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The Bioarchaeology of Health Crisis: Infectious Disease in the Past

Clark Spencer Larsen

Department of Anthropology, Ohio State University, Columbus, Ohio 43210-1106, USA; email: Larsen.53@osu.edu

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Abstract

Beginning some 10,000 years ago, humans began a dramatic alteration in living conditions relating especially to the shift in lifeway from foraging to farming. In addition to the initiation of and increasing focus on the production and consumption of domesticated plant carbohydrates, this revolutionary transformation in diet occasioned a decline in mobility and an increased size and agglomeration of populations in semipermanent or permanent settlements. These changes in life conditions presented an opportunity for increased transmission of pathogenic microbes from host to host, such as those that cause major health threats affecting most of the 7.5 billion members of our species today. This article discusses the bioarchaeology of infectious disease, focusing on tuberculosis, treponematosis, dental caries, and periodontitis, all of which continue to contribute to high levels of morbidity and mortality among the world's populations today.

INTRODUCTION

Infections caused by exposure to a remarkable diversity of pathogenic microorganisms—bacteria, parasites, and viruses—have long challenged human health. The ancestors of the modern pathogens associated with health crises have likely been present in settings occupied by hominins since the earliest members were moving about the African landscape beginning 6–7 million years ago. However, given the small numbers of individuals comprising social groups from then until at least the later Pleistocene and early Holocene, it is unlikely that the so-called crowd diseases—such as measles, influenza, or smallpox—could have been transmitted from person to person in a continuous fashion (Harper & Armelagos 2010). This is not to say that infectious disease did not contribute to hominin morbidity and mortality prior to the Holocene. Rather, other factors likely figured more prominently in life and death circumstances.

Fast-forward to the Holocene and the last 10,000 years or so, when the shift from foraging to farming first commenced in the Middle East, ultimately becoming a global cascade of subsistence changes associated with increases in population size and density, permanent settlement and reduction in sanitation and hygiene, and generally declining nutritional quality due to dietary focus on domesticated plant carbohydrates (e.g., maize in the Western Hemisphere, wheat in Europe and Asia, and rice in Asia). In combination, these circumstances facilitated pathogen transmission and the spread of infectious disease in ways largely not experienced by pre-Holocene humans (Larsen 1995, 2006). The growing number and size of sedentary farming communities packed into increasingly smaller territories created a critical mass for the evolution of pathogenic microbial organisms, their continuous transmission, and their adaptive success. These developments for pathogens laid the groundwork for increased morbidity and mortality for earlier and present-day human hosts (Cohen & Armelagos 1984, Cohen & Crane-Kramer 2007, Hutchinson 2016, Steckel & Rose 2002). It is at this point in human history where mostly individual health crises became the basis for community health crises and, later, global health crises in the modern era.

Bioarchaeology, the contextualized study of human remains from archaeological settings, is a relatively new field that has been actively engaged in developing an informed understanding of the role of infection and infectious disease in influencing health outcomes and living conditions over the last 10,000 years of human evolution. This record facilitates drawing inferences about individual, community, and regional health profiles having implications for today's quality of life around the globe. Today is an especially dynamic period in the bioarchaeological study of ancient infectious diseases, largely owing to the remarkable growth in interest in the field globally and the increased engagement between those who study skeletons (biological anthropologists) and those who study archaeological contexts (archaeologists). In addition, the technological, methodological, and theoretical breakthroughs are providing new answers to old questions (Larsen 2018). High on the list of these breakthroughs are the technological advances in sequencing microbial genomes and the molecular genetic record of the pathogenic microbes causing the infectious diseases (Feldman et al. 2016, Harkins & Stone 2015, Mühlemann et al. 2018, Stone et al. 2009, Vågene et al. 2018, Wagner et al. 2014, Warinner et al. 2014), microscopic analyses of skeletal tissues in disease diagnosis (Schultz et al. 2001, von Hunnius et al. 2006), and the use of isotopic signatures of carbon, nitrogen, and other elements to reconstruct diet and nutritional quality and migration as agents for the success and spread of pathogens (Katzenberg 2008, Schoeninger 2010). The growing understanding of health crises in the past is also benefitting from the broad perspective offered by the discipline of anthropology, especially regarding social, behavioral, economic, and political contexts for understanding health and health outcomes in all places and all times. Moreover, identification of the complex linkages between society, culture, and health in the past provides awareness of the complex factors that lead to health crises and other challenges facing us in the

present-day world (DeWitte 2016, Roberts 2016). More than ever, bioarchaeological analysis of past populations has important meaning for understanding health crises today, especially in light of the re-emergence of infectious diseases once thought to be on the decline (e.g., tuberculosis), those diseases still of considerable concern (e.g., influenza), and the emergence of health challenges from a range of new pathogens (e.g., Zika, H7N9, bird flu, Ebola, severe acute respiratory syndrome, and many others).

