antemortem tooth loss ($P \leq 0.0001$), as well as between age and periosteal lesions ($P \leq 0.0001$).

Table 13: Results of log-linear analysis of the interaction of periodontal disease, periosteal lesions, and age for males.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X PERIODONTAL DISEASE X PERIOSTEAL LESIONS	.858 (2)	0.651
AGE X PERIODONTAL DISEASE	23.162 (2)	0.0001
AGE X PERIOSTEAL LESIONS	15.136 (2)	0.001
PERIODONTAL DISEASE X PERIOSTEAL LESIONS	5.287 (1)	0.021

Table 14: Results of log-linear analysis of the interaction of periodontal disease, periosteal lesions, and age for females.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X PERIODONTAL DISEASE X PERIOSTEAL LESIONS	1.976 (2)	0.372
AGE X PERIODONTAL DISEASE	17.066 (2)	0.0001
AGE X PERIOSTEAL LESIONS	20.262 (2)	0.0001
PERIODONTAL DISEASE X PERIOSTEAL LESIONS	3.225 (1)	0.073

Table 15: Results of log-linear analysis of the interaction of periodontal disease, periosteal lesions, and age for sex combined blacks.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X PERIODONTAL DISEASE X PERIOSTEAL LESIONS	1.014 (2)	.0602
AGE X PERIODONTAL DISEASE	24.891 (2)	0.0001
AGE X PERIOSTEAL LESIONS	21.530 (2)	0.0001
PERIODONTAL DISEASE X PERIOSTEAL LESIONS	3.816 (1)	0.051

Table 16: Results of log-linear analysis of the interaction of periodontal disease, periosteal lesions, and age for sex combined whites.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X PERIODONTAL DISEASE X PERIOSTEAL LESIONS	.232 (2)	0.891
AGE X PERIODONTAL DISEASE	23.221 (2)	0.0001
AGE X PERIOSTEAL LESIONS	12.050 (2)	0.002
PERIODONTAL DISEASE X PERIOSTEAL LESIONS	3.331 (1)	0.068

Table 17: Results of log-linear analysis of the interaction of antemortem tooth loss, periosteal lesions, and age for sex combined blacks.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X AMTL X PERIOSTEAL LESIONS	.019 (2)	0.991
AGE X AMTL	37.598 (2)	0.0001
AGE X PERIOSTEAL LESIONS	21.530 (2)	0.0001
AMTL X PERIOSTEAL LESIONS	4.732 (1)	0.030

Table 18: Results of log-linear analysis of the interaction of antemortem tooth loss, periosteal lesions, and age for sex combined whites.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X AMTL X PERIOSTEAL LESIONS	5.013 (2)	0.082
AGE X AMTL	15.347 (2)	0.0001
AGE X PERIOSTEAL LESIONS	12.050 (2)	0.002
AMTL X PERIOSTEAL LESIONS	1.342 (1)	0.247

Table 19: Results of log-linear analysis of the interaction of antemortem tooth loss, periosteal lesions, and age for females.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X AMTL X PERIOSTEAL LESIONS	5.367 (2)	0.068
AGE X AMTL	21.667 (2)	0.0001
AGE X PERIOSTEAL LESIONS	23.124 (2)	0.0001
AMTL X PERIOSTEAL LESIONS	4.035 (1)	0.045

Table 20: Results of log-linear analysis of the interaction of antemortem tooth loss, periosteal lesions, and age for males.

INTERACTION	CHI-SQUARE (DF)	P VALUE
AGE X AMTL X PERIOSTEAL LESIONS	.055 (2)	0.973
AGE X AMTL	38.388 (2)	0.0001
AGE X PERIOSTEAL LESIONS	18.678 (2)	0.0001
AMTL X PERIOSTEAL LESIONS	6.691 (1)	0.010

Kaplan-Meier Survivorship

The results of the Kaplan-Meier analysis are listed in Table 21, the frequencies of individuals are reported in Table 22, and survivor curves are represented in Figure 1.

Individuals with carious lesion expression had a significantly greater probability of survival ($x^2 = 9.862$; $P \leq 0.002$). When individuals were differentiated based on sex, females with carious lesions had higher survivorship than females without lesions, males with lesions, and males without lesions ($P \leq 0.0001$) (See Tables 23 and 24). Females without lesions had higher survival than males without lesions ($x^2 = 3.773$; $P \leq 0.052$) (Figure 2). Females lesions had significantly higher survivorship than males with without lesions ($x^2 = 17.220$; $P \leq 0.000$) and males with lesions ($x^2 = 4.294$; $P \leq 0.038$). Males without lesions had significantly lower survivorship than males with lesions ($x^2 = 13.533$; $P \leq 0.0001$).

Table 21: Kaplan-Meier survival analysis results for carious lesion absence/presence.

Carious Lesion Expression	Mean Survival Time	95% CI (Lower limit-upper limit)
Absent	39.2	36.0-42.5
Present	45.4	44.3-46.4

Table 22: Frequencies of individuals with absent and present lesions.

AGE	ABSENT (%)	PRESENT (%)	TOTAL
14-19	7 (0.35)	13 (0.65)	20
20-29	20 (0.15)	115 (0.85)	135
30-39	23 (0.12)	162 (0.88)	185
40-49	14 (0.07)	199 (0.93)	213
50-59	14 (0.09)	145 (0.91)	159
60+	10 (0.06)	152 (0.94)	162
TOTAL	88 (0.10)	786 (0.90)	874

