Histological Identification of Syphilis in Pre-Columbian England

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ABSTRACT Microscopic analyses served to complement the macroscopic identification of venereal syphilis in two of four pre-Columbian skeletons from the site Hull Magistrates Court in England. Diagnosis was based on parameters presented by Schultz ([1994] Origin of Syphilis in Europe, Toulon: Centre Archéologique du Var, p. 63–67; [2001] Yrbk. Phys. Anthropol. 44:106–147; [2003] Identification of Pathological Conditions in Human Remains, New York: Academic Press, p. 75–109), which characterized venereal syphilis at a histological level. Observation of the microarchitecture of these samples allowed a more comprehensive approach to identification of the disease (processes). In most samples, Polsters and Grenzstreifen (or remnants of such structures) could be identified, suggesting the presence of a chronic, inflammatory disease such as venereal syphilis. Sinous lacunae were also observed in all histological samples, pointing to lytic activity (osteitis). The combination of both proliferative and destructive processes is pathognomonic for syphilis, and histological analyses provided a more accurate diagnosis of this infectious disease in these four individuals. As a result, the histological evidence suggests that venereal syphilis was present in England prior to 1492. This secondary form of evidence supports the macroscopic identification of the disease, and shows the power of a multimethodological approach to paleopathological diagnoses. Am J Phys Anthropol 129:559–566, 2006. © 2005 Wiley-Liss, Inc.

The origins of venereal syphilis have been passionately debated for centuries, but three hypotheses surrounding the emergence of syphilis have dominated the debate: the Columbian, pre-Columbian, and Unitarian. Generally, these hypotheses suggest that syphilis originated either in the New World (Crosby, 1969; Dennie, 1962; Goff, 1967; Harrison, 1959; Pusey, 1915, 1933) or the Old World (Cockburn, 1961; Hackett, 1963, 1967; Holcomb, 1937), or was present in both regions but evolved to accommodate different geographical and sociological environments (Hudson, 1963, 1965a,b, 1968), respectively. Each of these hypotheses has its merits, but only one should be the most consistent with the available data.

Of the four human pathogens, T. pallidum subspecies pallidum (venereal syphilis), T. pallidum subspecies endemicum (endemic syphilis or bejel), T. pallidum subspecies pertenue (yaws), and T. carateum (pinta), only the first three are important to paleopathologists, as they can alter bone. However, venereal syphilis has been called the Great Imitator, as both its clinical pathogenesis and skeletal alterations are quite similar to other diseases (e.g., tuberculosis, leprosy, hematogenous osteomyelitis, and Paget’s disease), especially when the whole skeleton is unavailable for observation. As a result, researchers need to depend on a number of analytical methods to help in the differential diagnosis. For convenience, when “syphilis” is used in the remainder of this text, only venereal syphilis and not endemic syphilis is being discussed. The aim of this study was to use histological methods of analysis to confirm a diagnosis of syphilis in four individuals from an English Medieval site.

Identification of syphilis in this study started macroscopically. This led to the need for a closer view of the histological appearance of the pathological skeletal elements in both pathological and nonpathological areas of the bones. A multiple methodological approach potentially provides better diagnoses of skeletal samples, both for the identification of disease and to assess the preservation of bone and its constituent parts. By using a top-down methodology, a more comprehensive view and a better understanding of how this infectious disease affects bone could potentially be ascertained.

The four skeletons used for this study originate from a cemetery site in Hull, Humberside, England (Hull Magistrates Court), dated between AD 1300–1450 via dendrochronology of the coffins, stratigraphy, and 14C (David Evans, personal communication). This study tests the hypothesis that venereal syphilis was present in the Old World prior to 1492 by diagnosis of pathological lesions.

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from Hull Magistrates Court. The secure pre-Columbian date, along with both macroscopic and microscopic identification of syphilis for some of the samples, helped provide further evidence that the pre-Columbian hypothesis can no longer be ignored. These findings are in accordance with other researchers who discovered human skeletal remains with treponemal disease in other Old World regions, dated prior to Christopher Columbus’ voyage in 1492 (Scotland: Cardy, 1997; Italy: Henneberg and Henneberg, 1994; Ipswich and Rivenhall, England: Mays et al., 2003; France: Palfi et al., 1992; Gloucester, England: Roberts, 1994; Kazakhstan: Schultz et al., 2003; Norwich, England: Stirland, 1991).

