Morbidity in the Marshes: Using Spatial Epidemiology to Investigate Skeletal Evidence for Malaria in Anglo-Saxon England (AD 410–1050)

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ABSTRACT

Concerns over climate change and its potential impact on infectious disease prevalence have contributed to a resurgent interest in malaria in the past. A wealth of historical evidence indicates that malaria, specifically Plasmodium vivax, was endemic in the wetlands of England from the 16th century onwards. While it is thought that malaria was introduced to Britain during the Roman occupation (AD first to fifth centuries), the lack of written mortality records prior to the post-medieval period makes it difficult to evaluate either the presence or impact of the disease. The analysis of human skeletal remains from archaeological contexts is the only potential means of examining P. vivax in the past. Malaria does not result in unequivocal pathological lesions in the human skeleton; however, it results in hemolytic anemia, which can contribute to the skeletal condition cribra orbitalia. Using geographical information systems (GIS), we conducted a spatial analysis of the prevalence of cribra orbitalia from 46 sites (5,802 individuals) in relation to geographical variables, historically recorded distribution patterns of indigenous malaria and the habitat of its mosquito vector Anopheles atroparvus. Overall, those individuals living in low-lying and Fenland regions exhibited higher levels of cribra orbitalia than those in non-marshy locales. No corresponding relationship existed with enamel hypoplasia. We conclude that P. vivax malaria, in conjunction with other comorbidities, is likely to be responsible for the pattern observed. Studies of climate and infectious disease in the past are important for modeling future health in relation to climate change predictions. Am J Phys Anthropol 147:301–311, 2012.

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Grant sponsor: British Academy; Grant number: ref SG090361.

Received 14 July 2011; accepted 29 October 2011

DOI 10.1002/ajpa.21648
Published online 20 December 2011 in Wiley Online Library (wileyonlinelibrary.com).
(300–600 AD) and the Middle-Saxon warm period (700–800 AD) were significant climatic events occurring during this time, which resulted in flooding of the lowlands and warmer temperatures (Rippon 2000, 2010; Cracknell, 2005), potentially providing an ideal environment for mosquito abundance. Using geographical information systems (GIS), we conducted a spatial analysis of the prevalence of cribra orbitalia and, for comparative purposes, dental enamel hypoplasia (regarded as a non-specific indicator of poor health) in relation to geographical variables (geology and topography) and historically recorded distribution patterns of indigenous malaria and the habitat of its mosquito vector Anopheles atroparvus. Spatial epidemiology using mapping applications such as GIS enable accurate mapping and overlaying of many types of data (Pfeiffer et al., 2010) and are particularly useful for archaeological data; since, samples are smaller than in clinical contexts, thus contextualisation is required on a wide scale to investigate underlying etiological factors.

MALARIA AND SKELETAL REMAINS

Direct evidence: biomolecular

Direct evidence for malaria can only come from the identification of the relevant Plasmodium species DNA in the remains of past victims of the disease. The DNA of Plasmodium falciparum has been retrieved from the soft tissues of Egyptian Mummies (e.g., Taylor et al., 1997; Nerlich et al., 2008) and skeletal remains from a 5th century AD infant cemetery in Umbria, Italy (Salares et al., 2004). However, current PCR systems do not appear to be able to amplify routinely the DNA of malaria pathogens from ancient bones (Zink et al., 2002). For example, Pinello (2008) sampled 159 skeletons from areas of known malaria endemicity in later medieval England, but failed to retrieve P. vivax DNA. Pinello concluded that the structure and pathogenicity of P. vivax might prohibit its study from archaeological skeletal material using current biomolecular techniques.

Another potential avenue for direct diagnosis from skeletal remains is the use of immunological techniques. These seek to identify antigens produced in response to the malaria pathogen and are frequently used as a diagnostic tool in clinical contexts. Claims for the successful identification of P. falciparum using such techniques have been made from soft tissue samples obtained from an Egyptian Mummy (Bianucci et al., 2008) and on archaeological bones dating to 16th century Italy (Fornaciari et al., 2010). However, positive test results can occur in the absence of the pathogen due to a range of diagenetic and contaminant factors and a number of authors have raised serious doubts as to the reliability of these techniques when applied to archaeological bone (e.g., Brandt et al., 2002; Setzer, 2010).