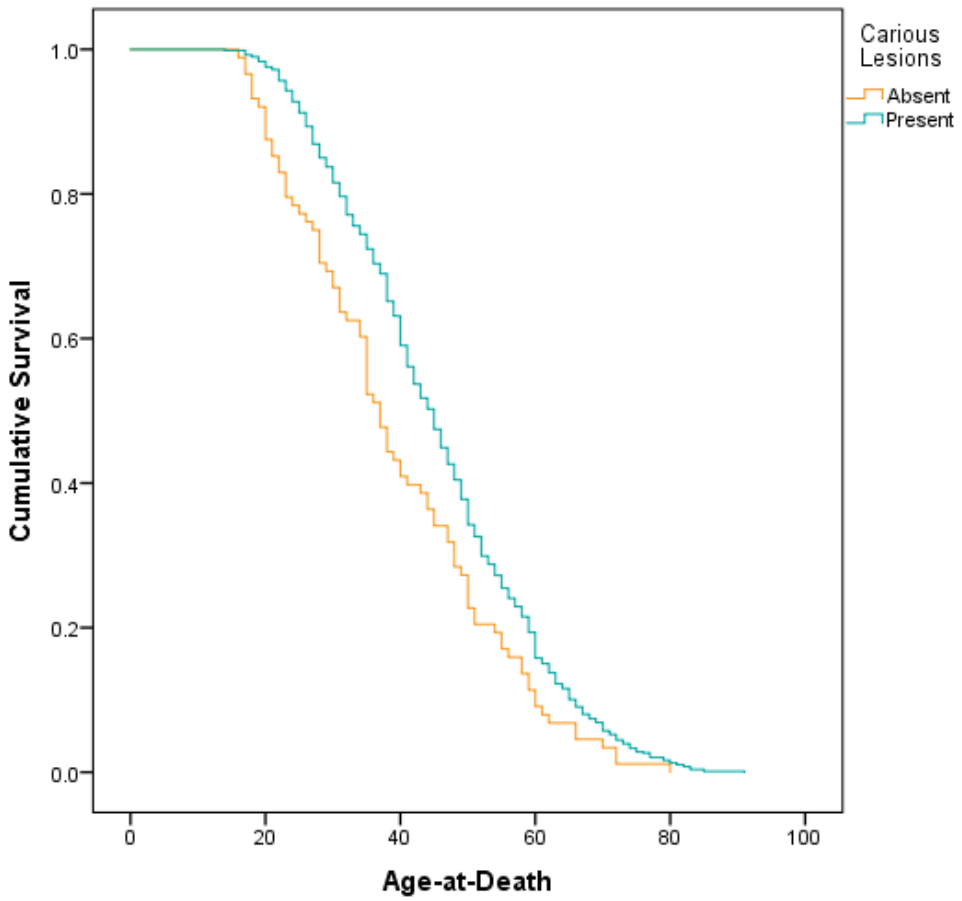

Figure 3: Survivorship curve based on carious lesion absence/presence.

Table 23: Kaplan-Meier survival analysis results for carious lesion presence/absence based on sex.

Sex	Carious Lesion Expression	Mean Survival Time	95% CI (Lower limit-upper limit)
Female	Absent	43.5	37.9-49.1
	Present	46.0	44.1-48.0
Male	Absent	36.7	32.9-40.5
	Present	45.0	43.8-46.2

Table 24: Frequencies of male and female individuals with absent and present lesions.

	MALES		FEMALES		
AGE	**ABSENT**	**PRESENT**	**ABSENT**	**PRESENT**	**TOTAL**
14-19	5 (0.25)	8 (0.40)	2 (0.10)	5 (0.25)	20
20-29	14 (0.10)	68 (0.50)	6 (0.04)	47 (0.35)	135
30-39	16 (0.09)	106 (0.57)	7 (0.04)	56 (0.30)	185
40-49	8 (0.04)	139 (0.65)	6 (0.03)	59 (0.28)	213
50-59	7 (0.04)	90 (0.57)	7 (0.04)	55 (0.35)	159
60+	5 (0.03)	93 (0.57)	5 (0.03)	60 (0.37)	162
TOTAL	55 (0.06)	504 (0.58)	33 (0.04)	282 (0.32)	874

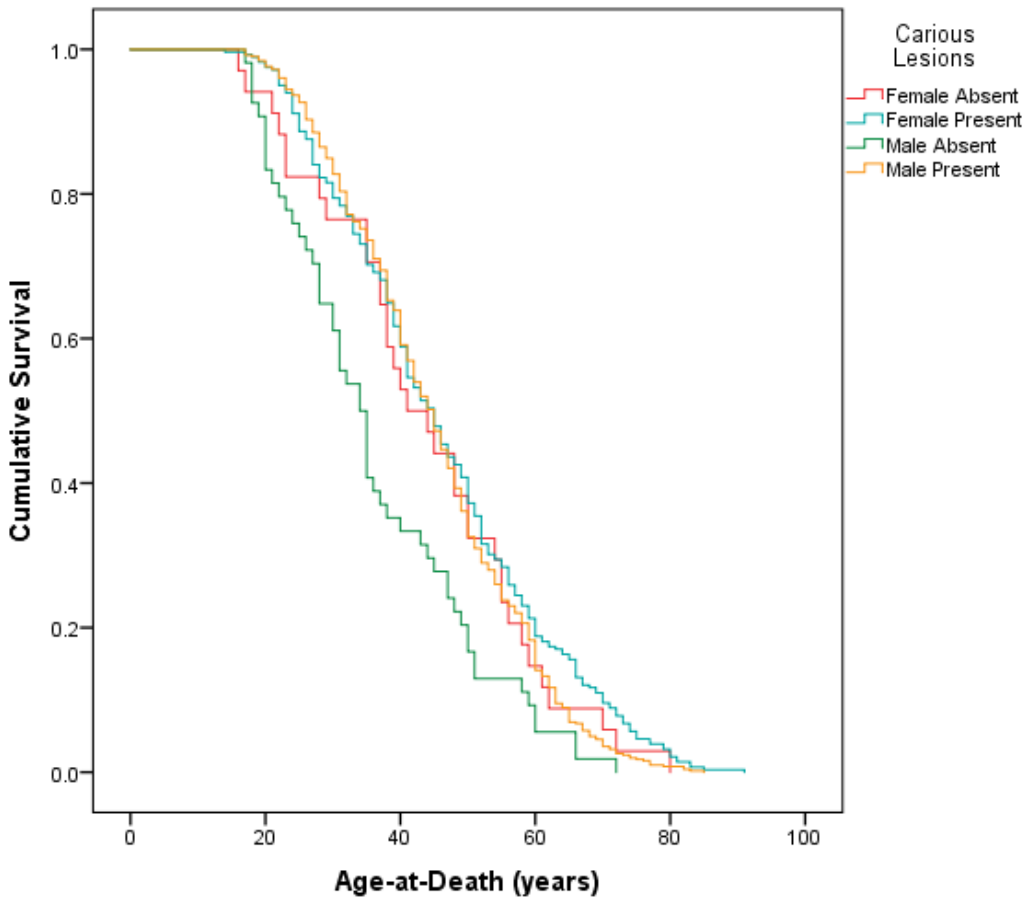

Figure 4: Survivorship curve based on carious lesion absence/presence based on sex.

Analysis was further completed on survivorship based on location of carious lesions (Tables 25 and 26) (Figure 3). Individuals with lesions at the CEJ/root had significantly higher survivorship than individuals without lesions ($x^2 = 16.061$; $P \leq 0.000$) and individuals with crown lesions ($x^2 = 26.460$; $P \leq 0.0001$). However, there is no significant difference in survivorship between individuals without lesions and those with crown lesions ($x^2 = 0.171$; $P \leq 0.679$).

Table 25: Kaplan-Meier survival analysis results between location of lesion formation.

