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# The Origin and Antiquity of Syphilis Revisited: An Appraisal of Old World Pre-Columbian Evidence for Treponemal Infection

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*ABSTRACT* For nearly 500 years, scholars have argued about the origin and antiquity of syphilis. Did Columbus bring the disease from the New World to the Old World? Or did syphilis exist in the Old World before 1493? Here, we evaluate all 54 published reports of pre-Columbian, Old World treponemal disease using a standardized, systematic approach. The certainty of diagnosis and dating of each case is considered, and novel information pertinent to the dating of these cases, including radiocarbon dates, is presented. Among the reports, we did not find a single case of Old World treponemal disease that has both a certain diagnosis and a secure pre-Columbian date. We also demonstrate that many of the reports use nonspecific indicators to diagnose treponemal disease, do not provide adequate information about the methods used to date specimens, and do not include high-quality photographs of the lesions of interest. Thus, despite an increasing number of published reports of pre-Columbian treponemal infection, it appears that solid evidence supporting an Old World origin for the disease remains absent. Yrbk Phys Anthropol 54:99–133, 2011. ©2011 Wiley Periodicals, Inc.

As Naples fell before the army of Charles VIII in 1495, a plague broke out among the French king's troops. Today, it is generally agreed that the disease described by contemporary writers was the first recorded epidemic of syphilis (Crosby, 1972; Quétel, 1990). When the army, composed largely of mercenaries, disbanded shortly after the invasion, the troops returned to their homes and disseminated the disease (Williams et al., 1927; Brown et al., 1970). By 1500, it was widespread across Europe (Pusey, 1933). Because the epidemic had emerged shortly after Columbus's return from the voyages of discovery, the theory that Columbus's crew had contracted the disease in the New World and brought it back to the Old World arose in popular and medical literature by the early 16th century. Some chroniclers also stated that the crew had shown symptoms of a novel disease and that an affliction resembling syphilis had been present on the island of Hispaniola from "time immemorial" (see Fernandez de Oviedo y Valdes, 1526; Las Casas, 1530; Díaz de Isla, 1539). The theory of a New World origin for syphilis remained popular for the next four centuries.

Serious doubts about this theory have been raised, however. Some critics argued for the pre-Columbian presence of syphilis in the Old World (Holcomb 1934, 1935). Others suggested reformulations of the New World origin theory (Crosby, 1969) or proposed sites of origin outside of Europe and the Americas (Livingstone, 1991). Over the past five centuries, the geographic and chronological origins of syphilis have remained subjects of vigorous debate in disciplines as diverse as physical anthropology, history, and microbiology (Meyer et al., 2002).

Because of concerns with the bias and incompleteness of documentary and ethnographic data, primary evidence—skeletal material and its specific context—plays a pivotal role in research seeking to elucidate the origin and antiquity of syphilis (Roberts, 1994; Siena, 2005). Unlike many other infectious diseases, syphilis and two closely related but nonvenereal diseases, yaws and bejel (endemic syphilis), generate distinctive lesions on the human skeleton (Hackett, 1976; Ortner, 2003). The body of evidence for treponemal disease in the archaeological record has, not surprisingly, increased over time as more and more skeletons have been recovered and studied. In the New World, several pre-Columbian cases had been documented by the early 20th century (Jones, 1876; Hrdlička, 1922; Williams, 1932; Haltom and Shands, 1938; Bullen, 1972), though these were scarce and in

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many cases their diagnosis was doubtful (Stewart, 1973; Hackett 1976; p 114; El-Najjar, 1979; p 616).[1] Since then, a growing number of cases have been unearthed in the Americas, several of which date to as early as 7,000 years BP (Powell and Cook, 2005a; Hutchinson and Richman, 2006). Some New World sites boast an estimated prevalence for treponemal disease of up to 50% (Cook, 1984; Powell, 2003). The high prevalence and youth of many of the affected skeletons, however, is inconsistent with a sexually transmitted form. Instead they suggest the presence of an endemic form similar to modern yaws or bejel (Baker and Armelagos, 1988).