Indirect evidence: skeletal

Cribra orbitalia refers to a condition that manifests as small holes (known as foramina) in the orbits of the skull. These foramina result from an expansion of the diploë (marrow hypertrophy) and a thinning of the outer cortex of the bone. A similar condition observed on the cranial vault is referred to as porotic hyperostosis, a term under which cribra orbitalia is sometimes subsumed. These lesions are commonly recorded in both child and adult skeletons from archaeological contexts.

The lesions in adult skeletons are believed to represent healed childhood episodes of the condition (Stuart-Mcadam, 1985, 1992).

For many years, cribra orbitalia has been interpreted as an indicator of iron deficiency anaemia resulting from poor diet, parasites, and/or a high pathogen load. Most interpretations of cribra orbitalia in past populations invoke a synergistic combination of all of these factors. Other conditions that result in a similar appearance to porotic hyperostosis are vitamin D or C deficiencies and infectious processes (Ortner, 2003; Lewis, 2007). In a histological study, Wapler et al. (2004: 336) noted that while 54.1% of macroscopically observed lesions in their study sample were associated with anaemia and hypertrophy of bone marrow, 32.4% were likely to have been produced solely through inflammation (osteitis). Diagnosis is also complicated by the interrelated nature of many deficiency diseases; for example folic acid deficiency will affect iron and vitamin C status (Fairgrieve and Molto, 2000). In such cases, it would be difficult to determine the precise etiology of cribra orbitalia lesions. Overall, therefore, there is the potential for misidentification of cribra orbitalia and misattribution of anaemia as being the sole agent of the lesions observed macroscopically in skeletal material.

While clinical literature in the 1960s and 70s reported radiological findings of porotic hyperostosis to be associated with iron deficiency anaemia (See, for example, Aksoy et al., 1966), it is now understood that only those anaemias linked to a significant and sustained increase in red blood cell production (erythropoiesis) can directly result in these lesions; iron deficiency results in suppression of the formation of marrow and new red blood cells and, therefore, cannot lead to porotic hyperostosis and cribra orbitalia (Walker et al., 2009, 111). Rothschild (2002, 609) has also argued that the hair-on-end sign (indicative of porotic hyperostosis) could only reflect “hyperregenerative marrow” and could not be attributed to chronic iron deficiency anaemia, since in this case “if there is inadequate iron for the production of blood cells, the marrow may actually be hypo-regenerative.” Rothschild (2002, 609) suggested that parasitic infection and hemorrhagic anaemia were among the causes of skeletal changes. Walker et al. (2009) consider both hemolytic and megaloblastic anaemias, the latter caused by vitamin B12 and B9 deficiencies, to have the potential to produce the levels of marrow hypertrophy necessary for macroscopic observations of porotic hyperostosis and cribra orbitalia (although this has been disputed by Oxenham and Cavill, 2010).

Clinical studies have observed that severe anaemia is one of the leading causes of morbidity and mortality in patients with malaria (Chang and Stevenson, 2004). Symptoms of malaria include cyclical fever and chills, headache, weakness, vomiting, and diarrhea. In vivax malarial patients, blood serum levels of magnesium, zinc and iron are significantly depleted (Balloch et al., 2011). The infection leads to hemolysis, the process of an abnormal breakdown of red blood cells that are subsequently removed by the spleen. When hemolysis exceeds the rate of erythropoiesis, an individual becomes anemic.

P. vivax parasites infect the immature red blood cells (reticulocytes) and generally cause long-term chronic infections and hemolytic anaemia but low mortality (Calton et al., 2008). In cases of malarial anaemia, the effects of hemolysis are further exacerbated by the accompanying dyserythropoiesis, where the production...
of new red blood cells is inadequate; bone marrow cells are increased but mature red cell output is insufficient (Abdalla and Pasvol, 2004: 63). Dyserythropoiesis results in the prolonging of anemia and is a frequently observed sequela of chronic malaria (Wickramasinghe and Abdalla, 2000; Abdalla and Wickramasinghe, 2004: 219). *P. vivax* parasites have a low biomass but studies have shown that for every infected red blood cell destroyed by *P. vivax*, ~32 noninfected red blood cells are removed from circulation (Anstey et al., 2009; Bassat and Alonso, 2011). Therefore, *P. vivax* causes severe hemolytic anemia in sufferers through a number of different mechanisms, including destruction of noninfected red blood cells, destruction of reticulocytes, and increased fragility of infected and noninfected red blood cells (Anstey et al., 2009: 221).