Carious Lesion Expression	Mean Survival Time	CI (Lower limit-upper limit)
No Lesion	39.2	36.0-42.5
Crown Lesion	41.0	39.2-42.9
CEJ/Root Lesion	47.1	45.8-48.3

Table 26: Frequencies of individuals with absent, crown, and CEJ/root lesions.

AGE	ABSENT (%)	CROWN (%)	CEJ/ROOT (%)	TOTAL
14-19	7 (0.35)	6 (0.30)	7 (0.35)	20
20-29	20 (0.15)	49 (0.36)	66 (0.49)	135
30-39	23 (0.12)	56 (0.30)	106 (0.57)	185
40-49	14 (0.07)	49 (0.23)	150 (0.70)	213
50-59	14 (0.09)	36 (0.23)	109 (0.68)	159
60+	10 (0.06)	28 (0.17)	124 (0.77)	162
TOTAL	88 (0.10)	224 (0.26)	562 (0.64)	874

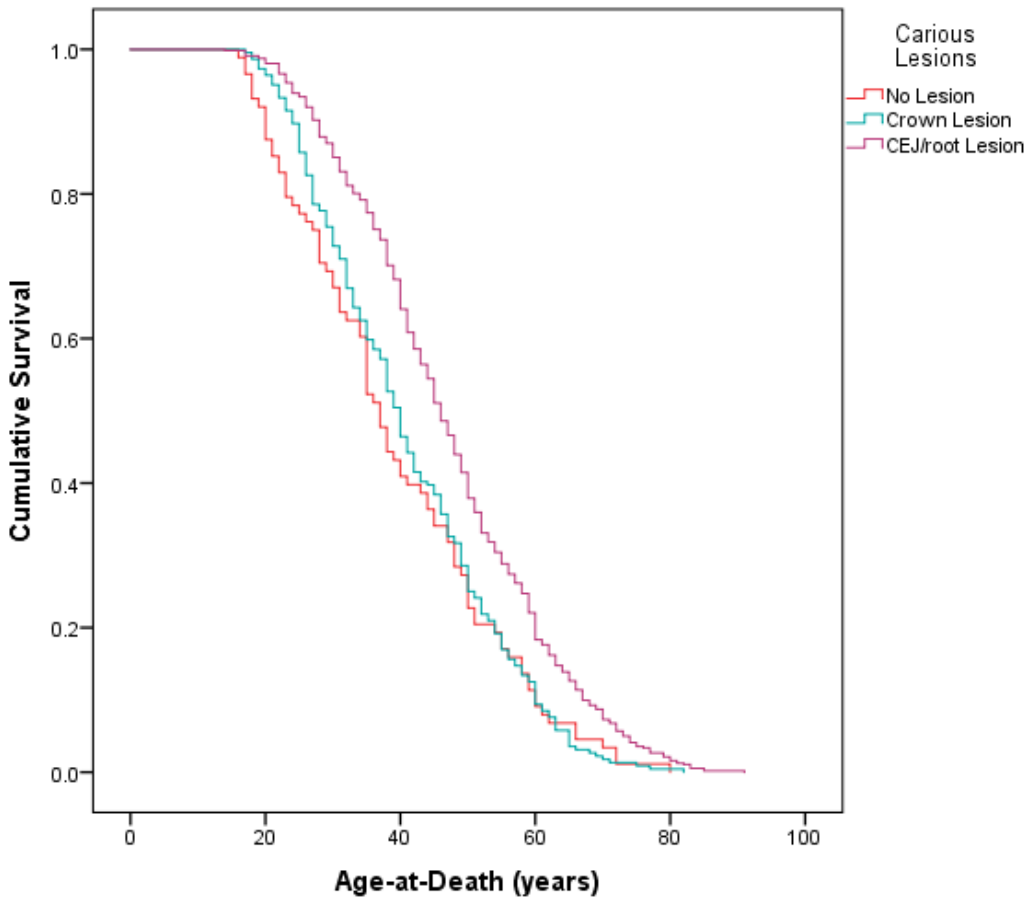

Figure 5: Survivorship based on lesion location.

Survivorship based on location of carious lesion expression differences between males and females was also examined. The results of the survivor analysis are reported in Table 27, frequencies of individuals are listed in Table 28, and survivor curves are represented in Figure 4. Females without carious lesions had higher survivorship than males without carious lesions ($x^2 = 3.773$; $P \leq 0.052$). Females with crown lesions had lower survivorship than females with CEJ/root lesions ($x^2 = 18.310$; $P \leq 0.0001$) and males with CEJ/root lesions ($x^2 = 10.961$; $P \leq 0.001$). Females with CEJ/root had

significantly higher survivorship than males without carious lesions ($x^2 = 24.517$; P ≤ 0.0001), males with only crown lesions ($x^2 = 19.591$; P ≤ 0.0001), and males with CEJ/root lesions ($x^2 = 6.532$; P ≤ 0.011). Males without lesions have significantly lower survivorship than males with CEJ/root lesions ($x^2 = 17.861$; P ≤ 0.0001). There is also a significantly higher survivorship among males with CEJ/root lesions than males with crown lesions ($x^2 = 9.355$; P ≤ 0.002).

These results indicate survivorship can be organized from lowest to highest as follows: males without lesions, females with crown lesions, males with crown lesions, females without lesions, males with CEJ/root lesions, and females with CEJ/root lesions.

Table 27: Kaplan-Meier survival analysis results for location of lesion expression based on sex.

Sex	Carious Lesion Expression	Mean survival time	95% CI (Lower limit-upper limit)
Female	None	43.5	37.9-49.1
	Crown	39.9	36.8-43.0
	CEJ/Root	48.3	46.0-50.6
Male	None	36.7	32.9-40.5
	Crown	41.6	39.4-43.9
	CEJ/Root	46.4	44.9-47.8
	Overall	44.7	43.7-45.7

Table 28: Frequencies male and female individuals with absent, crown, and CEJ/root lesions.