Despite the contributions that bioarchaeologists have made in the identification of pathogenic microbes and disease diagnosis generally, researchers do encounter limitations to reconstructing health and health crises in past populations. On the one hand, infection of the human host by a pathogen does not necessarily result in disease. That is, disease occurrence is based on a number of factors, especially the response of the host (Brown et al. 2011). Moreover, bioarchaeologists can never fully address health in the past, at least as the concept of health is understood in living societies. For example, self-perception of well-being is an important element of health but is unknowable for the people represented by their ancient skeletons. On the other hand, the suffering caused by physiological responses to infection—such as fever, nausea, bleeding, weakness, pain, and psychological stress—have varied, but largely universal social and behavioral outcomes, including a reduction in work capacity and increased pain and suffering. Thus, it is true that skeletons do not speak to us about the suffering endured when the individuals they represent were alive, but the universal responses to severe health crises that ancient skeletons display make it a certainty that circumstances of poor health in past populations elicited behavioral outcomes similar to what we see around the world today.

Extensive bioarchaeological evidence has accrued regarding infectious diseases (Grauer 2012, Larsen 2015, Ortner 2003, Powell & Cook 2005, Roberts & Buikstra 2003). This evidence is informed by the application of differential diagnosis for determining the probability of a cause of a specific pathological condition from a list of potential causes, all grounded in skeletal tissue and how it responds to pathogens (Ortner 2012). Social and behavioral contexts are central to the understanding of health outcomes as reconstructed from disease prevalence and patterns in human remains. Human remains in these contexts are growing the record of health profiles and quality-of-life conditions in the past, forming the backdrop to health profiles and life conditions today.

INFECTIOUS DISEASE IN PAST POPULATIONS

The study of infectious disease and past population health as represented by archaeologically derived human remains has its origins in investigations pursued in the nineteenth and early twentieth centuries, especially by medical practitioners interested in individual-specific disease diagnosis (various in Buikstra & Roberts 2012). Much of the early interest in skeletal pathology and infectious disease stems from a time when widespread attention was given to incurable or otherwise devastating infectious diseases, especially during the pre-antibiotic era of medicine. Today's population-oriented, epidemiological approach is informed by disease prevalence—the proportion of individuals affected at any given place and time. Prevalence is the baseline for inferring infectious disease and health outcomes, such as with regard to variation in sex, age, socioeconomic status, and spatial and temporal variation—all central elements of bioarchaeological inquiry (Agarwal & Glencross 2011, Armelagos 2003, Buikstra & Beck 2006, Larsen 2015, Milner & Boldsen 2017).

Population-based bioarchaeology of disease was first undertaken in a comprehensive manner by Earnest Albert Hooton (1930) in his landmark study of temporal, spatial, and cultural contexts of skeletal remains from Pecos Pueblo, New Mexico. His diagnoses and accounts of infectious disease were not especially sophisticated, even for the time. Hooton's population-based orientation

in comparative perspective was continued by his graduate students and former graduate students in a range of projects in the mid-twentieth century (see Larsen 2012). Their investigations and others set into motion decades of study of infectious disease as a basis for interpreting health and living conditions. Toward that effort, bioarchaeologists globally have developed a compelling body of research presenting regional and temporal patterns in the prevalence of infectious diseases in a wide range of settings (Cohen & Armelagos 1984, Roberts & Cox 2003, Steckel & Rose 2002).

DETECTING INFECTION AND INTERPRETING INFECTIOUS DISEASE PROFILES

A human skeleton recovered from an archaeological context displaying various pathological conditions may simply reflect that the person the skeleton represents survived the infection for a period of time long enough for visible pathological responses to develop. By comparison, a skeleton displaying no lesions may mean that the person succumbed to the illness before sufficient time had passed for lesions to develop. Thus, in determining disease prevalence from a sample of skeletons from an archaeological site, the observer collecting data and assessing levels of health would include only those persons with the lesions and not those without the lesions (Wood et al. 1992). However, solutions to issues surrounding biases have developed in recent years, such as thorough critical consideration of archaeological and historical contexts and application of epidemiological principles for addressing biases in the skeletal record (Milner & Boldsen 2017).

Identification of pathogen-specific ancient DNA (aDNA) also has considerable potential for the identification of specific infectious diseases. However, the presence of diagnostic aDNA by itself cannot determine whether a person had a specific disease. Its presence may simply reflect the person's exposure to the pathogen (Klaus et al. 2010). That said, new biomolecular approaches to disease diagnosis are now beginning to expand the evidence of disease-causing microbes, in some circumstances supporting the diagnoses of pathological conditions in skeletal remains (Bos et al. 2014, although see Wilbur & Stone 2012).