MATERIALS AND METHODS

The four skeletons (HMC94-SK0805, SK0932, SK1121, and HMC94-SK1216) used in this analysis came from burials excavated in 1994 (Evans, 2000) from a medieval Augustinian friary located on the Humber River on the east coast of England (Gillett and MacMahon, 1985), which is now the modern city of Kingston upon Hull (Fig. 1).

The age at death and sex information for these individuals from Hull was obtained from the original records documented by osteologists working on the site (Holst et al., unpublished Hull Magistrates’ Court draft report on the human skeletal remains), and confirmed by the primary author (Krogman, 1962; Loth and Iscan, 1989).

Histological thin sections were taken from visibly apparent pathological areas of individuals thought to have suffered from syphilis: the HMC94-SK0805 fibula, the HMC94-SK0932 proximal right humerus and an unidentified long bone fragment, the HMC94-SK1121 fibula and tibia, and two HMC94-SK1216 tibial fragments. Another important criterion we followed for sampling takes into consideration the destructive nature of this methodology. Areas were selected based on the least amount of damage that would ensue to the remains, and on ease of cutting (e.g., taking a piece from the end of an already broken bone, e.g., the HMC94-SK0932 unidentified long bone fragment). Ground thin sections of all bone samples were prepared in McMaster University’s Anthropology Hard Tissue and Light Microscopy Laboratory, following the protocol set out by Saunders and Pollet (1994). A brief explanation of the procedure is summarized here.

Approximately 1.5-cm sections of cortical long bone were cut from the original samples and cleaned with a solution of 90% distilled water and 10% Sandison’s fluid (95% ethyl alcohol, 1% aqueous formalin, and 5% aqueous sodium bicarbonate), followed by 100% distilled water in an ultrasonicator. Samples were then dehydrated in order to allow for proper embedding. Specimens were washed and placed in a desiccator and allowed to dry overnight. Next, they were embedded in a plastic resin (Epo-Kwick™ fast-cure epoxy and hardener, Buehler) and affixed to a glass slide with Thin Section Epoxy Part A and B™ (Hillquist).

The slide was allowed to dry for at least 24 hr, and another large cross-sectional cut was taken, leaving a very small thickness of embedded bone affixed to the slide. This was then ground and polished to a desired thickness (e.g., 30–50 μm) using Carbimet™ paper disks (320 grit) to allow for proper analysis under a light microscope. After the desired thickness was achieved, a coverslip was mounted onto the embedded specimen.

The prepared histological thin sections were observed at 100× magnification under a light microscope (Olympus BH-2), using polarizing filters. Photographs were taken with a mounted Polaroid digital microscope camera and imported into Adobe Photoshop 5.5 for analysis. A general assessment of bone quality was performed using a histological index designed by Millard (2001). This index ranks histological bone sections from 0–5, with the bottom of the scale (i.e., 0) signifying no original features identifiable except possibly Haversian systems, to the top of the scale (i.e., 5), where structures are very well-preserved and virtually indistinguishable from modern bone. The presence of a Maltese cross was also determined as a set criterion for observation, as it denotes good preservation of lamellae in osteon structures. Subsequently, the diagnostic criteria described by Schultz (1994, 2001, 2003) were used for assessment.

According to Schultz (1994, 2001, 2003, and references cited therein), criteria do exist for differentiating venereal syphilis from other specific and nonspecific inflammatory diseases when using light microscopy of ground thin sections of bone viewed under polarized light. Schultz (1994) states that the periosteal thickening of long bone shafts and the concomitant microscopic changes seen in venereal syphilis are a regular occurrence, most noted when the process of healing and remodeling of compact bone has not yet finished. The first criterion of Schultz (1994) is the presence of lines or band-like structures (“Grenzstreifen,” translated as “border stripes”) which separate the primary/original cortical bone from the active periosteal new bone layer laid down during bouts of infection (Fig. 1 in Schultz, 1994, p. 66; Schultz, 2001, p. 106). The next criterion is called the “Polster” (translated as “padding”). This structure represents pillow-like, polyp-like, or villous proliferations of very dense parallel lamellae found in the
highly thickened periosteal layer of cortical bone in the shaft of a long bone (Fig. 2 in Schultz, 1994, p. 67; Schultz, 2001, p. 107). Schultz (1984, p. 65) also suggests that syphilitic alterations of the microstructure of bone present with sinus resorption lacunae between the original bone surface and the newly calcified layers, but warns that these structures are also found in other nonspecific inflammatory diseases.

