Archaeological Evidence of Epidemics Can Inform Future Epidemics

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Abstract

The recent Ebola epidemic provides a dramatic example of the devastation and fear generated by epidemics, particularly those caused by new emerging or reemerging diseases. A focus on the control and prevention of diseases in living populations dominates most epidemic disease research. However, research on epidemics in the past provides a temporal depth to our understanding of the context and consequences of diseases and is crucial for predicting how diseases might shape human biology and demography in the future. This article reviews recent research on historic epidemics of plague and tuberculosis, both of which have affected human populations for millennia. Research on these diseases demonstrates the range (and differential availability) of various lines of evidence (e.g., burial context, diagnostic skeletal lesions, molecular data) that inform about past disease in general. I highlight how research on past epidemics may be informative in ways that benefit living populations.

INTRODUCTION

The recent devastating outbreak of Ebola virus disease, which began in December 2013, focused the world's attention on the dangers of emerging infectious diseases. Emerging diseases are those that are new to human populations or those that have existed previously but have increased rapidly in incidence or geographic distribution (Morse 1995). Dozens of diseases have emerged in recent decades, including HIV/AIDS, West Nile Virus, severe acute respiratory syndrome (SARS), and Ebola, and new diseases will certainly emerge in the future (Cleaveland et al. 2007, Morens et al. 2004). Emerging diseases cause concern, at least in part, because their newness produces uncertainty about the impacts they may have in both the short term (during and immediately following epidemics) and the long term (in the years and generations following epidemics).

Ebola virus was first identified in 1976 when it caused outbreaks in Sudan and Zaire [now the Democratic Republic of Congo (DRC)] (Ghazanfar et al. 2015); since first emerging, it has caused 25 known outbreaks (Farrar & Piot 2014). Although devastating at the local level because of high case-fatality rates, individual outbreaks of Ebola have, until recently, killed at most a few hundred people and have been limited spatially, occurring primarily in forested regions (Breman & Johnson 2014). The recent Ebola epidemic was unprecedented in terms of both its wide geographic distribution and the numbers of people affected. Thus far, there have been nearly 10 times the number of cases compared with those from all other outbreaks since 1976 combined (Tomori 2015). As of December 2015, there had been more than 28,600 cases and more than 11,300 deaths from the most recent Ebola outbreak (CDC 2015). The clinical course of the disease, transmissibility, and case-fatality rates of the recent outbreak did not differ from that of previous outbreaks (WHO 2014), and the variant of the virus that caused the outbreak did not differ from other variants responsible for earlier outbreaks in ways that would enhance virulence or transmissibility (Azarian et al. 2015, Olabode et al. 2015). The recent epidemic was more devastating than previous outbreaks not because the virus itself changed, but because of factors such as the relative ease of travel between urban and rural areas (where the outbreak began), failures in surveillance, delayed or insufficient control measures, inadequacies in health care delivery, and traditional beliefs regarding treatment of the sick and the dead that have played an important role in spreading the disease (Abramowitz et al. 2015, Agusto et al. 2015, Tomori 2015, WHO 2014). The scale of the recent Ebola epidemic raises questions about how well prepared we are for future epidemics of both known and unknown emerging diseases.

Emerging disease researchers have focused their attention primarily on how to cope with existing diseases; determining when, where, and why new diseases will emerge; and preventing the emergence of new diseases. Prioritizing current and future diseases is clearly important given that peoples' lives are at stake. Research on modern emerging diseases has revealed factors that affect emergence and the mortality patterns of recent emerging diseases (Engering et al. 2013, Fauci et al. 2005, WHO Ebola Response Team 2014). However, important questions remain about who is at highest risk of disease and death during emerging disease epidemics; the social, economic, biological, and environmental factors that lead to emergence and epidemics; how epidemiological patterns change following emergence; the interactions among emerging diseases, political-economic processes, and human biology; how such diseases affect the health and demography of human populations over the short and long term; and how the causative agents and their human hosts coevolve. These questions persist, in part, because researchers have focused almost exclusively on diseases that have emerged within the past few decades. Thus, we lack the temporal depth necessary to fully examine changes in the behavior of emerging diseases and the long-term interactions between pathogens and human hosts. Without a complete understanding of these factors, our ability to adequately respond to or prevent disease emergence is hindered.