Virtually all the skeletal documentation of infectious diseases in archaeological settings pertains only to those diseases that had significant duration during a person's lifetime. Some infectious diseases may take months or years for the skeletal tissues to display diagnostic characteristics (e.g., leprosy, tuberculosis, syphilis), whereas numerous other infectious diseases leave no visible skeletal signature, especially acute infectious diseases that cause rapid and devastating mortality (e.g., Black Death) (DeWitte 2016) and chronic infectious diseases that have profound health implications (e.g., hepatitis) (Mühlemann et al. 2018). Nevertheless, the bioarchaeological record of chronic infectious diseases with diagnostic skeletal signatures is increasingly abundant, providing a crucial perspective on the conditions of life and the challenges caused by the spread of pathogens among members of past populations.

SIGNATURES OF SPECIFIC INFECTIOUS DISEASE

For the remainder of this article, I focus on four infectious diseases, all caused by pathogenic bacteria: treponematosis (treponemal disease), tuberculosis, dental caries, and periodontitis (periodontal disease). These infectious diseases were chosen for this discussion owing to the comprehensive understanding of their etiology and the extensive record in the published literature of both diagnosis and hard-tissue presence in past and contemporary populations. These diseases represent those caused by a single pathogen (treponematosis, tuberculosis) and those caused by multiple pathogens (dental caries, periodontitis). As with many infectious diseases, these four examples present complex signatures representing long-term processes involving evolution of the

pathogen, its adaptation to humans, and its transmission. All four diseases have distinctive hard-tissue indicators conducive to differential diagnosis and characterization of health conditions over the last 10,000 years of human evolution. There is a small but growing literature on the bioarchaeology of other infectious diseases. For example, malaria is well documented in both historical and modern contexts. However, in my view, the presence of cranial lesions sometimes associated with the disease does not have the same paleopathological diagnostic precision or bioarchaeological breadth as the four diseases discussed here.

Collectively, these diseases are responsible for a considerable volume of morbidity, suffering, and mortality in the past, present, and foreseeable future. In this regard, the bioarchaeological, historical, and modern records reveal the high prevalence of treponematosis, tuberculosis, dental caries, and periodontitis in many contexts worldwide, which are often associated with sedentary groups living in challenging environments, including poor sanitation, undernutrition, and limited health care. Prevalence rates and morbidity for the infectious diseases discussed here are also remarkably high in some archaeological contexts, especially in settings where diets included significant presence of carbohydrates (see Larsen 2015 and below). In this regard, specific infectious disease can only rarely be linked with mortality. However, mortality in the present and last few centuries makes the clear association between a range of infectious diseases and cause of death, numbering in the millions globally on an annual basis (e.g., Morens et al. 2004), including the diseases discussed in this article (e.g., Abdellatif & Burt 1987, de Melo et al. 2010, DeWitte 2016). For example, some form of periodontal disease affected 90% of the world population in the first decade of the twenty-first century (Pihlstrom et al. 2005). The prevalences of dental caries, endemic treponematosis, and tuberculosis are also extraordinarily high in modern history (see de Melo et al. 2010, Frencken et al. 2017, Roberts 2015), affecting all human populations around the globe to one degree or another, but at especially elevated levels in challenged economic settings and those societies having limited health care and inadequate nutrition.

Treponematosis

Treponematosis, or treponemal disease, has been a focal point of the study of infectious disease and morbidity in past populations since at least the mid-nineteenth century (Jones 1876). Curiosity about the disease has served as a major driver for the development of method and theory in bioarchaeology, with considerable attention paid to the origin of venereal syphilis, caused by the bacterium *Treponema pallidum pallidum*. The other three treponemal diseases and their associated pathogens are endemic (nonvenereal) syphilis (*T. pallidum endemicum*), pinta (*T. carateum*), and yaws (*T. pallidum pertenue*) (Cook & Powell 2012, Hackett 1976, Mandell et al. 1990, Ortner 2003). Although painful and disfiguring, pinta is restricted to infectious processes associated with the skin only. The more virulent treponematoses—yaws, endemic syphilis, and venereal syphilis—produce an infectious response that commences as a skin infection and subsequently spreads to other soft tissues and eventually to the skeleton. The skeletal lesions involve proliferative and destructive processes, including but not limited to gummatous bone remodeling involving most commonly the flat bones of the cranium and periosteal inflammatory responses on tibiae diaphyses. The skeletal manifestations of advanced stages of venereal and nonvenereal syphilis are similar, so much so that the first studies of archaeological human remains displaying treponemal-like lesions in prehistoric Native American skeletons concluded that these individuals suffered from venereal syphilis (see Larsen 2012).