Megaloblastic morphological abnormalities of blood cells also occur as part of the dyserythropoietic process as a direct result of malaria infection (Abdalla and Wickramasinghe, 2004: 221). Of significance for studies of cribra orbitalia, these abnormalities cannot be differentiated from those caused by vitamin B12 or folate deficiencies (Abdalla and Wickramasinghe, 2004: 223–224).

In cases of chronic hemolytic anemia, marrow hyperplasia and reconversion from yellow to red marrow has been observed as a response to the hemolysis in an attempt to generate sufficient compensatory new red blood cells (Buckley, 2006). In nonadults, the conversion from red to yellow marrow is arrested. Radiological signs include a coarsened or accentuated trabecular pattern of bone marrow with widened medullary spaces and cortical thinning (Vigorita, 2008). The clinical literature regarding skeletal changes in response to malaria and associated hemolytic anemia is extremely sparse, although bone marrow is described as “extremely hypercellular” in chronic malaria (Pasvol and Abdalla, 2004: 44). There is no direct clinical evidence beyond marrow hyperplasia linking cribrotic lesions with *P. vivax*. This is because cribra orbitalia is not of significance in a clinical context and it is difficult to observe radiographically in living patients. Most discussion has been in the paleopathological literature. Angel (1966) first made the association between endemic malaria and high prevalences of porotic hyperostosis in the Mediterranean, although he initially suggested that thalassemia was responsible. Porotic hyperostosis is observed in genetic hemolytic anemias such as beta-thalassemia major and sickle cell disease. However, genetic anemia is rare in comparison to acquired anemia. Furthermore, the severity and distribution of the skeletal lesions associated with genetic anemias tend to be much greater than observed in acquired anemia, thus enabling these conditions to be differentiated in the paleopathological record. Hershkovitz et al., 1997; Lagia et al., 2007; Lewis, early view).

In conclusion, there is a clinically established association between *P. vivax* malaria, chronic anemia, and marrow hypertrophy. Previous paleopathological studies have noted an association between *P. falciparum* malaria (established using DNA) and porotic hyperostosis (Soren, 2003). The association between *P. vivax* malaria and hemolytic anemia has also been highlighted by Buckley (2006) in relation to porotic hyperostosis and cribra orbitalia in archaeological remains excavated from Polynesia. Furthermore, the clinical literature emphasizes the synergistic relationship between malaria and other infectious diseases, nutritional disorders and parasites, often termed “comorbidities” (Chang and Stevenson, 2004; Anstey et al., 2009), all of which are routinely implicated in the etiology of cribra orbitalia. It therefore seems highly probable that infection by *P. vivax*, in conjunction with other comorbidities, will produce the sustained increase in red blood cell production necessary to result in cribra orbitalia in skeletal remains. All other factors being equal, the prevalence of this condition should be higher in areas where malaria is endemic.

**MATERIALS AND METHODS**

A spatial epidemiological study of the skeletal remains was conducted to evaluate correlations between traditionally recognized nonspecific skeletal indicators of poor health (cribra orbitalia and enamel hypoplasia), geography, topography, and historically recorded evidence of outbreaks of malaria. A survey of Anglo-Saxon inhumation sites was undertaken using Historic Environmental Records (HERs) from 27 counties and district authorities in the east of England and these were mapped using GIS Arcview version 9.3 (Figs. 1 and 2). Subsequently, cribra orbitalia and, for comparison, enamel hypoplasia prevalence rates were collated from published and unpublished skeletal reports and linked to the survey data in the GIS database. The basic methodologies for recording the presence or absence of cribra orbitalia followed Brothwell (1981) or Stuart-Macadam (1991). For enamel hypoplasia, defects were most frequently recorded using Buikstra and Ubelaker (1994) and Brothwell (1981, 159). There will doubtless have been some interobserver variability in recording; however, because this study relies on presence/absence of lesions only, rather than degrees of severity, its impact should be minimal. The total number of sites for which cribra...
orbitalia crude prevalence rates (CPRs) were available was 46, comprising of the skeletal remains of 5,802 individuals. Sites were excluded where they contained fewer than 15 individuals and where bone preservation was notably poor. The basic age composition of the populations was also noted (Table 1).