However, emerging diseases are not just a recent phenomenon in human populations. Emerging diseases were also important in the past (indeed, all infectious diseases of humans were at some point emerging diseases), and the existence of archaeological evidence of past diseases and the persistence of some ancient emerging diseases to the present day provide ideal opportunities to examine long-term trends in emerging and epidemic disease dynamics. Research on past diseases can deepen the temporal scope of our understanding of the causes and consequences of emerging diseases and potentially provide tools for mitigating disease in living populations and for predicting how they may affect us. This review summarizes archaeological, bioarchaeological, and paleomicrobiological approaches to studying past diseases and outlines ways in which such research may benefit living people now or in the future.

ARCHAEOLOGY OF DISEASE

This article highlights research on plague and tuberculosis, both of which have affected human populations for millennia. The skeletal remains of the victims of past plague epidemics, including the medieval Black Death, are identified primarily by burial context, whereas the victims of tuberculosis can be identified via diagnostic skeletal lesions. Thus, studies of these two diseases leverage the most common evidentiary regimes available to anthropologists interested in health in the past and will provide illustrative examples of how informative such studies can be.

The Black Death

Few diseases in human history have generated as much interest as the Black Death (ca. 1347–1351), which killed 30–60% of people in Europe and thereby caused or accelerated dramatic changes in economic, political, and demographic conditions. Its effects elsewhere in the Old World are less well known, but we will learn more as scholars increasingly focus on evidence outside of Europe (Green 2014). The Black Death has been described as "one of the most dramatic examples ever" of an emerging infectious disease (Wheelis 2002, p. 971). Following the Black Death, there were periodic outbreaks of plague for centuries, though no other outbreak matched the mortality levels of the Black Death. We have abundant evidence from historical documents regarding the spatiotemporal spread of the epidemic in Europe. Because it was relatively short-lived and we know precisely when and where it occurred, we can examine the demographic, health, social, political, and economic conditions that existed at the time of the Black Death. Furthermore, mass burial grounds were established to accommodate the huge numbers of epidemic victims, and thus skeletal assemblages associated with the Black Death and later outbreaks of medieval plague are available for study. Without the historical and archaeological evidence linking these burial grounds to plague, bioarchaeological and molecular analyses of the disease would be difficult if not impossible. The Black Death killed too quickly to leave any visible, diagnostic skeletal lesions, thereby preventing paleopathological diagnosis of the disease.

Much of the published bioarchaeological research on the Black Death has been done using samples from the East Smithfield cemetery in London. The location, purpose, and dimensions of East Smithfield are recorded in historical documents. Reports of the Black Death preceded its arrival in London, and East Smithfield was established in anticipation of the high mortality that would result in the city (Grainger et al. 2008, Hawkins 1990). The Black Death arrived in 1349 and lasted in London until 1350; East Smithfield was used only during the Black Death, so most, if not all, of the people buried there were victims of the disease. East Smithfield was partially excavated in the 1980s as part of the larger Royal Mint site, and more than 600 individuals interred in single burials or mass burial trenches were excavated from the cemetery.

Several studies have compared East Smithfield to other nonepidemic (i.e., attritional) cemeteries or to model life tables to test the assumption that the Black Death was an indiscriminate killer (DeWitte & Wood 2008, Gowland & Chamberlain 2005, Margerison & Knüsel 2002, Waldron 2001). If this were the case, East Smithfield, and presumably other plague assemblages, would provide relatively unbiased skeletal samples that better represent once-living populations than is true of attritional samples. The latter are typically biased because mortality under normal circumstances tends to be selective, i.e., those with the highest relative risk of mortality [or what Vaupel et al. (1979) describe as frailty] are most likely to die at any particular age. The results of these studies were mixed. Some reveal differences between the age-at-death distributions of Black Death and attritional assemblages that suggest the Black Death was an indiscriminate killer and affected all age groups equally (Gowland & Chamberlain 2005, Margerison & Knüsel 2002). However, my research (e.g., DeWitte 2010, DeWitte & Hughes-Morey 2012, DeWitte & Wood 2008) and that of Waldron (2001) found similarities between the East Smithfield and attritional assemblages, which suggests that the Black Death, like most other causes of mortality, killed selectively and thus was not an indiscriminate killer. My colleagues and I used hazard analysis–based approaches, which are arguably more efficient and informative ways to assess skeletal data compared with the traditional life table–based approaches (Konigsberg & Frankenberg 2002, Milner et al. 2008, Wood et al. 2002) used in other studies of the Black Death. We also used transition analysis, a method of age estimation that avoids the biases associated with the traditional methods used in most other studies and that provides point estimates of age, even for the oldest individuals (traditional methods typically include open-ended terminal age categories and tend to underestimate older ages). We found that elderly people and frail people of all ages (i.e., those who had experienced physiological stress prior to the epidemic) were at elevated risks of death during the Black Death. We thus concluded that if something as devastating as the Black Death was apparently selective, then we should expect mortality to be selective under most conditions (DeWitte & Wood 2008).