Treponemal lesions are documented in archaeological skeletons around the world (Buckley & Oxenham 2016, Dutour et al. 1994, Harper et al. 2011, Larsen 2015, Powell & Cook 2005). There is an ongoing and often heated debate in the bioarchaeological community regarding the

origin of venereal syphilis. Three key competing hypotheses—Columbian, Pre-Columbian, and Unitarian—have emerged in the discussion. The Columbian hypothesis posits that either venereal syphilis or a progenitor nonvenereal syphilis began in the New World and was transmitted by Columbus's crew to the Old World on their return to Europe in the 1490s. The historical accounts describing a venereal syphilis crisis involving much of Western Europe beginning within a few years after Columbus's return supports this point of view (Harper et al. 2011, Hutchinson 2016). Powell & Cook (2005) argue, however, that an abundant skeletal record of treponemal disease in North America reveals no evidence for anything but the presence of endemic (nonvenereal) syphilis. If their assessment of the record is correct, then it seems unlikely that a venereal treponemal pathogen was transported from the New World to the Old World in the mid-1490s upon Columbus's return to Europe.

The skeletal pathology record is consistent with the notion that if the pathogen for nonvenereal syphilis was transported to the Old World from the New World, then it may have been a progenitor treponemal species that subsequently evolved into a fully venereal form once introduced to the Old World. However, only limited support for the Columbian hypothesis is indicated by the genomic similarity of yaws-causing strains from South America and strains that cause venereal syphilis (Harper et al. 2008; but see Mulligan et al. 2008). The phylogeny of modern strains of endemic and venereal syphilis is especially interesting owing to the strongly overlapping characteristics of skeletal pathology associated with both diseases. Early efforts have suggested the presence of pathogen-specific aDNA in archaeological human remains (Kolman et al. 1999). However, at least with today's technology, the biomolecular record representing treponemal disease is silent owing to the fragility of the spirochete structure of the bacterium and the near impossibility of extracting and identifying diagnostic DNA from ancient tissue samples (Bouwman & Brown 2005, Wilbur & Stone 2012).

According to the Pre-Columbian hypothesis, treponemal disease—both venereal and endemic—was already present in Europe and elsewhere in the Old World well prior to Columbus's explorations in the New World and his subsequent return to Europe (Mays et al. 2003, Roberts & Manchester 2005). Hackett (1976) suggested that the disease was simply not recognized owing to misdiagnosis by fifteenth-century physicians.

The Unitarian hypothesis argues that all treponemal diseases are closely related syndromes caused by a single, highly flexible pathogen capable of having different phenotypic expressions in human hosts (Hudson 1965). In this view, venereal syphilis arose as an evolutionary response to the combination of changing hygienic circumstances, which prevented general skin-to-skin contact, and changing social values following colonization. This hypothesis is highly unlikely, however, in large part because of the genetic differences between the pathogens that cause endemic syphilis, venereal syphilis, and yaws (Harper et al. 2011).

The burgeoning bioarchaeology of numerous newly excavated skeletal series around the globe and the restudy of existing collections in the last several decades provide a fresh look at the circumstances surrounding the origins and spread of venereal syphilis. The paleopathological evidence of endemic treponemal disease is represented by hundreds of individual cases in the prehistoric Western Hemisphere (Harper & Armelagos 2010, Powell & Cook 2005), ranging from far northern latitudes to far southern latitudes, but with an especially high prevalence in temperate, subtropical, and tropical regions in Eastern North America. By comparison, treponemal disease is minimally represented in Mesoamerica and South America (Klaus & Ortner 2014). This wide range of geographic distribution of treponemal disease suggests that there is no specific climate-based association.

In sharp contrast with the proliferation of known cases of treponemal disease in various contexts in the Western Hemisphere, Europe in particular and the Old World in general present a relatively

sparse picture of treponemal disease, especially for the pre-1493 period (Harper et al. 2011). From their review of 54 published reports, Harper and collaborators (2011) found that none of the samples studied from the Old World provided conclusive evidence for treponemal disease in skeletons having a pre-Columbian date. Since publication of their review, however, potential cases of treponemal disease in well-dated archaeological contexts have emerged in Europe, especially in England (Cole & Waldron 2011, Walker et al. 2015). Other cases from elsewhere in the Old World suggest the presence of treponemal disease (e.g., Hernandez & Hudson 2015).

Regardless of how the evidence of venereal treponemal disease origins is interpreted, the point remains that some form or forms of treponemal disease were widespread in prehistory. In Eastern North America, it is the most prevalent specific pathological condition, largely from agricultural communities but extending to earlier prehistory. Whether venereal or endemic, the condition was the basis for substantial morbidity, such as in the remarkable record of North America (various in Powell & Cook 2005) and within specific regions (e.g., Betsinger et al. 2017).

TB or Not TB?: Tuberculosis Is No Longer the Question

As with treponemal disease, tuberculosis is a chronic infectious disease, causing considerable morbidity and mortality in human populations past and present (and see above). The disease in humans is associated with mostly, but not exclusively, sedentary communities featuring agricultural-based subsistence economies (Roberts & Buikstra 2003). Moreover, like treponematosis, there is no clear association between tuberculosis and climate (Roberts & Buikstra 2003). However, there is a link between season of the year and the disease, a finding consistent with respiratory infections. In this regard, confinement to closed quarters, especially with other people, is conducive to the spread of respiratory and other infectious diseases.