In 1988, Baker and Armelagos performed a comprehensive review of the reported cases of treponemal disease in the New and Old Worlds. They documented an abundant, indisputable body of pre-Columbian New World finds—which has since been reaffirmed by Powell and Cook (2005a)—but a striking absence of Old World pre-Columbian finds. In the intervening decades, a steadily increasing number of cases of treponemal disease from the pre-Columbian Old World have been reported in the published literature. Many researchers have argued that these cases establish the antiquity of treponemal disease in the Old World (Dutour et al., 1994a; Brothwell, 2005). However, in contrast to Powell and Cook's (2005a) standardized evaluation of the New World evidence, the Old World finds await a critical review. Twenty-three years after Baker and Armelagos, this analysis revisits and reevaluates published skeletal evidence for treponemal disease in the pre-Columbian Old World. In the interest of approaching paleopathology as a scientific endeavor (e.g., Powell and Cook, 2005a; Rothschild, 2005), published cases of treponemal disease from Old World pre-Columbian archaeological sites were evaluated against standardized, preestablished, and explicit original criteria for the diagnosis of treponemal disease and the determination of dating. We present the results of this evaluation and discuss their implications for the origin and antiquity of syphilis.

## BACKGROUND

### Theories on the origin of syphilis

There are three primary explanations for the evolutionary history of *Treponema pallidum* ssp. *pallidum*, the bacterium that causes syphilis: the Columbian, pre-Columbian, and Unitarian. Though there are other, less well-known theories (e.g., Livingstone, 1991; Andre, 1994), we deal here only with the three major ones; of these three, the first two are the most accepted (see Meyer et al., 2002).

The "Columbian hypothesis" originated in 16th century Spanish accounts, as described in the introduction, and was popularized by Crosby (1969). It proposes that syphilis originated in the New World and was transmitted to the Old by Columbus in the 1490s. This is supported by 15th and 16th century accounts attesting to syphilis's rapid spread and extreme virulence in the early years of the epidemic, which some have argued suggests a novel infectious disease set loose on virgin populations (Hudson, 1963; Knell, 2004).

In contrast, the "pre-Columbian hypothesis" asserts that treponemal disease was present in the Old World before the 1490s (Holcomb, 1934, 1935; Hackett, 1963, 1967). It was either very mild or not distinguished from other bone-remodeling diseases, particularly one known as "venereal leprosy" (Buret, 1891; Sudhoff, 1925; Castiglioni, 1941; Hudson, 1961, 1964; Hackett, 1963). According to this theory, historical accounts indicating the emergence of a new disease in the 15th century can be attributed to an increase in the disease's virulence (Waldron, 2009) or to improved medical and lay recognition of syphilis (Steinbock, 1976), possibly because of the introduction of the printing press or an especially virulent New World strain (El-Najjar, 1979; Kampmeier, 1984). Several researchers have given this explanation a biocultural and evolutionary twist by proposing that sexually transmitted treponemal disease evolved in response to the social, cultural, and environmental changes that humans have experienced since the Pleistocene, such as increased population density and urbanization (Brothwell, 1981; Cockburn, 1961; Hackett, 1963; Willcox, 1972).

According to the "Unitarian hypothesis," the treponematoses are environmentally determined expressions of "a single and extremely flexible disease," with syphilis being a product of improved hygiene, which hindered the skin-to-skin transmission of the endemic treponematoses, as well as lax urban sexual mores (Hudson, 1963, 1965). Following early critique (Hollander, 1981; Morris, 1988), this theory was discredited by genetic evidence which shows that the three treponemal subspecies are genetically distinct and have evolved along different trajectories (Centurion-Lara et al., 2006; Gray et al., 2006; Harper et al., 2008a,b; contra Mulligan et al., 2008).

### Diagnosis

Choosing among these theories requires 1) recognizing treponemal disease in the skeleton; and 2) distinguishing between the skeletal lesions caused by each of the treponemal variants. These requirements are complicated by two limitations. The three treponemal syndromes manifest with very similar lesions (Powell and Cook, 2005b). Moreover, in most cases the skeletal lesions caused by the treponematoses are not even specific to this family of diseases. Both limitations are attributable to the skeleton's limited array of physiological responses to insult. Essentially, the skeleton can respond only with resorption, proliferation, and/or abnormalities in the growth and formation of bone. This means that different diseases can affect the skeleton in very similar ways. Below, we consider each complication individually, discussing its implications for the ability to distinguish among competing hypotheses.