Most studies of East Smithfield have focused on mortality patterns, but the cemetery has also been the subject of chemical analyses of migration. Kendall et al. (2013) analyzed strontium and oxygen stable isotopes to identify nonlocals in the East Smithfield assemblage and found 5 people (out of 30 sampled) who were outliers and thus likely immigrants from the hinterlands of London or more distant locales. Although the sample was relatively small, this study provides an example of the insights into life in the past (beyond revealing relative risks of death) that might be possible if we focus on epidemic burials. In the case of East Smithfield, given the very short duration during which the cemetery was used, the combination of skeletal sex, age-at-death, and pathology data and historical evidence would enable examination of the motivations (e.g., famine, warfare, disease, household economics) for and consequences of migration into London during a period for which too little is known about this important demographic phenomenon. There is still much more work to be done along these lines using large sample sizes that allow researchers to analyze the interaction of these variables.

The accessibility of exclusively pre–Black Death assemblages from London has also allowed researchers to examine demographic and, by inference, health conditions before the epidemic. This is important for understanding why the Black Death caused such devastatingly high mortality, particularly given the lack of discernible functional genomic differences between ancient and modern plague (see below). Bioarchaeological data from London reveal declines in survivorship and increases in mortality rates for adults in the thirteenth century compared with adults in the eleventh and twelfth centuries. These demographic changes occurred during a period of climate fluctuations and resulting famines, which might have reduced health in general such that the population was highly vulnerable to the emergence of the Black Death (DeWitte 2015).

Evidence that the Black Death targeted frail people of all ages, and evidence from historical documents indicating that standards of living (including diet) improved following the epidemic as a result of the depopulation that it caused, raised the question of whether health improved after the epidemic. Comparison of pre–Black Death (ca. 1000–1250 CE) and post–Black Death (ca. 1350–1540) cemeteries in London revealed decreases in risks of mortality and improvements in survivorship after the Black Death compared with pre-epidemic conditions (DeWitte 2014a,b). The exact cause of these trends remains to be determined, i.e., whether they were the result of improvements in diet, a harvesting effect [i.e., an increase in mortality among people with compromised health (Sawchuk 2010)], changes in human genetic variation associated with immune competence or disease susceptibility, or something else. Regardless, these demographic changes indicate underlying improvements in health as a result of the Black Death and, more generally, suggest that epidemics can have dramatic and long-lasting effects on human health and demography.

As mentioned above, there were periodic plague epidemics following the Black Death up through the eighteenth century, and some research has focused on burials associated with subsequent outbreaks in France. Analysis of sixteenth-century plague burials at Les Fédons in Lambesc, France, reveals an age profile that differs from those found in attritional assemblages and is similar to that of a living population (Castex 2008). These results, according to Castex (2008), indicate that plague mortality was nonselective with respect to age, at least in the context she studied. These findings contradict my own, which indicate elevated risks of mortality for the elderly and the frail during the Black Death. It is possible that patterns of selectivity during historical plague epidemics may not have been uniform across time or space. However, the different patterns estimated by these studies may reflect methodological differences. Castex uses traditional methods of adult age estimation [no ages above 29 were reported in Castex (2008)] and does not use hazard analysis, both of which mean that bioarchaeological examination of mortality patterns at the latest adult ages during historic plague epidemics in France is limited. Differences in observed plague mortality patterns may also be an artifact of sample size differences (Les Fédons, $n = 58$ versus East Smithfield, $n = 491$).