Tuberculosis is normally contracted via inhalation of airborne bacteria transported in droplets from an infected individual to a noninfected individual. Once inhaled, the pathogenic bacteria spread from the lungs throughout the body of the host, sometimes including their skeleton. The skeletal changes consistent with clinical manifestation of the disease occur well after—months to years—the original infection. The pattern of tuberculosis infection pertains to individuals showing destruction of marrow-rich spongy bone in bodies of vertebrae in the spine, causing collapse of the spinal column (Pott's disease) (Roberts 2012). Other, mostly nonspecific lesions associated with tuberculosis include apposition of new periosteal bone on the internal rib surfaces, endocranial surfaces of the flat bones of the cranium, and other bone surfaces (Roberts 2012).

The disease today is caused largely by two primary species of genus *Mycobacterium*: *M. tuberculosis* and, less often, *M. bovis*. Other species have been sporadically identified in association with humans (*M. canetti*, *M. africanum*) and other animals, both wild (*M. pinnipedii* in seals and sea lions) and domestic (e.g., *M. caprae* in goats, *M. bovis* in cattle) (Brosch et al. 2002, Roberts 2012). It has long been assumed that human tuberculosis emerged when the bacterial pathogen *Mycobacterium tuberculosis* evolved from a bovine taxon, *M. bovis*, a speciation event that took place in Europe and western Asia where populations first lived in close proximity with domesticated cattle in the Neolithic. However, molecular genetic analysis of tuberculosis strains indicates that *M. tuberculosis* is basal to *M. bovis* (Brosch et al. 2002). The analysis also shows that recent historical strains of *M. tuberculosis* are similar in Europe and the Americas, suggesting that tuberculosis in the modern era was introduced to the Western Hemisphere following sixteenth-century circumglobal exploration, replacing the other pathogenic, precontact strains in the New World. Analysis of the DNA strains of *Mycobacterium tuberculosis* in precontact Peruvian populations documents strong similarity with DNA strains from pinnipeds (seals/sea lions), indicating a role for sea mammals

in the transmission of the disease to native New World humans deep into prehistory (Bos et al. 2014).

It was long debated whether tuberculosis was present in native populations in the Americas, with earlier authorities arguing that the existence of the disease prior to European contact is unlikely (Cockburn 1963, Hrdlička 1909). However, Allison and collaborators' (1973) identification of acid-fast bacilli in tissues recovered from a Peruvian mummy dating to ca. AD 700 was the first to document the presence of the disease centuries before European contact. Along with the expanding record of molecular genetics of mycobacterial infection, observations of pathological lesions consistent with Pott's disease and other hard tissue pathology confirm that the Western Hemisphere included tuberculosis in its prehistoric infectious disease repertoire, potentially contributing to endemic disease and resulting in increased morbidity and mortality at crisis levels.

The extensive body of research showing skeletal lesions consistent with tuberculosis, especially beginning in the first millennium AD, documents significant presence of the disease in a wide range of settings globally (Pálfi et al. 1999, Roberts 2012, Roberts & Buikstra 2003). These findings generally match the growing aDNA record (Wilbur & Stone 2012), especially in precontact-era settings from mummies and skeletons in Chile and Peru (Bos et al. 2014, Klaus et al. 2010, Raff et al. 2006, Salo et al. 1994). Outside of the Americas, tuberculosis-specific aDNA is present in various bioarchaeological contexts (Roberts 2012). Like the Western Hemisphere, settings affected in Eurasia are largely later Holocene sedentary, agricultural communities. The presence of tuberculosis aDNA in the Neolithic speaks to the long history of the disease, extending to at least 5000–9000 YBP (Hershkovitz et al. 2008, Nicklisch et al. 2012), and is consistent with the earliest dated skeletal record, at least as it is represented in advanced stages of the disease (Canci et al. 1996).

The global distribution of aDNA is consistent with the presence of destructive vertebral and proliferative rib lesions in the late Holocene, especially in later prehistoric complex societies in the Peruvian Andes of South America (Allison 1984, Allison et al. 1981, Buikstra & Williams 1991, Klaus et al. 2010, Wilbur et al. 2008), beginning with the earliest examples dating to ca. 2000 YBP (Allison et al. 1981).

The most abundant presence and elevated prevalence of tuberculosis in bioarchaeological contexts has been reported for much of the northern Western Hemisphere north of Mexico, especially in North America east of the Mississippi River (e.g., Buikstra 1977, Cook 1984, Danforth et al. 2007, Eisenberg 1991, Katzenberg 1977, Lambert 2000, Milner & Smith 1990, Powell 1992), in the American Southwest (Bruwelheide et al. 2010, Hooton 1930, Stodder 1994, Stodder & Martin 1992), in the Great Plains (Williams 1994), on the Northwest coast (Cybulski 1990, Williams & Snortland-Coles 1986), and other settings (see Larsen 2015).