	MALES			FEMALES		
AGE	**ABSENT (%)**	**CROWN (%)**	**CEJ/ROOT (%)**	**ABSENT (%)**	**CROWN (%)**	**CEJ/ROOT (%)**
14-19	5 (0.25)	4 (0.20)	4 (0.20)	2 (0.10)	2 (0.10)	3 (0.15)
20-29	14 (0.10)	31 (0.23)	37 (0.27)	6 (0.04)	18 (0.13)	29 (0.21)
30-39	16 (0.09)	36 (0.19)	70 (0.38)	7 (0.04)	20 (0.11)	36 (0.19)
40-49	8 (0.04)	31 (0.15)	108 (0.51)	6 (0.03)	18 (0.08)	41 (0.19)
50-59	7 (0.04)	25 (0.16)	65 (0.41)	7 (0.04)	11 (0.07)	44 (0.28)
60+	5 (0.03)	21 (0.13)	72 (0.44)	5 (0.03)	7 (0.04)	53 (0.33)
TOTAL	55 (0.06)	148 (0.17)	356 (0.41)	33 (0.04)	76 (0.09)	206 (0.24)

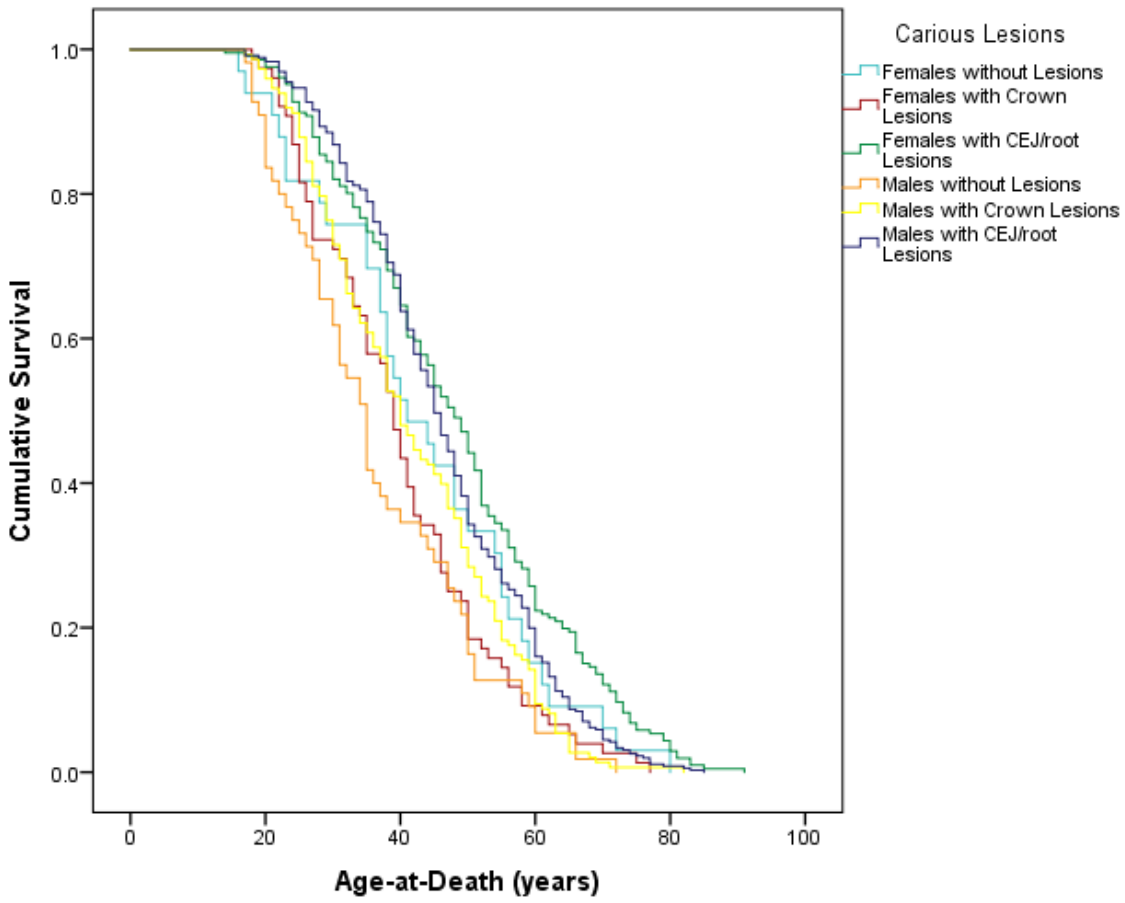

Figure 6: Survivorship based on carious lesion location based on sex.

Multivariate four-way ANOVA

Log- linear analysis was completed on individuals 19+ years. The results show there is an interaction between sex, periodontal disease, and carious lesions (Tables 29 and 30). As individual age, they are more likely to exhibit carious lesions ($x^2 = 11.558$; $P \leq 0.003$) and periodontal disease ($x^2 = 32.646$; $P \leq 0.0001$); furthermore, males are more likely to express periodontitis than females ($x^2 = 5.043$; $P \leq 0.025$). Logistic regression

demonstrated the directionality of the tests shows that males have greater periodontal disease frequency than females. Periodontal disease also appears to have a positive association with carious lesion type.

Table 29: K-Way and Higher-Order Effects

K	CHI-SQUARE	P VALUE
1	1343.251	0.0001
2	73.256	0.0001
3	15.489	0.078

Table 30: Relationship between periodontal disease, carious lesion expression, sex, and age.

INTERACTION	CHI-SQUARE	P VALUE
SEX X PERIODONTAL DISEASE	5.043	0.025
PERIODONTAL DISEASE X AGE	32.646	0.0001
CARIOUS LESIONS X AGE	11.558	0.003

A Wilks Lambda multivariate test demonstrated there was a significant difference in mean number of carious lesions dependent on periodontal disease, age, and sex ($F = 4.99$, $P \leq 0.0001$). This difference is significant for individuals displaying CEJ/root lesions ($F = 7.42$, $P \leq 0.0001$). Interaction plots demonstrates that this interaction is age specific for CEJ/root lesions (Figures 9 and 10). Figures 7 and 8 display plots for crown lesion association in males and females. Females have larger average number of teeth

affected by crown lesions when compared to males; however, there is not an association between crown lesions and periodontal disease in either males or females, as expected above.

Figures 9 and 10 show plots for CEJ/root lesion association in males and females. In both age groups, males appear to have greater average number of teeth with CEJ/root lesions. In reproductive aged males (19-49) (group 1), individuals with periodontal disease have larger average number of teeth with CEJ/root lesions. In post-reproductive age (50+) (group 2), males without periodontal disease have greater average number of teeth with CEJ/root lesions. Reproductive age females are similar to reproductive male as individuals with periodontal disease has greater average number of teeth with CEJ/root lesions. Post reproductive aged females, however, exhibit larger numbers of CEJ/root lesions in association to periodontal disease.