Bioarchaeological research focusing on burial patterns during historic epidemics has the potential to reveal how people responded behaviorally to plague mortality (Castex 2008). For example, in the East Smithfield cemetery, though the mass burial trenches are clearly different from typical medieval Christian burials, the individual graves are indistinguishable from those in contemporaneous nonepidemic burial grounds in Britain (Grainger et al. 2008). Throughout the cemetery, including within the mass trenches, all but two people are buried in standard medieval Christian fashion (prone, extended, and with their heads oriented west and feet oriented east). The bodies were stacked carefully within the trenches rather than tossed from the edges of the trenches (Grainger et al. 2008). The burial patterns in East Smithfield indicate that people took great care of the deceased (some of whom were in advanced stages of decomposition at the time of burial) and treated them with respect. Similarly, burials in putative plague burials in France dated to the fifth and sixth, fourteenth, and sixteenth centuries were very carefully performed and similar to non-plague mortality burials (Castex 2008, Kacki et al. 2011). Castex (2008, p. 30) describes these burials as reflecting "orderly management" in the face of crisis. However, burial trenches associated with the 1720–1721 plague epidemic in Provence contain bodies in a random orientation, which indicates that bodies were deposited from the tops of the trenches (Signoli et al. 2002). These different types of plague burials provide insights into the extent to which epidemic diseases can disrupt normal social processes, rituals, and behaviors surrounding death and burial, and the possible geographic or temporal variation in such disruption (or lack thereof).

Historic plague assemblages have allowed for molecular analyses of the causative pathogen. Several studies have extracted DNA diagnostic of the bubonic plague bacterium, *Yersinia pestis*,

from victims of historic plague epidemics, thus confirming the long-standing assumption that these epidemics (including the sixth-century Plague of Justinian and the Black Death) were caused by plague and revealing that humans have been affected by the disease for several thousand years (Bos et al. 2011, Drancourt et al. 1998, Haensch et al. 2010, Raoult et al. 2000, Rasmussen et al. 2015). Investigation of *Y. pestis*, including its molecular biology and behavior in the past, is particularly important because the disease is currently a widespread zoonosis (and thus cannot be eradicated), has genetic plasticity, can acquire antibiotic resistance, is considered a high-priority bioterrorism agent, and thus has "considerable potential to re-emerge" as a threat to living human populations (Smiley 2008, p. 256). Recent analysis of Bronze Age samples suggests that ancient strains lacked some key virulence genes found in those that caused later pandemics (including the Black Death), and thus earlier forms of the disease may have been less virulent or had different transmission mechanisms compared with more recent ones (Rasmussen et al. 2015). A draft genome of fourteenth-century *Y. pestis* reveals that it is ancestral to all known currently circulating strains that are pathogenic to humans (Bos et al. 2011). Comparison of the fourteenth-century strain to modern stains, however, has not revealed any genetic reasons for the extraordinarily high mortality levels associated with the Black Death. This serves to underscore the importance of bioarchaeological research for revealing the human context of the disease and potentially identifying factors beyond the pathogen itself that may explain changes in plague epidemiology (including decreasing mortality levels) that have occurred over the centuries.

Tuberculosis

Tuberculosis, which is considered a global epidemic disease by the World Health Organization (WHO 2015), has long fascinated anthropologists because of its antiquity, its effects on the human skeleton (and thus the possibility of identifying its victims based on skeletal lesions), the devastating toll it takes on contemporary human populations, and the role that biological, social, behavioral, and environmental factors play in determining susceptibility to and driving transmission of the disease. In 2014 alone, an estimated 9.6 million new cases of tuberculosis were diagnosed, and the disease killed 1.5 million people worldwide, an unacceptably high number given that most cases of the disease are curable (WHO 2015). In living populations, tuberculosis is characterized as a disease of poverty and of poor living conditions, such as overcrowding (Littleton et al. 2010; Roberts 2011, 2015), and there is an unfortunate stigma associated with the disease. The modern associations of tuberculosis with poverty and the attendant stigma also appear to have existed in the past (Roberts 2011), and their persistence is contributing to the reemergence of the disease, a phenomenon that will likely continue unabated in the future unless increased funding is devoted to controlling the disease. Reemerging diseases are those that have increased in incidence following a decline or that have expanded in geographic distribution (Feldmann et al. 2002). Tuberculosis is reemerging because of a variety of factors, including the HIV epidemic (and thus the increased prevalence globally of immune-compromised people), increased poverty in urban areas, immigration, and insufficient control measures (Faustini et al. 2006). Multidrug-resistant strains of tuberculosis are on the rise because of failures by people to properly complete lengthy therapeutic regimens (Fauci et al. 2005), which in turn results at least in part from insufficient health education, money, and access to medical care, all hallmarks of poverty (Roberts & Buikstra 2003).