The Old World is represented by a considerable number of cases of tuberculosis but especially those cases concentrated in Europe (summarized in Roberts 2015 and see Roberts & Buikstra 2003). There is also representation in the Middle East (Buikstra et al. 1993, Hershkovitz et al. 2008, Ortner & Frohlich 2008, Zias 1991), East Asia (Suzuki et al. 2008, Suzuki & Inoue 2007, Tayles & Buckley 2004), the Pacific (Pietrusewsky & Douglas 1994), and northwest Africa (Buikstra et al. 1993, Morse et al. 1964, Strouhal 1991). This evidence reveals a global development of tuberculosis that fits the pattern of mostly later Holocene occurrence, largely associated with farming communities where living conditions were compromised (Larsen 2015).

Oral Infectious Disease: Dental Caries and Periodontal Disease

The mouth is a highly dynamic reservoir of pathogenic bacteria, many of which have an important role in infectious diseases in the oral cavity and systemwide. In particular, dental caries is an

infectious disease process characterized by focal demineralization of the crowns and roots of teeth by organic acids produced by bacterial fermentation of dietary carbohydrates (sugars and starches). The bacteria linked to dental caries include a diverse array of oral pathogens but have been especially linked to *Streptococcus mutans* and *Lactobacillus acidophilus* (Aas et al. 2008, Burne 1998). Carious lesions are the pathological condition caused by the infection and commence with small, barely discernible demineralization on the tooth surface that subsequently develops into small pits. These pits expand in size and may extend into the tooth's pulp chamber as the infectious process continues. Unlike treponemal disease or tuberculosis, where identification and origin are hotly debated by bioarchaeologists, dental caries is well understood, at least in terms of cause, effects, and broad regional and temporal patterns.

Dental caries requires both essential and modifying factors. The essential factors are (*a*) teeth having surfaces exposed to the oral environment; (*b*) aggregation of indigenous oral bacteria (e.g., *S. mutans*), salivary glycoproteins, and plaque; and (*c*) diet (Bowen 1994, Burne 1998, Rowe 1982, Sheiham 2001). Modifying factors include occlusal-surface complexity (molars are more complex than other teeth), degree of tooth wear, presence of enamel defects, hormonal effects, food texture, oral pH, salivary flow and composition, and (in recent history) fluoride introduced into drinking water (Burt & Pai 2001, Hara & Zero 2010, Rowe 1982, Woodward & Walker 1994). Food characteristics, including its composition, consistency, and manner of preparation, are leading influences in the development of dental caries. In this regard, the relative amount of carbohydrates consumed, the degree of reliance on domesticated plants, and the preparation of these foods into soft-textured, easily masticated foods via extended cooking practices explains the variation in caries prevalence in bioarchaeological and other contexts as the collective package driving the caries process (see also Hara & Zero 2010).

Carious lesions are among the most well-documented pathological conditions arising from an infectious disease process in populations drawn from archaeological contexts. Carious lesions have been observed in populations from every continent, representing a diverse array of groups with different subsistence foci (Hillson 2008, Larsen 2015). Beginning with Turner's (1979) analysis, broad comparisons of populations drawn from archaeological contexts have revealed consistently higher (but not universal) prevalence in farmers than in foragers (Hillson 2008, Larsen et al. 1991, Lukacs 2012, Milner 1984). These comparisons show links between elevated caries prevalence and a strong commitment to the production and consumption of domesticated plant carbohydrates (e.g., maize, wheat, rice) and their products.

Not all domesticated plant carbohydrates appear to be equally cariogenic. For example, populations drawn from archaeological contexts that consumed maize in the New World appear to have higher rates of dental caries (Cucina et al. 2011, Lambert 2000, Larsen et al. 1991, Milner 1984, Steckel & Rose 2002) than prehistoric rice farmers in East Asia (Domett & Tayles 2007, Oxenham et al. 2006, Pietrusewsky & Ikehara-Quebral 2006). Moreover, some Western Asian and European settings show lower prevalence of dental caries in early farmers than in populations in North America (Eshed et al. 2006, Lubell et al. 1994). That being said, the general pattern of the infection shows a consistent trend of increased dental caries prevalence in a wide range of studies globally, especially wherever and whenever food is acquired via cultivation of or access to plant carbohydrates, mostly of domesticated origin.