Anglo-Saxon environmental and topographical data was extrapolated within a 2 km circumferential buffer zone for each site using British Geological Society official and bedrock geology digital map layers at 1:50,000 scale obtained through the EDINA geology digimap service. Slope data was obtained from the ShareGeo Open website (www.sharegeo.ac.uk) SRTM Slope DEM for Great Britain and was recorded for the central point of each site.

Historical data from a British Museum (Natural History) survey carried out in 1900 AD noting the locations of *Anopheles maculipennis* (now known as *Anopheles atroparvus*) mosquito in England was mapped on GIS (Lang, 1918). Since this early study was not systematic, these data were cross-referenced with a second contemporaneous survey of the distribution of “ague” in England (Nuttall et al., 1901).

**Spatial distribution**

**Methodology.** This study uses the general approach taken in clinical spatial epidemiological studies as outlined by Pfeiffer et al. (2010). The sample of 46 cribra orbitalia CPRs were mapped and tested for clustering or spatial autocorrelation (SA). SA is a measure of “the degree of spatial similarity observed among neighboring values” (Pfeiffer et al., 2010: 34). Ideally, true prevalence rates (TPRs) should be used in paleopathological research due to these rates accounting for differential

bone preservation across sites. Unfortunately, the sample of TPRs of cribra orbitalia gathered from the literature was too small to be used for SA investigation. Since CPRs can be affected by differential bone preservation, CPR values were statistically assessed against the known corresponding TPR values in the study sample using both Pearson’s r ($r^2 = 0.68$, two-tailed $P$ value is $<0.0001$) and Spearman’s Rank ($r^2 = 0.72$, two-tailed $P$ value is $<0.0001$) correlations (Fig. 3). These tests confirm that there is a highly significant correlation between the two datasets. Given that the majority of the population sizes are large and that populations of poor preservation were excluded, it is considered here that the CPRs should be reliable proxies for TPRs.

The distribution of sites was first analyzed to detect any spatial clustering irrespective of prevalence values using the average nearest neighbor tool in GIS (De Smith et al., 2007). The average nearest neighbor test calculates an index based on the average distance from each point to its nearest neighboring point. The nearest neighbor ratio was 0.93 with a $P$ value of 0.36 and a $Z$ score of $-0.914010$ (standard deviation), demonstrating that the selected sites were randomly distributed across the study area.

Due to the small sample size, only global estimates detecting first order effects in SA were made. A first order effect is defined as “one that produces a variation in point density in response to some causal variable” (De Smith et al., 2007). This is exemplified by environmental conditions acting as habitats for vectors that may cause disease. Second order effects are locally produced and are a measure of the interaction between neighbors and are used, for example, in the epidemiological analysis of contagious diseases (De Smith et al., 2007). Factors correlating with the spatial distribution of a disease, such as habitat, could however be placed in either category depending on the scale upon which the environmental variables are analyzed and how narrow an area a factor is confined to (Pfeiffer et al., 2010: 14).