Unfortunately, with recent microscopic analyses of other paleopathological samples, some of the structures “indicative” of syphilis were shown to be present in other diseases. For example, Schultz and Roberts (2001) observed Polster-like and Grenzstreifen-like structures in histological thin sections of leprous bones. To differentiate, Schultz (2001, p. 126) stated that leprous Polsters are “rudimentarily developed and relatively flat” (Fig. 8E in Schultz, 2001, p. 127) in comparison to syphilitic Polsters (larger and more pillow-like, with organized lamellae).

The Grenzstreifen-like structures in leprous appear to be thinner (less lamellae) and will not show alterations in the subperiosteal bone or the endosteal bone or trabeculae (no osteoclastic changes in both) (Schultz, 2001, p. 128). Grenzstreifen-like structures can also be found in nonspecific inflammatory diseases (e.g., hematogenous osteomyelitis), but can be differentiated via their manner of production: syphilitic Grenzstreifen are band-like structures laid down in a very slow manner, creating a solid mass of newly built bone vs. an aggressive, rapidly laid down, and often disorganized (combination of newly built bone with old bone structures) appearance in nonspecific inflammatory diseases (Schultz, 2001). Grenzstreifen can also be observed in microscopic analyses of skeletal remains of individuals suffering from endemic syphilis. This discussion shows that there is a fine line between diagnosing syphilis and other infectious or inflammatory diseases.

RESULTS

Macroscopic observations

HMC94-SK0805. This is an edentulous male (approximately 40–61 years of age) with eburnation on most joint surfaces. The third to eleventh thoracic vertebrae are ankylosed as a result of ossified spinal ligaments. Osteoarthritis is present in the cervical and upper thoracic spine. All upper limbs (humeri, radii, ulnae, and clavicles) show osteitis and/or periostitis to varying degrees. All lower limbs (femora, tibiae, and fibulae) also show osteitis and/or periostitis, with the right fibula displaying an irregular topography produced by these two pathological changes. Even several metatarsals have spongy periostitis and osteitis.

HMC94-SK0932. This individual is a male, aged approximately 36–45 years. The remains are fragmentary, with no complete long bones. The observed frontal bone fragments have what appear to be healed remnants of caries sicca lesions. Carious lesions are present on several teeth, and the right first premolar is angled perpendicularly to the norm. The dorsal distal aspect of the left humerus has a large area of ballooned osteitis with some periostitis, while the anterior aspect contains spongy periostitis. Small areas of osteitis were also observed on the shafts of the left radius and ulna. The left femur and both tibiae present with extensive osteitis, with striated and spongy periostitis present only on the tibiae. Several areas of osteitis were also noted on the right fibula.

HMC94-SK1121. This individual is a 25–39-year-old female with slight cribra orbitalia in the left orbit. All upper limbs, including the scapulae and right clavicle, display areas of osteitis and/or periostitis. All lower limbs show signs of marked osteitis (irregular topography) and striated and spongy periostitis.

HMC94-SK1216. This individual is a young adult male approximately 17–25 years of age. No complete long bones exist for this individual. The skull presents with classic caries sicca lesions on the frontal bone. Most of the lesion is erosive, with several small areas beginning to heal. The left side of the nasal cavity contains spongy periostitis on the outer and inner rims. A symmetrical lesion of spongy periostitis, and possibly osteitis, can be found on the lower border of the mandibular body, just inferior to the molars. An erosive cloaca/sequestrum is present on the acromion process of the right scapula. The right clavicle has extensive periostitis at the midshaft region. The right and left humeri have areas of osteitis and periostitis at the distal dorsal ends of their shafts. The right and left radii, as well as the left ulna, have extensive osteitis and periostitis (spongy and striated) over most of their shafts, with several cloacae/sequestra (except for the right radius, with only two erosive holes which do not penetrate to the medullary cavity). These cloacae may be evidence of gummatus lesions often found in syphilis. The shafts of the femora, tibiae, and left fibula all show very extensive osteitis and periostitis (striated and spongy), with the presence of “snail tracks.” This excess osseous material has made these bones quite heavy.

Histological observations

Of the four specimens, observations of more than one area of the skeleton were completed for two individuals (HMC94-SK0932 and HMC94-SK1121). A summarized view of the results is presented in Table 1.