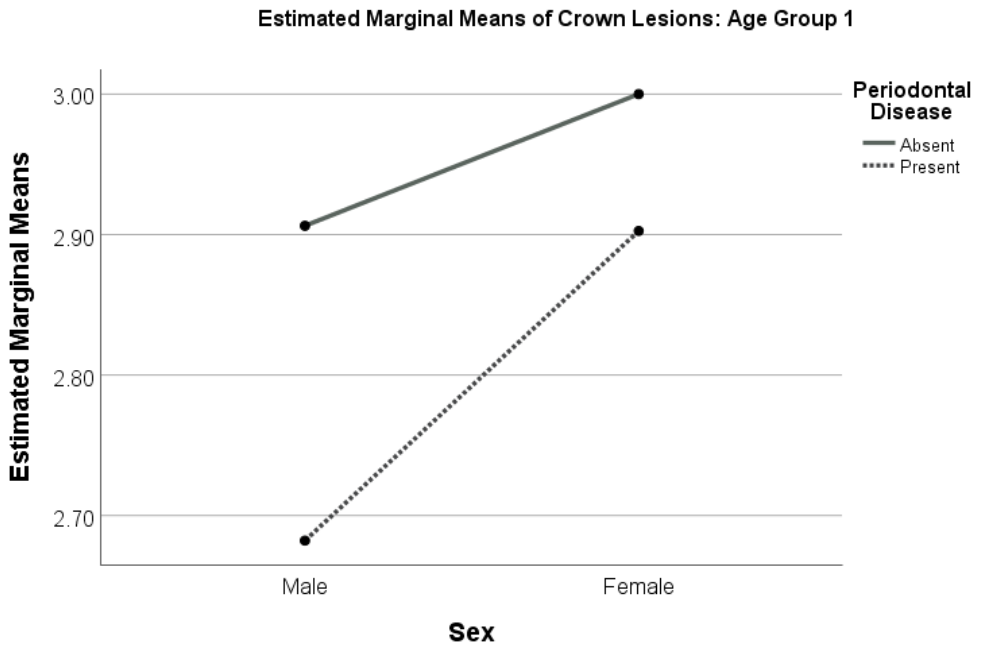

Figure 7: Average number of teeth with crown lesions between reproductive aged males and females.

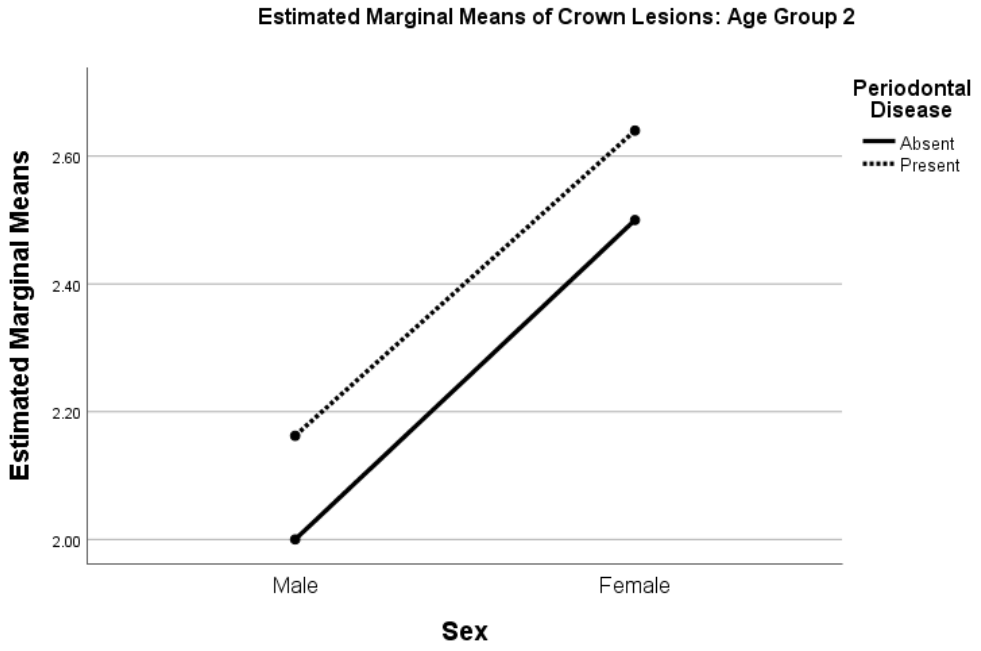

Figure 8: Average number of teeth with crown lesions between post-reproductive aged males and females.

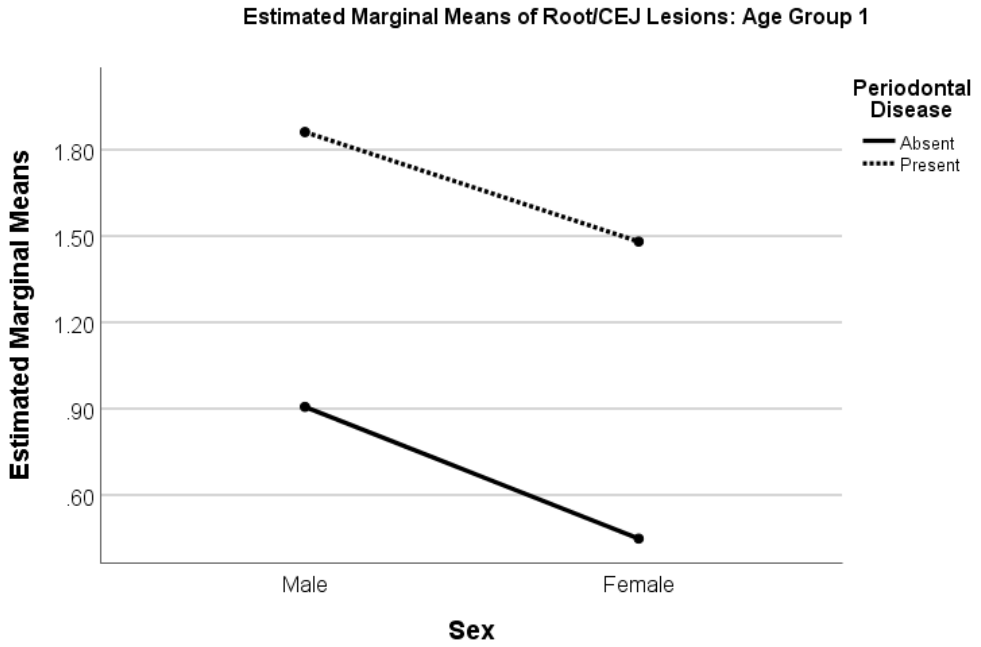

Figure 9: Average number of teeth with CEJ/root lesions between reproductive aged males and females.