Periodontal disease (periodontitis) is an infectious disease process involving periodontal soft tissues (gingiva or gums) caused by acidic by-products of bacteria accumulating on tooth surfaces, commencing with plaque buildup and subsequently leading to inflammation of the tissues anchoring the teeth in the alveolar bone of the upper and lower jaws. The bacterial colonies comprising plaque include *Streptococcus mutans*, *Porphyromonas gingivalis*, and other pathogenic organisms (Enwonwu 1995, Slots 2004). The associated inflammatory responses in the gums and alveolar

bone lead to alveolar bone loss and ultimately tooth loss. Given the common causal microbial sources of dental caries and periodontal disease, it is not surprising that dental caries and periodontal disease prevalences mirror one another, and both infections are elevated when comparing earlier foraging populations with later farming populations (DeWitte & Bekvalac 2011).

Comparison of oral health outcomes for developing countries and their traditional communities in the process of replacing their traditional diets with Western, carbohydrate-enriched diets shows considerable increases in periodontal disease and associated antemortem tooth loss (Clarke et al. 1986, Donnelly et al. 1977, Hunter & Arbona 1995, Ronderos et al. 2001, Walker et al. 1998). Sampling of archaeological populations whose subsistence focused on agricultural foods similarly reveals a near-universal pattern of increased rates of periodontal disease and tooth loss (Blau 2007, Douglas & Pietrusewsky 2007, Klaus & Tam 2010, Larsen 2015, Sakashita et al. 1997) compared with hunter-gatherers, whose diets were high in animal sources of protein (Costa 1982, Scott 1991). As seen with the pattern of infection as it relates to tooth crowns and roots, past populations having made the shift from foraging to a diet based at least in part on agricultural products express increased periodontal disease resulting in significant antemortem tooth loss (Cohen & Armelagos 1984, Cohen & Crane-Kramer 2007, Larsen 2015, Patterson 1984, Rose et al. 1993).

TRACKING THE BIOARCHAEOLOGY OF SOCIAL VARIATION IN PAST POPULATIONS: INFERENCES ABOUT HEALTH AND WELL-BEING

The bioarchaeology of infectious disease gives a robust picture of the downstream consequences of poor nutrition and health as inferred from prevalence variation in oral infectious diseases. For example, access to animal sources of protein and consumption of carbohydrates vary substantively along the lines of sex and gender. Many archaeological series document a dominant, but not universal, pattern of greater dental caries prevalence in women than in men in agricultural-dependent populations (Larsen 2012, 2015; Lukacs & Largaespada 2006; Stantis et al. 2016). This distinctive pattern has also been identified in traditional and Western populations (Ferraro & Vieira 2010, Lukacs 2012). The record suggests that pregnancy and lactation and impacts of hormonal changes and reproductive factors related to these circumstances explain this variation. That is, the oral environment during pregnancy, including the presence of more cariogenic bacteria and lower pH, as well as the altered buffer effect of saliva owing to these circumstances, may elevate caries prevalence (Lukacs & Largaespada 2006). On the other hand, although sex differences in the oral environment likely influence dental caries outcomes, investigation of traditional societies, prehistoric and ethnographic, also reveals patterns of dietary variation based on sex and gender, which shows the centrality of access to carbohydrates in both hunter-gatherers and agriculturalists in explaining oral health outcomes (Da-Gloria & Larsen 2017, Lambert & Walker 1991, Walker & Hewlett 1990).

One recent investigation documents patterns of oral infectious disease associated with high-status and low-status native populations in a seventeenth-century Spanish mission context on the southeastern US Atlantic coast (Winkler et al. 2017). Individuals interred nearest the ritual nucleus of the church—the altar—were high-status persons in life. These individuals express lower dental caries prevalence than do individuals interred farthest from the ritual nucleus. These findings reveal a pattern of increased levels of oral infectious disease in individuals having relatively elevated maize consumption (see also Klaus & Tam 2010, White 1994). In contrast, high-status individuals in Dynastic Egypt, Yin-Shang-period China, and Edo-period Japan express greater prevalence of dental caries than do low-status individuals, which shows that access to domesticated plants was associated with high social position (Leigh 1934, Sakashita et al. 1997, Suzuki et al. 1967). Clearly, these circumstances pertain to the role of dietary patterns in promoting oral infectious disease.

CONSEQUENCES OF INFECTION AND INFECTIOUS DISEASE: LINKING ORAL AND SYSTEMIC HEALTH

There are significant, chronic effects that relate to the response of the immune system in individuals who have experienced infectious disease. In particular, chronic infections, such as those discussed in this article, stimulate systemic inflammatory responses that have long-term health consequences (Crespo et al. 2017, Fowler et al. 2001, Weston 2012). The inflammatory processes focus on containing the pathogen and its systemic effects, especially those involving increased morbidity and mortality relating to chronic health conditions, including but not limited to cardiovascular disease, diabetes, and respiratory diseases (Dhadse et al. 2010, Kuo et al. 2008). These findings show that virtually any inflammatory condition, including dental caries and periodontitis, has downstream systemic effects that compromise an individual's general health and increase their susceptibility to chronic disease in later life. These compromises result in increased frailty and early death. Thus, although inflammation is largely considered a natural response to infection, serving to heal the body, the result is a long-term detriment to systemic health.