We start with the ability to differentiate among the three treponemal syndromes using dry bone. Considerable overlap in lesion type, distribution, and frequency between the variants has been reported for modern human populations in the biomedical literature (Ortner, 2003). Some researchers argue that the variants are merely very difficult to distinguish in dry bone (Steinbock, 1976; Anderson et al., 1986). Potential differences in the types of treponemal lesions, their distribution across the skeleton, and the frequency with which they occur in the three variants have been reported (e.g., Steinbock, 1976; Zimmerman and Kelley, 1982). Some of these have been incorporated into a method for differentially diagnosing the treponematoses in the archeological record known as SPIRAL (Rothschild and Rothschild, 1995). However, the basic assumptions of SPIRAL have

[1]A discussion of the history of research on syphilis within the field of paleopathology can be found in Buikstra and Cook (1980) and Cook and Powell (2006).

met with criticism (Heathcote et al., 1998; Cook and Powell, 2005). To the best of our knowledge the method has also not been independently tested (but see Rothschild and Rothschild, 1997, 1998; Rothschild et al., 2000; Rothschild, 2005), and many researchers maintain that the diseases are indistinguishable on the basis of lesions in dry bone (Rokhlin and Rubasheva, 1938; Hudson, 1958; Hackett, 1976; Webb, 1995; Ortner, 2003). Epidemiological differences between the diseases, such as mean prevalence and age of infection, have been tentatively employed in the analysis of large skeletal samples (Cook, 2005; Powell and Cook, 2005a; Powell et al., 2005). However, it should be noted that even if population-level characteristics of the diseases were firmly established, they would be insufficient for making a diagnosis with any certainty in individual cases (Mays et al., 2003) or small groups of skeletons in the archaeological record (Ortner, 2003).

Without doubt, the ability to successfully identify venereal syphilis in the pre-Columbian Old World would be ideal for resolving the debate over its origin and antiquity. However, with no reliable, evidence-based method of distinguishing between the treponemal diseases in skeletal remains, we make no attempt to assign a specific cause. On the one hand, this limits the specificity of the conclusions that can be drawn. While one can state there is evidence of pre-Columbian treponemal disease in a sample, one cannot state that there is evidence of syphilis. On the other hand, and more importantly, this policy ensures that the conclusions drawn do not extend beyond the data.

The second limitation, that most lesions caused by the treponemes are not specific to this family of diseases, is also difficult but more manageable. Differential diagnosis between treponemal disease and other insults, infectious and otherwise, is complicated by a host of factors. There is the limited range of physiological responses that bone is capable of, already mentioned. While lesions that can be used to diagnose treponemal disease do exist, they are rare. Overall, skeletal involvement occurs in only 1–20% of cases of treponematosis (Aufderheide and Rodrìguez-Martìn, 1998), depending on the specific disease, and diagnostic lesions account for few of the total observed. Lesions can also vary in appearance based on their state of healing, the individual's immune response to the pathogen, the duration of active infection, and whether coinfection exists (Mays, 1998; Ortner, 2003). In addition, many skeletons of individuals afflicted with treponemal disease will be represented in the archaeological record by only a bone fragment or a single skeletal element, making a definitive diagnosis challenging and often impossible (Merbs, 1992).

These issues have consistently complicated studies that attempt to use skeletal evidence to trace the antiquity of treponemal disease and have fueled the debate over the existence of Old World, pre-Columbian treponemal disease (Powell and Cook, 2005b). Luckily, however, an evidence-based system of recognizing *Treponema*-specific skeletal lesions is available, as discussed in the next section. Though most cases of treponemal disease throughout history will not produce such lesions, in geographic regions where the diseases were present, and where large skeletal samples have been recovered and analyzed, a number of individuals with pathognomonic lesions should be evident, as is the case in the New World (Baker and Armelagos, 1988; Powell and Cook, 2005a).