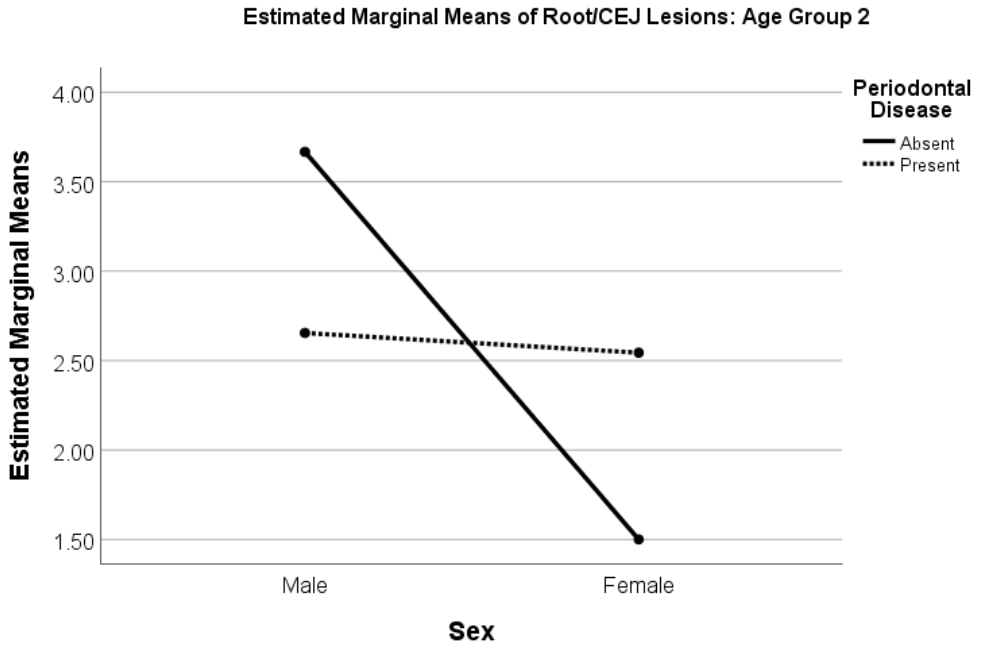

Figure 10: Average number of teeth with CEJ/root lesions between post-reproductive aged males and females.

CHAPTER 5: DISCUSSION

Relationship between Periodontal Disease and Periostosis

The results from this study indicate that there is a positive relationship between periodontal disease and age as well as antemortem tooth loss and age. This is consistent with previous findings, which indicate an increased alveolar bone resorption and tooth loss within individuals over 40 years, especially among females (Abdellatif and Burt, 1987; Hildebolt and Molnar, 1991; Strohm and Alt, 1998; Spahr et al., 2006; Meyer et al., 2008; Liang et al., 2010; DeWitte and Bekvalac, 2011). As individuals age, teeth are exposed to the oral environment for longer durations. Particles in food consumed adhere to the teeth, providing an ideal reservoir for bacteria if the biofilm is not removed. This can trigger an inflammatory response that results in alveolar bone loss, and degradation to the periodontal ligament and root cementum (Greene, 1963). As these fibers are broken down, periodontal disease and eventual tooth loss occur (Clark, 1990; Williams, 1990; Hildebolt and Molnar, 1991; LeResche and Dworkin, 2002). Inflammatory responses in the oral cavity can, furthermore, be influenced by life-history events, such as menopause. Post-menopausal women experience a reduction in sex hormones that regulate bone health. Therefore, resorption can occur, resulting in age-related increases of periodontal disease and antemortem tooth loss.

Periostosis also appears to be age-related within this sample. Since periosteal lesions manifests as a non-specific indicator of infection, it has been used to examine health and longevity within several populations (DeWitte, 2014a; DeWitte 2014b; Grauer, 1993). Individuals in this study were originally analyzed based on presence of periostosis. However, there were several individuals who only exhibited lesions unilaterally. These individuals may have had lesions due to injury rather than systemic illness. When unilateral periosteal lesions are removed from the analysis, there is still a significant association with age. Here, there was a larger number of older individuals with periosteal lesions when compared to younger individuals. This is because healed periosteal lesions were found within the older cohorts, potentially indicating the ability to survive physiological stressors throughout their lives. Other studies also demonstrated a positive association between age and periosteal lesions. In samples from medieval London cemeteries that dated to pre-black death (ca. A.D. 1000-1300) and post-black death (ca. A.D. 1350-1530) older individuals contained more periosteal lesions when compared to those in younger cohorts (DeWitte, 2014b). The lesions could have indicated that individuals with increased longevity were associated with substandard health over the lifespan, and were thus subjected to more lesions. Alternately, the periosteal lesions could be the accumulation physiological stressors that the individual was able to endure. A study of St. Helen-on-the-Walls cemetery from York, England (ca. A.D. 1100-1550) also postulated that age-related lesion manifestation could be the result of enduring physiological stressors throughout life (Grauer, 1993).

While the results indicate a positive association between periodontal disease and periosteal lesions, this correlation is not supported when factoring for age. Both periosteal lesions and periodontal disease were found to have a significant relationship. Thus, it can be concluded that the link between periodontal disease and periostosis is age-related. As an individual increases in age, the likelihood of developing periodontal disease, as well as periostosis increases but this is done independently of each other. This contradicts findings from a sample in London (A.D. 1350-1538) that found a significant association between periosteal lesions and periodontal disease, when age was factored (DeWitte and Bekvalac, 2011). Other studies examining the relationship between periodontal disease and systemic illnesses have also found varying results, which is potentially related to confounding factors.

For instance, research focusing on heart disease and periodontitis have postulated that oral bacteria are able to obtain systemic passageway into the body through compromised gingival tissue (Li et al., 2000; DeWitte and Bekvalac, 2010; Hajishengallis and Hajishengallis, 2013). Once in the circulatory system, bacteria are able to gain access to the heart. While most studies have found a significant association between cardiovascular disease and periodontitis, there are studies that have contradictory results. Studies focusing on cancer have also found adverse results, with some results indicating there was no, or low, association between periodontal disease and various forms of cancer (Meyer et al., 2008; Mai et al., 2016; Michaud et al., 2017). The association between birth outcomes and periodontal disease has many significant results, but there

are studies that do not demonstrate significant association between adverse birth outcomes and periodontal disease.

Adverse results can be due to factors that are not controlled for, such as the effects of smoking, alcohol, drugs, intake of medicine, family history, severity of periodontal disease, race, and socioeconomic class, or the sample might not have been representative of the population (Van Winkelhoff and Slots, 2000; Pihlstrom et al., 2005; Williams et al., 2008; Pizzo et al., 2011; Michaud et al., 2017). These factors can be difficult or impossible to control for in archaeological samples. Enamel hypoplasia and femoral length were used in a previous study as proxies of environmental factors have on overall health, such as unsanitary conditions and social status (DeWitte and Bekvalac, 2011). Enamel hypoplasia are pits and furrows in the enamel due to stress factors preventing ameloblasts from secreting new enamel. These defects are not remodeled throughout life and provide information on childhood stress events (King et al., 2005). The authors did not find a significant association between enamel hypoplasia and pathological conditions in the sample examined (DeWitte and Bekvalac, 2011).