In this case, global effects in cribra orbitalia CPR were calculated using Moran’s $I$ to assess the SA between attribute values in adjacent areas (Pfeiffer et al., 2010: 46). This method assumes heterogeneity of the distribution of the population and also requires a normal distribution of data. To meet these requirements prevalence rates have been used rather than raw counts so that there is no bias in skewed population distribution. The rates were transformed using square root values, the recommended method for transforming percentage rates have been used rather than raw counts so that there is no bias in skewed population distribution. The rates were transformed using square root values, the recommended method for transforming percentage rates between 0 and 30% (Gómez and Gómez, 1984: 307) and the resulting Gaussian distribution of the data was confirmed by carrying out the Kolmogorov-Smirnov test for normality ($KS = 0.12; P > 0.10$) and the Shapiro-Wilk test for normality ($W = 0.95; P = 0.05$). Moran’s $I$ was calculated using a zone of indifference weighting, so that the influence of points within a specified distance band were weighted more highly and that there was a sharp drop off in influence from those points laying outside the band. The appropriate distance band value was calculated by GIS by formulating $Z$ scores for a series of incremental band values of increasing distance from each point taking into account the values of its neighbors. This process identifies the maximum SA or maximum clustering of values. The value correlating with the last increase in those $Z$-scores (standard deviations) is the appropriate distance band value, in this case 61.1 Km.
Getis Ord General G and Gi* tests were also used to explore any clustering further and to identify clustering of high (hot spots) and/or low values (cold spots). These tests were run also using the zone of indifference weighting to ensure continuity in the conceptualization of spatial relationships and comparability with Moran's I.

**RESULTS**

The Moran's I global test of variation revealed a statistically significant level of SA of the cribra orbitalia CPR values (Z = 3.39; <0.001). Having identified a trend in SA, the distribution of values was analyzed using the Getis Ord General G and Gi* tests to identify hot or cold spots in clustering. The Getis Ord General G test indicated a statistically significant clustering of high values in the sample data (Z = 2.92; <0.01). Hot and cold-spots identified through the Getis Ord General Gi* test are illustrated in Figure 4. One statistically significant (P < 0.05; Z score > 1.96) hot spot is identified in the Cambridgeshire region and one cold spot (P < 0.05; Z score < -1.96) in the Northumbrian area.

To evaluate this distribution, some associated environmental factors potentially relating to the contrasting rates were analyzed. Northumbria is mainly hilly with a hard-rock coastline, whereas Cambridgeshire is flat and associated with the Fens, an open coastal lowland area greatly affected by marine and freshwater flooding in the past. Historically, the coastal lowlands are also known to have provided an ideal habitat for mosquitoes.

**Geographical factors associated with hotspots**

**Methodology.** The second part of this study aims to explore the relationship between geographical factors...
and the distribution of cribra orbitalia CPRs. In order to objectively quantify this relationship, the variables of slope, surface soil type and the historical presence or absence of the *A. atroparvus* mosquito were analyzed using spatial distribution and statistical analysis.

The 481 observations of *A. atroparvus* mosquitoes as collated by Lang (1918) were mapped and categorized where possible according to the frequency noted (Fig. 5). An interpolated map of the distribution of *A. atroparvus* was created (Fig. 6). Missing values were interpolated according to the average value of at least 10 nearest neighbor scores. Neighboring points were selected equally in all directions on the basis that spatial dependence was isotropic and weighted according to their proximity. This map ignores any constraints on mosquito abundance placed by the local environment or elevation and represents a “smoothed” version of the data at a national level. Although anopheles mosquitoes have been observed to fly only a maximum of 12 km, and more generally only 4.5 km (Kaufmann and Briegel, 2004: 140), it is likely that the extent of malaria is greater than that of the minimum extent of the mosquito habitat because people, animals and mosquitoes all migrate. In this context, the interpolation map is a useful indicator of the full extent of malarial transmission.

In Figure 6, observations of “ague” during the 19th century (Nuttall et al., 1901) have been overlain onto the interpolated map of *A. atroparvus* distribution to assess consistency between the two datasets. The distribution of “hot” and “cold” spots for cribra orbitalia values were subsequently overlain onto the interpolation map of *A. atroparvus* observations to examine any spatial correlations between prevalence and *A. atroparvus* distribution (Fig. 7).

The observations of the distribution of *A. atroparvus* mosquitoes collated by Lang (1918) were not the result of a systematic study but were merely a record of positive sightings, as Lang himself stressed. In order to more accurately define the locales most likely to present a suitable habitat for *A. atroparvus* mosquitoes, a 50 m resolution map was created based upon a query that searched for the full extent of superficial soil types containing the plotted points of *A. atroparvus* observation that were of a slope of less than 1° (i.e., of flat topography) over a 3 × 3 m² moving panel. Mosquitoes are weak fliers, generally reaching no higher than 5–6 m up...
from ground level, very often keeping much closer to
ground level (Service, 1971). This map represents, there-
fore, the minimum extent of the most likely areas of
mosquito habitats or wetland marsh (Fig. 8).