Because it can produce diagnostic bony lesions [though only approximately 3–5% of those with untreated tuberculosis develop such lesions (Resnick & Niwayama 1995)], tuberculosis provides an example of a disease in the past that can be investigated using skeletal material in the absence of corroborating documentary or mortuary evidence. This method of investigation is not currently feasible for most diseases that do not produce bony lesions, though that may change with the

development of relatively inexpensive, minimally destructive molecular screening methods, such as immunoassays for plague (see, for example, Bianucci et al. 2008, Kacki et al. 2011). There is an extensive body of bioarchaeological literature on tuberculosis, far too large to summarize sufficiently here. Readers interested in comprehensive discussions and descriptions of the paleopathological evidence of tuberculosis and the spatiotemporal distribution of the disease in the past should refer to Roberts & Buikstra (2003), Roberts (2012), Roberts (2015), Stone et al. (2009), and references therein.

Bioarchaeological research on tuberculosis demonstrates how such work in general is invaluable in terms of clarifying the context of disease, which has important implications for understanding and predicting the existence and behavior of diseases in living populations (Roberts & Buikstra 2003). Examination of trends in the prevalence and skeletal manifestation of tuberculosis in the past improves our understanding of how environmental and cultural factors affect the dynamics of infectious disease in the absence of antibiotics and other effective medical interventions (Anastasiou & Mitchell 2013, Matos & Santos 2015, Pálfi et al. 2015)—i.e., the context that characterized much of our coevolutionary history with infectious diseases and that still exists within some populations today. Roberts & Buikstra (2003), for example, emphasize the role of particular living conditions in promoting the rise of tuberculosis in medieval Europe and the New World. High population density, poverty (with attendant poor diet and living conditions), and contact with animals appear to have allowed tuberculosis to flourish in the past and, as mentioned above, contribute to its persistence in living populations.

Archaeological evidence also contributes to an understanding of the population-level effects of tuberculosis. The antiquity and persistence of tuberculosis provide an excellent opportunity to examine how natural selection shapes patterns of disease susceptibility between populations. Analysis of the association between urbanization (assessed using archaeological and historical data) and a genetic polymorphism (present in living populations) associated with resistance to tuberculosis indicates that populations with longer histories of urbanization are more highly adapted with respect to disease resistance (Barnes et al. 2011). Other work more directly addresses heterogeneity within populations in the past, which ultimately can affect outcomes at the population level and coevolutionary dynamics between humans and tuberculosis. Blondiaux et al. (2015), for example, reveal reduced survival in general for people with tuberculosis lesions in a large skeletal sample from France dated to ca. 200–1500 AD; however, the effect varies by sex, with females exhibiting higher survivorship, perhaps because of the general immune-boosting effects of estrogens. Examination of variation in the skeletal presentation of the disease in the past can provide insights into how the virulence of the pathogen (which is potentially accessible via ancient DNA analyses) and factors that affect individual susceptibility (such as diet) interact to produce disease outcomes (Donoghue et al. 2015, Wilbur et al. 2008).

Bioarchaeological examination of the interaction between tuberculosis and leprosy in medieval Europe exemplifies how the study of disease ecology in the past (including the presence of contemporaneous circulating pathogens) is important for understanding disease patterns. Leprosy declined in Western Europe in the late medieval and early modern periods (Roberts & Manchester 2005), and close similarities between ancient and modern strains of the disease suggest that the decline did not occur solely because of genetic changes in the pathogen (Harkins & Stone 2015). Instead, the decline of leprosy may have been a consequence of the rise in the prevalence of tuberculosis. Like tuberculosis, leprosy is caused by a mycobacterium (*Mycobacterium leprae*), and some evidence indicates that cross immunity occurs between the closely related bacteria. This finding has led to the suggestion that exposure to tuberculosis provides protection against leprosy and, thus, that as tuberculosis increased in the past, fewer people suffered from leprosy (Chaussinand 1948, Lietman et al. 1997). However, ancient DNA evidence of coinfection with both diseases

suggests, alternatively, that immune suppression resulting from leprosy infection may increase the risk of mortality from tuberculosis, thereby leading to observed declines in the numbers of people suffering from leprosy (Donoghue et al. 2005). Mathematical modeling lends support to this latter hypothesis (Hohmann & Voss-Böhme 2013). Recognition of the importance of these and other endogenous and exogenous factors that shape disease susceptibility, prevalence, and outcomes is an important step toward reducing or eliminating the burden of tuberculosis in living populations (Roberts & Buikstra 2003).