Enamel hypoplasia and femoral length were not used in this study; however, results were examined based on sex and race to determine if there were any underlying factors in the results. Numerous studies have examined the difference in immune responses between males and females. The immune system is expensive to maintain and has potential trade-offs with reproductive efforts in females. Studies have demonstrated consequences in immune system response within pregnant or lactating females because energy is focused on caring for the young (Prentice and Prentice, 1988; Promislow and

Harvey, 1990; Lunn, 1994; Sheldon and Verhulst, 1996; Lycett et al., 2000; Charnov et al., 2001; McDade, 2003; McDade, 2005; French et al., 2009).

While race should not be compared based solely on a genetic difference, there might be biological consequences that arise due to sociocultural racism (Gravlee, 2009). Race has been embedded into the way in which people identify social, economic, and even political structures. These cause inequalities between groups that have the potential to cause embodied consequences related to health, psychosocial stress, and socioeconomic status. Differences in responses to systemic stress, therefore, would not be the result of genetic variance but rather how institutional racism may become embodied within individuals (Gravlee, 2009).

Several studies have found differences between races and health outcomes. Those focusing on periodontal disease have found differences in pervasiveness of severity of disease based on race and geographic location (Strohm and Alt, 1998; Irfran et al., 2001; Loos, 2005; Meyer et al., 2008; DeWitte and Bekvalac, 2011).This might be due to environmental factors, such as socioeconomic inequality, access to education, frequency of dental visits, psychological stress, BMI, diabetes, and nutritional intake (Strohm and Alt, 1998; Boyd and Madden, 2003; Pihlstrom et al., 2005; Demmer and Desvarieux, 2006; Eshed et al., 2006; Meyer et al., 2008; Johansson and Ostberg, 2015; Hujoel and Lingstrom, 2017; Sun et al., 2017; Siddiqui et al., 2017; Petersone-Gordina et al., 2018). These factors can have detrimental impacts on health and survivorship.

Additionally, studies have focused on other illnesses that have differing impacts on racial groups. There have been differences observed in cardiovascular disease, trauma,

diabetes, cancer, and pre-term births (Wong et al., 2002; Pihlstrom et al., 2005; Gravlee, 2009). Thus, race in this study is tried to identify any negative environmental factors that could have influenced biological responses to physiological stress. These factors are especially relevant to the individuals here, as the they lived during periods of extreme racial segregation within the United States. The results on this work, however, indicate that there were no underlying factors that were the result of sex or race. Antemortem tooth loss and periosteal lesions are still associated with increased age.

Here, no significant relationship between periosteal lesions and periodontal disease was observed when accounting for age. This contradict the findings conducted by DeWitte and Bekvalac (2011). There are several confounding factors in skeletal collections that could not be controlled for, which might have provided more information on the potential relationship found in the previous study (DeWitte and Bekvalac, 2011). Here, even when controlling for sex and race, the study did not find any significant association.

Carious Lesion Expression and Survivorship

The findings in the second portion of this study indicate a relationship between location of carious lesion expression and survivorship. In the sample from the Terry Collection, individuals with one or more lesion survived longer, on average, then individuals who did not exhibit any lesion formation. Individuals without lesions had a mean survival of 39.2 years, while those with lesions had an increased average survival of 45.4 years of age. These results differ from those that report increased mortality risk in

association with carious lesion presence (DeWitte and Bekvalac, 2010). It is, however, important to note that dental caries is a chronic infectious disease (Hillson, 2008). Lesions associated with chronic infectious conditions such as periostosis have differing rates of survivorship. For example, a study examining survivorship in pre-black death and post-black death populations, found an association between the manifestation of periostosis and mortality (DeWitte, 2014b). Individuals with periosteal lesions were found to have survived significantly longer than individuals without any lesion present. These results might be occurring because individuals possessing evidence of skeletal lesions were able to survive physiological stressors long enough for mechanisms in the skeleton to react (Wood et al., 1992). Individuals without lesions, thus, had higher frailty and succumbed to the stress before the body had time to enact a proper immune response. The results in this study indicate that individuals without lesions had higher frailty and were not able to survive stress events when compared to individuals with CEJ/root lesions. This does not mean that every individual without lesions is indicative of higher frailty but that as a group overall these individuals were more susceptible to stressors than individuals with lesions. Furthermore, dental caries is an age-progressive disease, the longer duration that an individual is exposed to microbiota within the oral cavity, the more susceptible they are to dental caries (Caselitx, 1998; Lanfranco and Eggers, 2010; Powell, 1998). Individuals able to survive longer would, therefore, be expected to experience more lesions than an individual of higher frailty.

When individuals are separated based on sex, there are distinctions in survivorship between males and females with active or healed lesions that might be

suggestive of life-history parameters. Males without lesions have the lowest rate of survivorship, while females with carious lesions at the CEJ/root have the highest rate of survivorship. Several studies have examined the relationship between female sex hormones and carious lesion formation. During pregnancy, the placenta drives an increase in estrogen and progesterone production. These hormones rise 100-fold from the beginning of pregnancy, which causes gingival inflammation and changes to immune responses. Vascular tissues become enlarged to allow immune cells to permeate into the oral cavity to fight gingivitis. T-helper cells also are affected by hormonal changes. These cells are a source of cytokines and decrease slightly during pregnancy (Laine, 2002). Sex hormones are also linked to oral chemistry, diet, and immune environments (Watson et al., 2010; Lukacs and Largaespada, 2006; Lukacs, 2011). For instance, females have been found to have slower saliva flow rate when compared to males, which increases food clearance time. This can lead to increased carious lesion rates. Lukacs and Largaespada (2006) posits this difference is due to sex hormones suppressing saliva flow. However, these changes to dental caries frequencies between males and females do not affect survival.

A study examining dental caries in a Maya population from Xcambó in the Yucatan Peninsula compared carious lesion frequency by sex in an Early Classic (A.D. 250-550) and Late Classic (A.D. 550-750) sample (Cucina et al., 2011). There were differences in lesion frequency in the Early Classic that might have been the result of food procurement. During the Late Classic, resources would have been equally available

between males and females; thus, carious lesions were more likely due to physiological factors rather than sex differences in dietary consumption.