To quantify the relationship between cribra orbitalia
and the geographical variables, each Anglo-Saxon cemetery
site was subsequently scored as “Malarial” or “NonMa-
larial,” according to whether one or more 50m grid squares
positive for malarial habitat or an identified “malarial”
location point of historically observed “ague” fell within a 2
km buffer zone around each site (Table 1). Statistical anal-
ysis using a two tailed Fisher’s Exact Test was undertaken
to identify any meaningful correlation between “malarial”
and “nonmalarial” categorization and cribra orbitalia
CPRs. The same process was undertaken using dental
enamel hypoplasia CPRs to identify any similarity or dif-
fERENCE in environmental associations between the two
conditions. Where two sites were located within the same 2
km buffer zone and the geology types present were consist-
similarly different across the zone, an average was taken of the
CPRs for each buffer zone to maximize the population size
associated with each zone, thus helping to overcome any
inconsistencies in archaeological sampling and resulting in
a more representative prevalence rate. The final cribra
orbitalia CPRs and dental enamel hypoplasia CPRs were
categorized as above or below average for the purposes of the
statistical test (Dunn and Clark, 2009:141–164).

RESULTS

GIS spatial distribution mapping indicates a similar
distribution pattern in the historically observed locations
of “ague” outbreaks and the inverse distance weighted
interpolated map of A. atroparvus distribution in Eng-
land. It can be inferred from the overlap in distribution
that the two proxy measures for the likelihood of
malaria are reasonably reliable in assessing the extent
of historical malaria and malarial habitats in England.

The spatial distribution of the hot- and coldspots in
crebra orbitalia CPRs identified by the Getis Ord General
Gi* test plotted against the interpolated values of
A. atroparvus presence identifies the cribra orbitalia
hotspot as occurring in an area positive for A. atroparvus
and, thereby, “ague.” Conversely, the cold spot for cribra
orbitalia occurred in an area negative for A. atroparvus
and “ague.” An association between high prevalence
rates in cribra orbitalia and areas positive for A. atropar-
vus and, thereby, “ague” is demonstrated.

The Fisher’s exact test identified a statistically signifi-
cant association between areas identified as “malarial”
or “nonmalarial” (using the geographical factors of slope
and superficial soil types in association with the location
points of historically recorded A. atroparvus and Ague)
and Anglo-Saxon cemetery sites with above or below av-
erage cribra orbitalia CPR’s (two-sided P value = 0.0077). In contrast, no statistical relationship between
the “malarial” or “nonmalarial” cemetery sites and den-
tal enamel hypoplasia CPRs was observed (two-sided
P value = 0.7098).

American Journal of Physical Anthropology
DISCUSSION

The interpretation of cribra orbitalia lesions has long been a matter of debate in the paleopathological literature, mainly due to the lack of a clinical base from which to interpret them. Spatial distribution analysis of cribra orbitalia using GIS provides a new perspective from which to interpret these lesions. There is a similarity in spatial distribution between the historically recorded presence of the malaria vector *A. atroparvus*, “ague,” and the cribra orbitalia hotspots at a national level. Further, there is a statistically significant correlation between cribra orbitalia CPRs with more specific geographical locales, including the factors of slope and superficial soil types, suggesting that wetland populations had a lower health status than those in dryland areas. Individuals living in low-lying and Fenland regions exhibit overall higher levels of cribra orbitalia than those in nonmarshy locales, in particular, Northumbrian populations in areas of hard-rock coastline. The lack of any corresponding correlation between dental enamel hypoplasia and geographical location suggests that specific disease processes related to local environmental factors produced cribra orbitalia lesions, and were either distinct from or more sensitive to these factors than those producing dental enamel hypoplasia.