***Skeletal lesions specific to acquired[2] treponematosis.*** Treponemal disease manifests in three stages: primary, secondary, and tertiary. In all stages, tissue damage is believed to be caused by both localized and systemic inflammation (LaFond and Lukehart, 2006; Radolf and Lukehart, 2006). However, distinctive skeletal lesions occur only in the tertiary stage. Primary infection rarely involves the skeleton, producing only mild, nondiagnostic lesions: periosteal reactions or subperiosteal bone deposition (e.g., Ehrlich and Kricun, 1976; Meier and Mollet, 1986; Hoeprich, 1994). Secondary stage infection also produces periosteal reactions, as well as osteitis, or inflammation of the inner structures of bone, though both often heal spontaneously and completely remodel (Hazen, 1921; Ortner, 2003; Powell and Cook, 2005b; but see Rothschild and Rothschild, 1995). Tertiary infection involves periosteal reactions, osteitis, and osteomyelitis, an infection originating in the marrow. Some individuals also manifest gummata, focal necrotizing lesions that may be caused by a hyper-allergenic response to treponemes or their antigens (Jaffe, 1972; Resnick and Niwayama, 1995; Musher and Baughn, 1998; Salazar et al., 2002).

Tertiary lesions can appear in many forms, but they are characteristically bilateral and systemic. They predilect a range of skeletal elements, including long bone shafts, ribs, the sternum, scapulae, the medial portions of the clavicles, the cranium, and the hands and feet. Excessive periosteal deposition can cause pseudo-bowing of the tibia (saber shins, boomerang leg), and less commonly, the radius and ulna (Hackett, 1936). Joint involvement, such as Charcot's joints, which are often accompanied by a dramatic proliferation of new bone (Todd, 1926; Resnick, 1988; Reginato, 1993), and arthritis have also been documented in the clinical and archaeological record (Rost, 1942; Sengupta, 1985; Yakinci et al., 1995). Cranially, treponemal disease can cause palatal perforation and rhinomaxillary destruction (gangosa), periosteal reactions on the maxilla (goundou), and *caries sicca* on the cranial vault (Csonka, 1953; Murray et al., 1956; Taneja, 1968; Hoeprich, 1994). This latter lesion develops in a sequence; over time, gummatous focal destruction, necrosis, pitting, osteitis, and excessive sclerosis, or healing, can produce a grossly thickened cranial vault covered in confluent pits and radially grooved stellate scars, which can take on a "worm eaten" appearance (Hackett, 1976; Steinbock, 1976; Ortner, 2003). There are six progressive stages in the *caries sicca* sequence: the initial lesions of clustered pits which lead to confluent pits, progressing to focal superficial cavitation, serpiginous cavitation, nodular cavitation,[3] and eventually, with extensive sclerosis, to classic *caries sicca* (Hackett, 1976, 1981).

As the treponematoses have such a varied effect on the skeleton, establishing which lesions are specific to them has been historically problematic. In this study, we follow the guidelines established by Hackett's (1976) seminal work, in which skeletons of clinically diagnosed cases of treponemal disease, cases of other pathological conditions, and healthy controls were compared. To date, this is the only published study wherein the specificity of various skeletal lesions to treponemal disease was rigorously tested, and it revealed two diagnostic

[2]Noncongenital.

[3]Serpiginous cavitation and nodular cavitation are also known as circumvallate cavitation (Hackett, 1976).