As seen in Table 1, preservation of osteological structures at the microscopic level is relatively poor for these samples. In fact, the majority of these samples show limited birefringence, and some even lack recognizable histological features under polarized light. Preservation of some samples is mixed within a single section, as is most apparent when comparing internal to external areas of bone. Only samples HMC94-SK0805 and HMC94-SK1121 illustrate the presence of well-preserved Havarian systems with lamellar bone, creating the Maltese cross under polarized light and lamellae within the different areas (i.e., interstitial, periosteal, and endosteal) (Fig. 2A,B). Specific alterations caused by diagenesis were observed for several samples. For example, microorganism focal destruction in the form of Wedl canals (described by Hackett, 1981) was observed in both samples of HMC94-SK0932 and in the fibula of HMC94-SK1121. Additionally, foreign materials (e.g., soil particulates, crystals) within lacunae and/or Havarian systems are visible in all samples. Fungal and/or microorganism intrusion of unknown origin is also present in several samples.

Red/brown staining of surfaces, both endosteal and periosteal (more prevalent), was observed to some extent in all samples (Fig. 2B, see color online version), which made observations of the periosteal surface difficult to record. This external staining is most striking in samples HMC94-SK0805 and HMC94-SK1121, which consequently have the best preservation of histological structures.
TABLE 1. Summarized results of histological analyses

<table>
<thead>
<tr>
<th>Sample</th>
<th>Histological index (Millard, 2001)</th>
<th>Preservation</th>
<th>Venereal syphilis changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMC94-SK0805 fibula</td>
<td>5</td>
<td>Maltese cross</td>
<td>Grenzstreifen</td>
</tr>
<tr>
<td>HMC94-SK0932 right humerus</td>
<td>2</td>
<td>Few</td>
<td>Unobservable</td>
</tr>
<tr>
<td>HMC94-SK0932 long bone, pathological</td>
<td>3</td>
<td>Medium</td>
<td>Unobservable</td>
</tr>
<tr>
<td>HMC94-SK1121 fibula</td>
<td>4</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HMC94-SK1121 tibia</td>
<td>4</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HMC94-SK1216 tibia fragment 1</td>
<td>1</td>
<td>For those observable osteons</td>
<td>+</td>
</tr>
<tr>
<td>HMC94-SK1216 tibia fragment 2</td>
<td>1</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

1 Histological index: 0, no original features identifiable, except that Haversian canals may be present; 1, Haversian canals present; small areas of well-preserved bone present, or lamellate structure is preserved by pattern of destructive foci; 2, some lamellate structure is preserved between destructive foci; 3, some osteocyte lacunae preserved; 4, bone is fairly well-preserved, with minor amounts of destructive foci; 5, very well-preserved, virtually indistinguishable from modern bone. Few, small number of observations; +, observable; +?, possible presence; –, none observed.

As previously mentioned, the lack of good osseous preservation led to some difficulties in discerning microscopic structures indicative of syphilis. However, several samples provide histological appearances that point to chronic, episodic, osteoclastic, and osteoblastic processes characteristic of syphilis. For example, Grenzstreifen and/or cement lines separating the original compact bone from the newly built bone were tentatively observed in the HMC94-SK0805 fibula (Fig. 2A) and tibial fragment 1 of HMC94-SK1216 (Fig. 2C), but were confidently identified in the HMC94-SK1121 fibula (Fig. 2D,E). Sinous lacunae were also identified within the Grenzstreifen for the HMC94-SK1121 fibula. Polsters were also tentatively observed in HMC94-SK0805 (Fig. 2A) and HMC94-SK1216 tibia fragment 1 (Fig. 2C), but were confidently identified in the HMC94-SK1121 fibula (Fig. 2F) and tibia (Fig. 2G–I) when using the criteria of Schultz (1994). Those Polsters identified in HMC94-SK1121 bone samples contain densely packed lamellae, indicative of this structure.

Some general trends indicative of abnormal processes caused by inflammation were also noted in these histological sections. Areas of focal destruction (i.e., osteoclastic) were observed in all sections (e.g., HMC94-SK0805 in Fig. 2B, and HMC94-SK1216), and the long bone pathological lesions of HMC94-SK0932 (Fig. 2J) and HMC94-SK1216 tibial fragment 2 (Fig. 2K) are excellent examples of the mixture of both the destructive and proliferative processes known to syphilis.