There are a few outliers of high values of cribra orbitalia that do not correspond to marshland environments, but this is to be expected given the vagaries of archaeological sample composition and more significantly, the range of etiological factors that cause these lesions. One such site (Marina Drive) is a small sample of a mid-late Saxon date with a relatively high proportion of nonadults (58.1%), which may partly explain the higher levels of cribrotic lesions observed here, since cribra orbitalia is often more frequently observed in nonadults. The quantification of cribra orbitalia prevalence rates may lead to paradoxical issues; a population of high comorbidity and health stress is likely to have a high rate of childhood mortality and archaeologically would be manifest in the presence of higher numbers of nonadults. To compare prevalence of cribra orbitalia per population, age-related mortality is not considered here, nor is the question of the extent to which morbidity provides a life-sustaining adaption to an environment and the extent to which this is represented by cribra orbitalia lesions. However, to ensure that there are not biases in the date presented here due to different proportions of nonadults/adults between the cemetery sites, an examination of the demographics between the “malarial” and “nonmalarial” populations was undertaken. There is no statistically significant difference in the proportion of nonadults (Unpaired t test \( P = 0.80 \)) and no age-related effects contributing to the correlation observed. A lack of higher numbers of subadults in the “malarial” populations may be explained by the fact that *P. vivax* infections are associated with low mortality but chronic morbidity. However, it is not possible to quantify sampling issues with regard to preservation and limited excavations, where nonadults are frequently observed to be under-represented (Buckberry, 2000).

Another factor for consideration is that this study rests on the assumption that individuals interred within Anglo-Saxon cemeteries, and the pathologies their skeletal remains display, are related to the local environment of the cemetery site. However, it is possible that any number of individuals interred in a particular cemetery migrated into the area after childhood, when it is generally accepted that cribra orbitalia lesions are formed. There is currently little scientific knowledge of Anglo-Saxon migration; we can only state that from the present limited isotopic studies, groups do appear to contain individuals of both local and nonlocal origins. Significantly, for cribra orbitalia prevalence, studies have indicated that subadults were most frequently local individuals (Montgomery et al., 2005).

The results of this study correspond to those by Gowland and Garnsey (2010) of cribra orbitalia and enamel hypoplasia in Roman Italy. Cribra orbitalia has long been recorded in particularly high frequencies in Mediterranean populations (Keenleyside and Panayatova, 2006; Walker et al., 2009) and is most often interpreted as resulting from an inadequate weaning diet and poor sanitation (e.g., Salvadei et al., 2001, Fucchini et al., 2004). Gowland and Garnsey (2010) found that sites with the highest recorded prevalence of cribra orbitalia coincided with marshy areas where malaria is believed to have been endemic. Likewise, no corresponding pattern was observed with respect to enamel hypoplasia. Gowland and Garnsey (2010) concluded that cribra orbitalia prevalence at many sites in Roman Italy were associated with acquired hemolytic anemia caused directly by malaria.

It should be recognized that the anemia of *P. vivax* malaria is complex in etiology. Contemporary research demonstrates that areas in which malaria is endemic contain a wide variety of coexisting diseases and are referred to as hotspots for comorbidity (see, for example, Kazembe et al., 2007). Many of these co-occurring diseases cause anemia as part of their own pathological
processes, and in addition may interact with and exacerbate malarial anemia in the individual (Anstey et al., 2009: 222). For example, the severity of anemia has been observed to increase with coinfection of intestinal parasites (Echeverri et al., 2003). However, although the importance of comorbidities in contributing to severe and fatal vivax malaria is likely to be underestimated (Da Silva Ventura et al., 1999; Fenn et al., 2005; Fernandez et al., 2008; Anstey et al., 2009: 225), malaria itself is believed to be the most common cause of severe anemia (Pasvol and Abdalla, 2004: 31).

During the Anglo-Saxon period, the dramatic flooding and later rise in temperature occurring as a result of changing climatic conditions would have created ideal habitats for mosquito abundance but concomitantly unstable and unsanitary living conditions for people, such as is seen in marginalized fishing communities today (Verduijn, 2000, Westaway et al., 2009). That the Fenlands were indeed a treacherous area of wetland during the Saxon period was recorded in the early eighth century in the Life of St. Guthlac;

“There is in the Midland district of Britain a most dismal fen of immense size, which begins at the banks of the river Granta not far from the camp which is called Gronte (Cambridge) and stretches from the south as far north as the sea. It is a very long tract, now consisting of marshes, now of bogs, sometimes with black waters overhung by fog, sometimes studded with woodland islands and traversed by the windings of tortuous steams.” (Felix’s Life of Guthlac, cited by Hill, 1981:11).