The association between infectious disease and mortality is strongly inferred in bioarchaeological study. DeWitte & Bekvalac's (2010) analysis of skeletal remains from the medieval St. Mary Graces cemetery, in London, shows a strong association between oral infection (dental caries and periodontal disease) prevalences and early death. That is, individuals who had oral infections showed earlier age-at-death than did individuals without oral infections. Moreover, the increased systemic inflammation burden is suggested by the presence of localized postcranial infections and periodontal disease in the population (DeWitte & Bekvalac 2011). In this setting, the combination of strong reliance on plant carbohydrates in diet, poor oral hygiene, and poor living conditions generally contributed to increased morbidity and mortality.

OPPORTUNITIES AND CHALLENGES GOING FORWARD

The bioarchaeological study of infectious disease is the most important retrospective picture of the physical manifestations of health crises as they pertain to infectious disease, especially for chronic conditions. Human remains present a compelling picture of challenges to earlier societies and key developments that have shaped health outcomes, most of which have their origins in the dietary transition from the consumption of nondomesticated foods derived from hunting, gathering, and collecting to the consumption of domesticated dietary carbohydrates. The transition to agriculture had enormous implications for how humans organize themselves socially; the circumstances led to an increase in population size and concentration, permanent long-term settlement, and the increasing role of infectious diseases in influencing health outcomes, including health crises for individuals and their communities.

Bioarchaeologists are proficient in describing the osteological indicators of health outcomes, especially with regard to contextualizing the important circumstances that environment, social and cultural elements, and community organization provide for inferring health outcomes. The revolution in dietary reconstruction via stable isotope data gives new and growing understanding of nutritional outcomes, which is important for characterizing the consequences of infection and infectious disease for well-being. The study of aDNA in ancient diseases has advanced appreciably in the last decade, presenting us with an increasingly accurate documentation of the evolution of pathogens. This evolutionary record is foundational for understanding the spread of infectious diseases, explanations for success of the pathogenic organisms that cause them, and implications for the future of the world's populations today.

New biomolecular analytic approaches are beginning to inform our understanding of the mechanisms and interactions of immunological shifts that are taking place in individuals that

have chronic infections, including those represented by archaeological remains. For example, advances pertaining to aDNA and protein analysis are opening new windows onto the history and evolution of some infectious diseases (e.g., tuberculosis, plague, malaria, periodontal disease; see DeWitte 2016, Feldman et al. 2016, Fornaciari et al. 2010, Warinner et al. 2014). That said, bioarchaeological science needs to develop means of investigating systemic inflammation. Such a development stands to give a more comprehensive understanding of the biological processes underlying the origin of the skeletal and dental lesions described by bioarchaeologists. Toward that goal, newly developing experimental research by Crespo and collaborators (2017) on chronic infections (e.g., tuberculosis) focuses on identifying shifts in systemic levels of inflammation-related proteins (cytokines). In this regard, in vitro exposure of peripheral blood mononuclear cells from healthy, noninfected individuals to bacterial cultures having pathogenic bacteria—*Mycobacterium tuberculosis*, *Mycobacterium leprae*, and *Porphyromonas gingivalis*—resulted in a clear shift in the immunological performance when exposed to the oral pathogen, *P. gingivalis*. This pioneering experimental research suggests that the proinflammatory cytokine proteins associated with immunological responses increased when immune cells were pretreated with mycobacterial lysates (a medium containing bacterial antigens) and subsequently exposed to an oral pathogen (*P. gingivalis*) associated with periodontal disease. Individuals with chronic systemic infectious diseases (e.g., tuberculosis) experience increases in immune response when exposed to oral pathogenic bacteria. It is these increases that produce inflammation and negative systemic health consequences.

Experimental immunology has considerable potential for developing new understanding of infectious disease, the relationship between host and pathogen, and patterning in immune function in both contemporary and past populations. Regarding the latter, we know that native farming communities in the colonial-era Americas suffered enormous losses owing to epidemics and a confluence of other negative circumstances contributing to stress and an overall decline in life conditions (Baker & Kealhofer 1996, Cameron et al. 2015, Hutchinson 2016, Larsen 1994, Larsen & Milner 1994, Verano & Ubelaker 1992). Historical, archaeological, epidemiological, and immunological evidence suggests that the virulence of epidemic diseases was worsened by the confluence of oral and systemic infectious diseases, both native and introduced, in these settings. Similarly, the increasingly poor oral health of medieval Europeans may be an element that contributed to mortality during plague outbreaks, including the Black Death, which resulted in the loss of life of some 30–60% of the population (DeWitte 2016). These new windows into the role of infectious disease and associated health crises for individuals, communities, and regions offer opportunities to understand the deep history of human health.

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