As with historical plague, tuberculosis research includes ancient DNA analysis of victims of the disease. One of the values of paleomicrobiological analyses of tuberculosis using skeletal samples with good chronological control is that it allows for calibration of the timing of the emergence of various strains and lineages within the *Mycobacterium tuberculosis* complex (MTBC) (Baker et al. 2015, Donoghue et al. 2015, Harkins & Stone 2015). This procedure is informative about the phylogeny and evolution of the pathogen itself (Bouwman et al. 2012), and it also helps clarify how long humans have faced the disease and how human demography and behavior (including migration and contact events) in the past have shaped the distribution of tuberculosis (Donoghue 2011, Donoghue et al. 2015). Paleomicrobiological approaches have allowed scholars to examine the origin and spread of the disease among humans, which remain matters of debate despite decades of research (Hershkovitz et al. 2015). Whether the MTBC recently jumped from a zoonotic source or is an heirloom pathogen that dispersed, along with humans, from Africa much longer ago is, according to Harkins & Stone (2015), one of the "most enduring questions in pathogen evolution" (p. 144).

Until recently, scholars generally believed that tuberculosis in humans developed from a bovine form (*Mycobacterium bovis*) at the time of domestication, given the apparent increase in the prevalence of tuberculosis in the archaeological record during the Neolithic period (Donoghue et al. 2015, Roberts 2012). However, phylogenetic analysis of the MTBC indicates that *M. tuberculosis* is the more ancestral lineage compared with *M. bovis* (Donoghue 2011, Gagneux 2012). Human paleopathological and ancient DNA evidence from ancient Egypt reveals an absence of *M. bovis* in the samples and that tuberculosis infections caused by *M. africanum* predate those caused by *M. tuberculosis* (Donoghue 2011, Zink et al. 2003); there is also evidence of human tuberculosis prior to animal domestication in ancient Syria (Baker et al. 2015). These lines of evidence, in addition to others, are inconsistent with the view that *M. tuberculosis* evolved from *M. bovis*. Recently, MTBC DNA isolated from pre-Columbian Peruvian samples was shown to be most closely related to *Mycobacterium pinnipedii* (Bos et al. 2014), i.e., tuberculosis adapted to seals and sea lions and distinct from forms that are adapted to humans (Harkins & Stone 2015). This evidence suggests that tuberculosis was transmitted, at least in some cases in this population, to humans from pinnipeds rather than having arrived in South America with people who migrated from Asia over the Bering Land Bridge. This also suggests that there may have been temporal and geographic variation in the mechanisms that introduced tuberculosis into human populations. Although at this point there continues to be debate surrounding the questions of when and how tuberculosis made the transition to human hosts, it is clear that bioarchaeological and paleomicrobiological research can provide crucial evidence.

POTENTIAL BENEFITS TO LIVING POPULATIONS

As fascinating as research on past diseases is in terms of understanding life and, particularly, health in the past, archaeological evidence of past epidemics might also be informative in ways that benefit living populations. Research focusing on disease in the past clarifies how the diseases that currently affect us originally spread to and among humans and how diseases have affected

us demographically, biologically, and socially. Investigations of epidemics in the past provide a temporal depth to our understanding of disease dynamics and consequences and the social, biological, and environmental circumstances that give rise to epidemics [or, syndemics, if we view all these factors as an integrated whole (Singer 2010, Singer & Clair 2003)], all of which is necessary for fully understanding epidemics that occur in contemporary populations and that will inevitably occur in the future (Herring & Swedlund 2010b). Indeed, Noymer (2010, p. 137) argues that it is only by focusing on disease in the past and taking a long-term perspective that we can observe the true effects of epidemics.