Adaptation to wetland environments during the Early and Middle Saxon period is thought to have involved a transient and seasonal pattern (Rippon, 2002: 58). Excavations of Anglo-Saxon settlements demonstrate that those dwelling on the Fen-edge, exploiting the fertile wetland and coastal lowlands, would have lived in wooden housing with earthen floors, in close proximity to livestock, with animals usually housed within the same dwelling (Carr et al., 1988). Surrounding areas of stagnant water and a relatively warm climate would also have provided an ample habitat for the mosquito A. atroparvus, especially where artificial reclamation may have extended mosquito breeding grounds (Sérandour et al., 2007). This mosquito has been shown to over-winter in dwellings in close proximity to their blood meals (humans or animals), thus usually infecting several inhabitants of the same domicile (Reiter, 2000; Huldén et al., 2005). The ability to thrive in the ever-changing marshlands is a testament to the resilience and ingenuity of the local populations. Nonetheless, reclaiming the wetlands would have been a hazardous occupation and would have presented a number of serious health risks to the resolute inhabitants.

Climate is a critical factor influencing infectious disease prevalence. Although archaeological skeletal data-sets are compromised by taphonomic factors as well as interpretational and etiological complexities, they provide our only means of analyzing this relationship over longer time-periods. By linking skeletal evidence with the increasing quantities of data available for past ecology and climate, we can essentially “populate” this environmental evidence and examine the impact of climate change fluctuations on the health and demography of past peoples. While we may be technologically far-removed from those living in the past, these data may provide an important dimension for modeling future health in relation to climate change predictions.

CONCLUSIONS

This research has used the techniques of spatial epidemiology in a paleopathological context to address the issue of morbidity in the wetlands in relation to the putative presence of malaria. The study has highlighted a number of important and significant methodological and interpretive findings, which may be summarized as follows:

1. There is a statistically significant correlation between cribra orbitalia prevalence and underlying geology and topography in eastern England.
2. There is no such correlation with enamel hypoplasia, indicating that it is not generalized health stress that resulted in the observed cribrotic lesions, but specific conditions that are causing acquired anemia.
3. There is a spatial correlation between elevated levels of cribra orbitalia and putative evidence for historically recorded A. atroparvus and malaria.
4. Environmental evidence indicates that temperature and precipitation in marshland areas during the early to mid-Anglo-Saxon period would have provided favorable breeding conditions for A. atroparvus.
5. We hypothesize that endemic malaria, in conjunction with related comorbidities, are responsible for the observed pattern of cribra orbitalia. These data potentially provide the earliest indirect evidence for malaria in England.
6. Future developments in biomolecular techniques may allow Plasmodium vivax to be detected directly in archaeological bone, but this is not yet possible.
7. Given the nonspecific etiology of many skeletal indicators of health stress a consideration of specific local conditions may ultimately aid in deciphering more context-specific etiological causes. Generalized interpretations that more often abound in the paleopathological literature are not always helpful in understanding the prevalence and distribution of these lesions.
8. Spatial epidemiological studies using GIS are not common in palaeopathology, but can be an invaluable tool for integrating historical, geographical, and paleopathological variables.

ACKNOWLEDGMENTS

For data and contextual information, the authors thank Abby Antrobus, Anthea Boylston, Victoria Brown, Jo Buckberry, Anwen Caffell, Andrew Chamberlain, Andy Chapman, Stephen Coleman, Elizabeth Craig, Nick Crank, Natasha Dodwell, Corinne Duhig, Holly Duncan, Naomi Field, Julia Habeshaw, Gail Hama, Betina Jakob, David Klinge, Tom Lane, Andrew Newton, Rose Nicholson, Natasha Powers, Charlotte Roberts, Brett Thorn, and Judith Walton. They would also like to thank all HER staff. The authors are extremely grateful to Tim Thompson, Andrew Millard, Graham Philip, Peter Rowley-Conwy, Mike Church, the editors at AJPA, and two anonymous reviewers for their insightful comments on earlier drafts of this article. All errors remain their own. This research was funded by the British Academy (ref SG090361).

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