**DISCUSSION**

Multiple lines of evidence in support of a hypothesis are fundamental in physical anthropology, especially paleop...
Differential diagnoses of macroscopic observations

It must be recognized that when other infectious diseases (e.g., tuberculosis) are ruled out in the differential diagnoses of individuals in this study, treponemal diseases (i.e., yaws and endemic syphilis) other than venereal syphilis are still important alternative diagnoses. However, when climate and geography (latitude and longitude, and rural vs. urban environment) are considered, it is more likely that these individuals suffered from venereal syphilis rather than other treponematoses. Yaws today is a disease that affects people living in a tropical/subtropical humid area with a warm climate, and endemic syphilis is more common in temperate and subtropical nonhumid rural areas of the world (Aufderheide and Rodríguez-Martín, 1998); there is no evidence that either of these environments existed in Hull in the Medieval period, and so it is highly unlikely that either condition affected these indi-
individuals, unless they were migrants from some other parts of the world. Current research is exploring this possibility.\(^2\)

Since caries sica is a distinctive indicator of syphilis (Hackett, 1975), no differential diagnosis is needed for HMC94-SK0932 and HMC94-SK1216. Additionally, caries sica, in combination with the involvement of multiple bones in the postcranial skeleton in the form of both proliferative and destructive lesions, also lends itself more to the diagnosis of venereal syphilis than any other disease.

Diffuse response to infection, which may be of a nonspecific nature, was noted by the presence of periostitis and osteitis for all upper and lower long bones of individual HMC94-SK0805. This individual also presented with several ankylosed thoracic vertebrae, which may be diagnosed as diffuse idiopathic skeletal hyperostosis (DISH) due to its appearance (similar to “dripping candle wax,” i.e., smooth calcification of bone), its positions on the spine (antero-laterally to the right side), and the greater age of the individual (Aufderheide and Rodriguez-Martin, 1998).

The presence of this manifestation does not exclude a diagnosis of syphilis in other regions of this individual, as the specific cause of DISH is unknown (but see Rogers and Waldron, 2001). Involvement of the metatarsals may suggest leprosy, but since the lesions in this area of the skeleton are more proliferative (periostitis), leprosy can be ruled out, as it usually causes more destruction.

Individual HMC94-SK1121 presents with cribra orbitalia, which may be caused by a nutritional deficiency and/or infection (Stuart-Macadam, 1992). Infection is prevalent in this individual, as all upper and lower long bones are affected by periostitis and/or osteitis to such an extent that in some cases, the topography of the bone is completely altered. These characteristics help to rule out tuberculosis (normally destructive) and hematogenous osteomyelitis (normally involving one bone), and are more characteristic of syphilis.

**Histological identification of syphilis**

Differential diagnoses can be more definitive with the addition of microscopic analysis. When this additional approach was applied to sections of bone from the skeletons in this study, their microarchitecture showed both proliferative and osteolytic processes in the forms of periostitis, osteitis (compact bone involved), and osteomyelitis (medullary cavity involved), which are indicative of an inflammatory process. Although Polsters and Grenzstreifen are also supposedly present in leprosy and hematogenous osteomyelitis (normally involving one bone), and are more characteristic of syphilis.

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2However, there have been claims of endemic syphilis in temperate regions (e.g., Jehreen, 2001).
not a static entity. For example, it was observed that some of the Polster formations in the tibia and fibula of HMC94-SK1121 contained Haversian canals (Fig. 2F,G). In this same individual, several Polsters were enveloped by new bone proliferation (e.g., Fig. 2I), making their identification difficult, as they were no longer distinct extensions of the periosteal surface. Generally, the presence of osteons and osteoblastic activity points to a sufficient lapse of time allowing for remodeling. The presence of osteons is only very briefly introduced by Schultz (1994, p. 65) when he states, "It seems that, in the cases of syphilitic inflammation, bone remodeling could also produce newly built Haversian systems. However, this could only be possible, if active disease is no longer in progress." In a later publication, Schultz (2001, p. 128) stated that the microscopist will see "vestiges of an extensive remodeling process" as the disease progresses, but does not provide the reader with examples of such occurrences. As a result, most of the criteria of Schultz (2001) are based on active forms of treponemal disease that are not indicative of the range (i.e., from active to latent to healed) that paleopathologists and/or histopaleopathologists come across when observing skeletal lesions in the archaeological record. Since syphilis is such a prolonged disease with many stages, it seems imperative that a discussion of chronic, prolonged exposure to inflammation be addressed.