Examining mortality patterns associated with disease in the past can reveal how individuals, in general, vary in their susceptibility to disease and risk of death during epidemics. For example, as described above, research on the medieval Black Death reveals that risks of death during the epidemic were highest among those who were already sick or malnourished; these results suggest that we should expect such variation in risk under all mortality conditions, catastrophic and otherwise (DeWitte & Wood 2008). In the case of tuberculosis, there is considerable variation between and within populations with respect to access to adequate medical care for the disease; consequently, there has been a failure globally to control a disease for which there is effective medication and one that we have the potential to control (Roberts & Buikstra 2003, WHO 2015). Given that tuberculosis appears to have been common among groups of lower socioeconomic status in the past and given its current association with poverty, elimination of poverty in living populations would contribute to control of the disease (Roberts & Buikstra 2003). Such findings can and should encourage us to attend to heterogeneity in risk in living populations. By revealing who might be most vulnerable during epidemics and determining which factors most significantly affect negative health outcomes or risk of mortality, research on past epidemics can help motivate action (e.g., increased and more equitable access to medical care and distribution of food and other resources to those people in greatest need) in advance of crises to ameliorate their potential devastating effects.

Evidence of short- and long-term demographic and health trends during and following past epidemics allows us to understand the power that epidemic diseases have to shape populations and the role that human demography may play in disease dynamics and evolution. Such evidence can inform models of the evolution of virulence in emerging pathogens (Ebert 1999) and help to resolve questions about whether changes in emerging disease epidemiology are the result of human adaptation, changes in human demography or behavior, changes in nonhuman animal host population dynamics, or evolution of the causative pathogens (Alizon et al. 2009, André & Hochberg 2005, Grenfell et al. 2004). Improved understanding of these issues may enhance our abilities to mitigate current diseases by, for example, revealing which pathogen or host factors can feasibly be altered to reduced risks of human mortality.

Genetic research on past epidemics may also provide tangible benefits to living populations. Genomic research involving pathogenic organisms, in general, often raises concerns that the results will be misused, e.g., to threaten public health, as was feared when the genome of the 1918 Spanish influenza virus was published and used to reconstruct the virus (Taubenberger et al. 2005, Tumpey et al. 2005, van Aken 2007). However, in that case, the US Department of Health and Human Services, in consultation with the National Science Advisory Board for Biosecurity (NSABB), decided that the scientific benefits of the research outweighed potential risks (Shea 2007). The National Research Council Committee on Genomics Databases for Bioterrorism Threat Agents (2004) recommends maintenance of open access to pathogen genome databases as a way to ensure security, and research on ancient pathogens can contribute to this goal and also potentially yield medical benefits. In addition to providing insights into pathogen evolution and functional biology, pathogen genomic data allow for the rapid and cost-efficient development of

vaccines and drug therapies (Moriel et al. 2010, Seib et al. 2009, Sette & Rappuoli 2010). For example, the drug ST-246, developed using pathogenic orthopoxyvirus genomic data, was used to treat a child who developed life-threatening eczema vaccinatum after exposure to the smallpox vaccine (Vora et al. 2008, Yang et al. 2005), and research using genomic data has identified vaccine antigens for *Escherichia coli* (Moriel et al. 2010), serogroup B meningococcus (Giuliani et al. 2006), and *Treponema palidum* (McKevitt et al. 2003). Ancient biomolecule research will potentially contribute to existing genome databases and may ultimately have public health benefits by providing tools for developing therapeutics, particularly if virulent forms of ancient diseases reemerge. Such research may also allow us to predict future genetic changes in pathogens, which could contribute to our ability to control diseases (Anastasiou & Mitchell 2013).