markers. The first are the final three stages of the *caries sicca* sequence, long believed to be diagnostic of treponemal disease (Virchow, 1858, 1896; Williams, 1932; Stokes et al., 1944; Goff, 1967): serpiginous cavitation, nodular cavitation, and *caries sicca*. The lesions found in the first three stages of the *caries sicca* sequence were deemed only suggestive of treponemal disease, as they are also found in other conditions. The second diagnostic feature is the combination of osseous expansions and nodes with superficial cavitations on the long bones. Expansion of a bone, resulting in cylindrical or fusiform enlargement, is caused by florid new bone deposition, often because of osteitis. It can involve the whole circumference of a long bone. Nodes are localized enlargements from remodeled sub-periosteal deposition, which can be small (4–5 cm) or involve up to half of a skeletal element. In the diagnostic form, these are combined with superficial cavitations, or shallow lytic pitting on the surface of a bone. Hackett found that variations upon this pattern that lacked the superficial cavitations—both rugose and finely striated nodes and expansions, and coarsely striated and pitted expansions on long bones—were not diagnostic but instead strongly suggestive of treponemal disease. Hackett (1976; p 79–93) thus denoted these as "on trial" characteristics. Other lesions documented in treponemal cases, such as tibial pseudo-bowing and striated cortical expansions were also shown by Hackett, and later by Webb (1995), to be nonspecific for treponemal disease. Therefore, in this study the only two macroscopic features considered diagnostic of treponemal disease were the later stages of *caries sicca* and nodes with superficial cavitations.

Some recent studies have asserted that microscopic indicators are also useful in diagnosing treponemal disease. These microstructures include polsters, pillow-like structures of newly built bone found on the cortex of long bones shafts, and grenzstreifen or grenzlinie, band-like structures which divide the original cortex from newly deposited bone, such as polsters (Schultz, 2001). These features are certainly useful for distinguishing between treponemal lesions and pseudopathologies caused by taphonomic processes (Schultz, 2003). However, in the single study performed to assess their specificity to date, grenzlinie were identified in cases of osteomyelitis and leg ulcers, and polsters were identified in non-syphilis related periosteal reactions (Weston, 2009). These structures have also been reported in leprosy (Blondiaux et al., 2002). Therefore, we did not employ them as diagnostic indicators of treponemal disease.

For the purposes of this study, we assume that the lesion types associated with treponemal disease have been fairly constant throughout history. Certainly, infectious diseases should not be presumed to produce precisely the same pattern of skeletal lesions in each affected environment, cultural context, or human population (Buikstra and Cook, 1980; Ortner et al., 1992; Heathcote et al., 1998). This had led some to wonder whether treponemal disease was highly variable in expression and severity in the past, thus impeding diagnosis with modern criteria (e.g., Weaver et al., 2005). However, dozens of clinical studies on the natural history of treponemal disease, hundreds of physicians' case papers, and, for syphilis in particular, the accounts of chroniclers, laiety, and physicians over the past five centuries all faithfully describe the general suite of skeletal involvement discussed above (Powell and Cook, 2005b). Consequently, we feel comfortable proceeding with the two diagnostic macroscopic criteria described above.

***Signs of congenital syphilis.*** The presence of congenital infection is widely regarded as evidence that venereal syphilis existed in a given region and time period (Mays, 1998). Among others, Merbs (1992) and Erdal (2006) have emphasized that its presence is critical to confirming the existence of Old World pre-Columbian syphilis. This is because, of the treponematoses, only syphilis is regularly transmitted transplacentally (Fiumara et al., 1951; Ingraham, 1951; Diday, 1959). Yaws and bejel may occasionally be transmitted during pregnancy or childbirth (Akrawi, 1949; Hoeprich, 1994), but this appears to be exceedingly rare. Grin (1956) attributed the treponematoses' differential capacity for congenital transmission to differences in the average age at infection for the venereal and non-venereal forms. Yaws and bejel are typically acquired during childhood, meaning the initial bacterial load has dramatically decreased—thus lessening the probability of transmission—by the time childbearing age is reached. In contrast, syphilis is primarily acquired after the onset of sexual maturity, so the probability of a high bacterial load during pregnancy is considerably higher. This hypothesis is supported by clinical data indicating that the vast majority of cases of congenital syphilis result from primary or secondary stage maternal infection (Fiumara, 1975). Given this evidence and the strong emphasis placed on congenital syphilis in the debate over the origins of syphilis, we too consider skeletal evidence specific for congenital treponematosis to be a strong proxy for the presence of venereal syphilis. Determining which skeletal lesions are specific to the condition, however, presents a problem.