Longitudinal studies do not, however, show significant differences in saliva flow during pregnancy and cannot be attributed to increased carious lesion frequency (Laine, 2002). Changes in pH can result in demineralization, when coupled with decreased remineralization – lower levels of calcium and phosphate— this can result in an increase of *mutans streptococci* later in pregnancy. These changes within the oral cavity are not primary reasons for higher frequencies in carious lesions among females because the development of dental caries takes years, while the duration of pregnancy is only nine months. A study of Late/Final Jomon hunter-gatherers examined the differences between carious lesion frequencies in males and females (Temple, 2011). Hunter-gatherers are often assumed to not have significant differences in carious lesions frequencies between sexes. Sexual division of labor, such as food preparation activities in some populations, can cause females to consume greater quantities of cariogenic foods. While reproductive factors could be influencing sex-specific differences in dental caries frequency, it was not the primary contributor. Instead, differences in food procurement was the cause of sex-specific differences in the Jomon sample. Whether individuals were affected by reproductive factors or food practices, females are usually at greater risks for carious lesion formation when compared to males. Since females typically have higher carious lesion frequency, and carious lesions are associated with higher survivorship, it is not unexpected to find females with lesions had lower frailty in this sample. This study does observe a difference in survivorship in females around age 30, during reproductive years.

This might correspond to the hormonal fluctuations mentioned above; thus, providing information on life-history events within females.

Survivorship was, moreover, examined based on carious lesion manifestation. Results from this work show individuals with lesions on the CEJ/root were able to survive significantly longer when compared to those with no lesion formation or lesions only on the crown. These individuals might have been able to survive stressors long enough for gum recession, due to periodontal disease, to occur, which exposes the CEJ and root to microbiota of the oral cavity. Once bacteria are able to adhere to the lower portions of the teeth, carious lesions can begin to form (Watson et al. 2010). Individuals in this study, without carious lesions, or lesions only on the crown, have an increased frailty and are not able to survive long enough for these changes in the oral cavity to occur. Periodontal disease, which exposes the tooth root, appears to be associated with hormonal changes in females; thus, location of carious lesions might provide information on sex-specific morality and life-history events. This might be affected due to the age at which individuals get periodontal disease, which occurs, typically, later in life.

When the results from this study were differentiated based on sex *and* lesion manifestation, males without lesions had the greatest frailty while females with CEJ/root lesions had the highest survival rate. Based on mean survival time, males without lesions have an average age of survival around 36.7 years and females with CEJ/root lesions average survival was 48.3 years of age. Furthermore, survival time was affected by crown lesions when compared to CEJ/root lesions. The survival curves in this study indicate there is a potential age-related pattern in the expression of carious lesion location. When

examining the survival curves between carious lesion location based on sex, there is a difference in post-menopausal women. By age 60, more females exhibited carious lesions located at the CEJ/ root are surviving that than any other groups of females or males. This might be indicative of hormonal changes to the periodontium and alveolar bone that expose further portions of the tooth. Females who are able to initiate a proper immune response, might be able to survive longer with these lesions. These results were confirmed through the Wilks Lambda test and interaction plots.

Reproductive factors here have the potential to contribute to alveolar bone loss in women, further magnifying the likelihood of cariogenesis. Here, females have clear associations between CEJ/root lesions, age, and periodontal disease. These results are consistent with interpretations by Watson et al. (2010) work with an Early Agriculturalist group (1600 B.C.- A.D. 200) from northwest Mexico and found that females had more carious lesions along the CEJ line when compared to males. In examining males in this study, however, a dietary model has a strong explanatory power in instances of CEJ/root lesion presence within males that are not affiliated with periodontal disease. This does not appear to be related to changes in sex hormone levels influencing periodontal disease.

Sex hormone changes during menopause can result in changes in alveolar bone mineral density, which leads to reabsorption of the bone and tooth exposure. Once exposed, the tooth is vulnerable to bacteria in the oral cavity. Other studies have also found sex-hormonal changes in post-menopausal females to be related to alveolar bone reabsorption and antemortem tooth loss. Post-menopausal females are not able to benefit from hormones that normally help retain bone health. Several studies have found that

when post-menopausal women receive hormonal treatments, there are not significant differences observed in alveolar bone mineral density (DeWitte, 2012; Hildebolt et al., 2002; Hildebolt et al., 2004). These studies indicate there is a difference in periodontal disease that is age-specific. Carious lesions located at the CEJ/root appear to be the result of periodontal disease; therefore, carious lesions might also give indications of life-history events such as menopause.

The results of this study suggest a relationship between carious lesion manifestation and survivorship. This is important because previous studies have not incorporated how the distinction in carious lesion location has on differential survival between individuals. Further studies based on various geographical and temporal populations could provide additional information on how lesion location affects survivorship and life-history events. Studies focusing on carious lesions location in relationship to periodontal disease in post-menopausal women might provide additional evidence of carious lesion expression being influenced by life-history parameters.

CHAPTER 6: CONCLUSIONS

The results from the first part of this study aimed to examine systemic illness through the relationship of periodontal disease and periosteal lesions. While numerous studies have demonstrated a potential spillover effect in cytokine production, leading to the dissemination of illness, this study was unable to find an association between poor oral health and periostosis. Here, an association was found between periodontal disease and periostosis; however, results indicate this relationship is biased by age. As individuals age, the frequency of periodontal disease and periosteal lesions increases. In the case of periostosis, age increases were specific to individuals with healed lesions, which the preponderance of cases where individuals displayed periodontal disease also had healed periosteal lesions. These results were, therefore, different than those found in previous studies and did not indicate a hyperinflammatory response. Periosteal lesions manifest as a result of several diseases. Since differential diagnosis was not completed on each individual there is a possibility that a specific disease is associated with periodontal disease rather than general observations of periostosis.

The second part of this study aimed to identify survivorship associated with carious lesion manifestation. Results of this study demonstrated that individuals with carious lesions had greater survival than individuals without carious lesions present. This result differs from previous findings. The pattern of survival observed here is influenced

by carious lesion manifestation and life-history parameters. Females with carious lesion formation had the highest survivorship, while males without lesions had the lowest survivorship. When carious lesions were differentiated by lesion type, individuals with CEJ/root lesions had the highest survivorship. This result was found to be sex specific, with females exhibiting CEJ/root lesions having greater survivorship when compared to all other groups.

Here, survivorship was observed to be driven by two issues: lesion manifestation and sex. Previous studies suggest that CEJ/root lesions are associated with age-specific periodontal disease in females. Results from a four-way MANOVA found a significant interaction between CEJ/root lesions and age, sex, and periodontal presence. In males, CEJ/root lesions were independent of periodontal disease. In females, however, CEJ/root lesions were dependent on this periodontitis. Reproductive and post-reproductive aged women experience alveolar bone loss due to changes in sex hormones. During pregnancy hormonal increases result in inflamed gingival tissue and changes in immune response, whereas post-menopausal women experience decreased hormones that decrease bone mineral density, including within the alveolar bone. All of this supports an argument that the relationship between carious lesions and survival is influenced by lesion manifestation and sex-related life history factors.

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BIOGRAPHY

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