Finally, ancient disease research can be used to raise public awareness about the powerful effects that diseases have had and can continue to have on our species. Disease epidemics are not new, and they will continue to affect and potentially devastate human populations in the foreseeable future. We should make better use of and further our capabilities to predict, prevent, and control infectious disease epidemics rather than waiting until diseases present immediate and severe threats or failing to act when diseases threaten people in other parts of the world. This action is particularly important given the current global interconnectedness, which can put people at risk of diseases that emerge in distant locales. Unfortunately, according to the Institute of Medicine and the National Research Council, "the public and government officials have short attention spans and are challenged by competing interests for limited resources," and thus emerging disease surveillance and research in general are not often prioritized (Keusch et al. 2009, p. 188). Archaeological research on past epidemics has the potential to help bring about change. Epidemic diseases in the past, such as the Black Death, provide dramatic and fascinating examples that capture the public's attention and imagination, and this public focus should be leveraged in ways that can lead to positive change. We can dispel views of past epidemics as historical curiosities completely disconnected from circumstances that exist today. We should emphasize that current and future interactions between humans and infectious diseases are a continuation of a struggle that our ancestors faced, successfully or not, in the past. Archaeological research on disease allows us to highlight the similarities between past and present conditions that give rise to epidemics, and we can provide information about what happened during past epidemics to motivate action in the face of epidemics or even before epidemics occur in living populations. Such action may include not only increased spending on disease research, but also efforts to reduce socioeconomic disparities in access to food, medical care, and other resources that affect susceptibility to and mortality from infectious disease. This is not an endorsement of using knowledge about past epidemics to incite irrational fear in people today, and we should be careful to avoid speculation about the likelihood that an epidemic as devastating as the Black Death will occur again in the future. Instead, we should promote the informed application of empirical and highly engaging evidence of the context and consequences of past epidemics to encourage preparedness and positive action in living populations.

FUTURE DIRECTIONS

Research on past human diseases has improved our understanding of human health in the past and provides us with information that might produce tangible benefits for living people. Moving forward, there are several possible directions that bioarchaeologists can take to extract the maximum amount of information available from skeletal data and to leverage recent technological, methodological, and analytical advances in the field. There should be an increase in population-level (paleoepidemiological) studies of past diseases that allow for intersectional analyses of age,

sex, diet, health status, socioeconomic status, and other factors that might influence disease outcomes. That is, in addition to considering case studies of diseases, researchers should examine large, more broadly representative samples from past populations, which would allow for the estimation of more accurate and informative demographic and health statistics. There has been a call, for example, for such studies of tuberculosis, particularly assessing the association between developmental stress (indicating dietary stress) and disease (Roberts 2012, Roberts & Buikstra 2003). Stable isotope analysis can produce high-resolution dietary data and thus allow investigators to examine the interaction of diet and disease (including, but not limited to, tuberculosis). Bioarchaeological isotopic studies are often done using small sample sizes; however, in the future, studies using sufficiently large samples would allow for more accurate inferences at the population level. More generally, the application of analytical approaches such as hazard analysis, which are commonly used in the demography and epidemiology of living populations and which accommodate the small samples typical of bioarchaeology, can reveal population-level associations between mortality and diet, stress, and other factors in the context of past epidemics (e.g., Blondiaux et al. 2015, DeWitte & Wood 2008). It is also important for bioarchaeologists to use methods of age estimation that provide estimates of the oldest ages (rather than open-ended terminal age categories that are typical of traditional methods). Doing so would allow researchers to examine morbidity and mortality trends in subjects at later adult ages (e.g., Blondiaux et al. 2015) and thus for a more representative sample of past populations than is possible with traditional methods.

Future work should also include a greater integration of bioarchaeological, paleomicrobiological, and human ancient DNA data. Analyses of ancient biomolecules are becoming more efficient and are capable of producing genomic information that enables large-scale comparisons between ancient and modern strains of pathogens (Bos et al. 2011). It is also possible to examine patterns of coinfection with multiple pathogens in the past (Devault et al. 2014, Warinner et al. 2014) and to examine human genetic variation with respect to disease susceptibility and resistance using ancient samples (Donoghue et al. 2015). Currently, however, bioarchaeology and paleomicrobiology are too often done independently of one another. Paleopathological evidence is typically used to identify candidates for paleomicrobiological analyses. However, few ancient biomolecule studies take advantage of the holistic perspective that bioarchaeology brings to the study of human life and health in the past and its ability to yield information about the human context of disease and spatiotemporal variation thereof that can affect disease dynamics. Better integration of the fields will allow for investigations of syndemics in the past—i.e., analysis of the outcomes of the interaction of host characteristics (diet, health, genetic variation), sociopolitical and economic conditions, and infectious pathogen genomics and functional biology—in ways that inform our understanding of past epidemics and have practical, beneficial applications for living people.

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Annual Review of Anthropology

Volume 45, 2016

Contents

Anthropology of Language and Communicative Practices

Sociocultural Anthropology

Indexes

Errata

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