As with acquired treponemal infection, the skeletal manifestations of congenital infection are varied. Many affected fetuses are spontaneously aborted, prematurely born, stillborn, or die shortly after birth (Fiumara, 1952). In surviving children, infection is divided into two stages: early (lasting from birth to 2 years) and late (typically from ages 2–15). In the early stage, skeletal lesions can develop as soon as 8-months postpartum (Ghadouane et al., 1995; Rasool and Govender, 1989), often beginning with systemic periosteal reactions (Hackett, 1957), osteomyelitis, and symmetrical osteochondritis (Caffey, 1939). The latter appears radiographically as decalcified subchondral bone in the epiphyseal or joint area, often with pathological fractures in the metaphyseal area of long bones, adjacent to the joint area, and results in pseudoparalysis of the affected limbs (i.e., Parrot's pseudoparalysis; Jaffe, 1972; Reginato, 1993). In the tibia, this can produce distinctive rarefactive lesions (Wimberger's signs) which are highly suggestive of congenital syphilis (Jaffe, 1972), though similar fractures and lesions can occur in battered child syndrome (Kleinman et al., 1986; Kleinman and Marks, 1996). Late stage infection includes both cranial and postcranial lesions. Postcranial lesions range from sternoclavicular thickening (Higoumenakis sign) to true tibial bowing (from differential growth of the anterior tibia), flaring scapulae (Fournier, 1886; Jaffe, 1972), periosteal reactions on the hands and feet (dactylitis), gummata, osteomyelitis, and syphilitic arthritis. Cranial lesions can include a collapsed nasal bridge (saddlenose), prominent bossing on the frontal bone (Parrot's sign), a high, arched palate, and a disproportionate maxillae and mandible (Fiumara and Lessel, 1970).

Dental defects, or "stigmata," are also present. These features include Hutchinson's incisors as well as Fournier and Moon's molars. Darkened enamel and reduced tooth size also occur but are non-specific (Hillson et al., 1998). While Fournier's molars can be caused by other conditions, Moon's molars and Hutchinson's incisors are often considered to be strongly indicative of congenital syphilis in the paleopathological literature (Kranz, 1927; Hillson et al., 1998). Because of their strong link to congenital syphilis and the tendency for teeth to preserve well, these dental defects are considered the most helpful feature for diagnosing congenital syphilis in the archaeological record (Cook, 1994). Their frequent presence in post-Columbian skeletal samples (Jacobi et al., 1992; Powell and Cook, 2005b; p 48) suggests that they should also be present in large pre-Columbian skeletal samples if syphilis was prevalent in the living populations.

Problematically, however, there are no rigorous studies of the specificity or sensitivity of congenital lesions in the published literature, as has been noted previously by Mays (1998). This is probably due, in large part, to the relative scarcity of infant and juvenile skeletons clinically diagnosed with various *in utero* conditions (but see Ortner, 2003). This makes it difficult to compare lesions in cases of congenital syphilis to those found in healthy and diseased control groups. Even in the absence of such formal studies, evidence questioning the specificity of these features has emerged. For example, though Hutchinson's incisors are routinely considered to be diagnostic of congenital syphilis in the paleopathology literature, contemporary case studies demonstrate that notched and tapering incisors may be found in a number of other, noninfectious conditions (Torgersen, 1951; Bargman et al., 1970; Lindenbaum and Bobrow, 1975; Walpole et al., 1990). Indeed, on the whole, abnormal tooth formation has long been considered a non-specific phenomenon in dentistry, related to a number of local and systemic developmental disturbances (Kreshover, 1960). Similarly, several other lesions associated with congenital syphilis, such as systemic periosteal reactions, osteochondritis, and saddle-nose, can also occur in other conditions, such as tuberculosis (Ortner, 2003). Therefore, until a rigorous analysis of the specificity of various congenital syphilis lesions has been published, we concur with other researchers who have stated that it is impossible to be certain of a diagnosis based on skeletal remains alone (Steinbock, 1976; p 106) or based on the presence of just one lesion associated with congenital syphilis (Ortner, 2003). While the criteria used in our study favor cases with multiple indicators of the disease, we recognize that none provides proof of the affliction.