As pointed out earlier, Polsters are not just indicative of syphilis, but can also be found in endemic syphilis, leprosy, and hematogenous osteomyelitis (Schultz, 2001). Schultz (2001, p. 126) contrasted the latter two with treponemal infection by their slight difference in morphology. It is these authors' belief that any disease which entails episodes of inflammation or infection, and is of a chronic relapsing nature, will present with similar bony reactions, especially when an increase in vascularization occurs. This was identified by Schultz (2001) when he acknowledged that endemic syphilis also manifests Polsters and Grenzstreifen. It is also believed that further, more extensive histological research will reveal that yaws also presents with these formations. As a result, histology should never be used as a first line of evidence, but instead, in concert with other forms of proof to provide a more thorough and accurate diagnosis.

As summarized in Table 1, poor histological preservation and hence diagenesis were at issue when observing several of the samples. Researchers must be aware of these processes in order to understand why the histomorphological (as well as chemical and molecular) nature of bone has been altered. The presence of Wedl canals reveals invasion by microorganisms of the bone (Hackett, 1981), and infiltration of lacunae with crystals, fungi, and other unknown debris provides prime opportunities for osseous destruction, which is quite apparent in some of these samples. However, even with the effects of diagenesis, some general observations (e.g., an overall increase in osteoclastic and osteoblastic reactions) were still deemed possible, and helped provide evidence of an inflammatory process at the microscopic level.

A noted visible red/brown staining found in thin sections of HMC94-SK0805 and SK1121 is believed to be attributable to the tannins in vegetable dyes used in the over-garments and their reaction with the surrounding soil (alluvial warp clays). Discoloration of coffin wood from textile contact was also noted for several other burials at the Hull Magistrates Court site (David Evans, personal communication). However, without any chemical and mineral analyses of the soil, it can also be hypothesized that the discoloration may be the result of iron compounds. It has been noted by Schultz (2001, p. 117–118) that osseous contact with iron can enhance bone preservation, which is interesting, since those thin sections most affected by the staining were also the best preserved for this sample set.

CONCLUSIONS

Since the inception of the three main theories of the origins of syphilis, evidence for and against them has been rather common. Skeletal evidence from recent excavations in Europe was able to push back the clock concerning a pre-Columbian presence of syphilis in the Old World. As excavations continue around the world, it is believed that more evidence will be garnered which clearly shows the presence of syphilis or treponemal precursors prior to 1492.

Bone alterations allow paleopathologists to identify disease in the past. However, some manifestations will mimic several diseases. When uncertainty arises in the diagnosis, it is recommended that a microscopic approach be used to differentiate disease processes. In fact, microscopic analyses served to complement the macroscopic identification of syphilis in these historic skeletal samples from England. The diagnosis was based on histological parameters presented by Schultz (1994, 2001, 2003) and those believed by the authors to resemble syphilis during the chronic state. In most samples, Polsters and Grenzstreifen, or remnants of such structures, could be identified, suggesting the presence of a chronic, inflammatory disease such as syphilis. Sinous lacunae were also observed in all histological samples, pointing to lytic activity (osteitis). The combination of both proliferative and destructive processes in certain regions of the skeleton is pathognomonic for syphilis, and lends itself to a better diagnosis of this infectious disease within these individuals. It must be pointed out that a diagnosis of syphilis at the microscopic level is supported for two individuals (HMC94-SK0805 and HMC94-SK1121), but only if the variations observed in this study are in line with what may be expected for the disease in a chronic state. This statement should be read as tentative, because the paleohistopathological literature (which is primarily based on active forms of the disease) does not provide guidance for observing the variations of Polster and Grenzstreifen structural formations. This is especially so for features related to the different stages of infection (i.e., acute or chronic) or even development (e.g., active, latent, or healed). Observations in this study revealed that these histological structures are localized and variable in size and shape, and can be changed or hidden by the dynamic nature of bone remodeling. More studies which use bone microscopy to identify diseases, particularly treponemal diseases, will eventually fill this void and provide a better database for comparison.

Microscopic evidence of syphilis in these individuals ultimately increases the paleopathological methodological repertoire, which can be used as a basis for comparison for future histological studies. In addition, it illustrates the fact that a range in variation for both size and shape does exist in the presentation of the characteristic structures (e.g., Polsters and Grenzstreifen) associated with treponemal infection. Finally, by illustrating the presence of treponemal disease via both macroscopic and histological approaches, we can confidently state that this infectious disease was in the Old World prior to 1492.
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LITERATURE CITED