## Dating

When establishing a pre-Columbian case of treponemal disease, the date is just as important as the diagnosis. A variety of methods are employed to determine the chronological age of the skeletons of interest. Many finds are dated using indirect evidence: associated artifacts, archaeological and architectural features, stratigraphic provenience, and increasingly, radiocarbon dating of associated organic matter. Radiocarbon dating can also be used to directly date the skeletons themselves. In the context of the debate over the Columbian or pre-Columbian origin of syphilis, in which accurate and precise dates for the limited remains bearing tell-tale marks of treponemal infection are desired, the strengths and weaknesses of each method must be carefully considered.

***Indirect dating methods.*** Dates premised on artifacts or features, including burial mound characteristics or architectural structures with known temporal provenience, are frequently reported but can generate time ranges accompanied by substantial error. Archeologists and historians are often unable to determine accurately the period wherein architectural structures were initiated, fell into disuse, or wholly abandoned. More problematically, even compelling archaeological or architectural evidence can be misleading. For example, in the United Kingdom, archaeological evidence at a number of sites indicates that burial may have continued at religious centers after their closure during the reformation and dissolution of monasteries (Stones, 1989; Andrews, 1993; James, 1997; Maynard and Ivens, 2002; Hall, 2008), an event often thought to neatly circumscribe the dates for burials at such sites. Burial at some sites may have continued even after cemeteries and churchyards had been converted to other uses such as grange or manor land (Maynard and Ivens, 2002). Evidence of continued burial at some sites is conspicuous—such as the scattered glass from windows smashed during the reformation intermingled randomly in burial layers at an abbey in Scotland (Stones, 1989)—but in most cases it is probably less so and may be missed entirely, particularly where the stratigraphy is ambiguous.

Artifacts recovered in association with skeletal remains can often provide narrow date ranges, such as when stylistic markers are tied to specific time periods, but they can also be problematic. For example, dendrochronological dating of wood or coffins associated with skeletal remains can be inaccurate, as coffins may have been produced before the individuals' deaths or even recycled, making burials appear older than they actually are (Schiffer, 1986). Coins, jewelry, or tools recovered with a burial may also have been manufactured prior to the date of death. This problem can be especially acute when researchers seek a very narrow time interval for a burial (Schiffer, 1987).

***Radiocarbon dating.*** For the past four decades, radiocarbon dating has provided an objective method of dating remains in the absence of, or independent of, associated artifacts and features and has played an increasingly important role in debates over the origin and antiquity of syphilis. However, it has become apparent that there are uncertainties inherent in radiocarbon dates (Arneborg et al., 1999). Many dates generated before the 1980s are of limited value, because the introduction of the accelerator mass spectrometry (AMS) technique subsequently increased the accuracy and precision of this method. However, AMS dates must still be interpreted carefully when the goal is to assign a narrow time-interval. In addition to the analytic uncertainty incorporated in the 95% confidence intervals that accompany point estimates (Higham et al., 2006), antemortem consumption of marine foods by a given individual is now understood to generate dates that can be hundreds, or even thousands, of years too old. This marine "reservoir effect" is caused by delayed exchange rates between atmospheric $CO_2$ and ocean biocarbonate and the dilution effect caused by the mixing of surface waters with upwelling deep water that contains 'old carbon' (Hedges and Van Klinken, 1992; Molto et al., 1997; Cook et al., 2002). The reservoir effect can affect direct dates generated from human bone collagen, due to consumption of marine resources, as well as indirect dates that rely on marine resources such as shells.

Correcting for reservoir effects is complicated. First, the relative proportions of marine and terrestrial dietary contributions must be assessed. This is typically accomplished by analyzing the carbon isotopic signatures ($\delta^{13}$C) in the dated bone collagen. Marine foods are typically enriched in $\delta^{13}$C relative to terrestrial resources (Krog and Tauber, 1974; Schoeninger et al., 1983). Using carbon isotopes, the percentage of a specimen's diet derived from marine foods is roughly approximated using linear mixing models that assume $\delta^{13}$C "endpoints" of $\sim -21$ and $-12$‰ for 100% terrestrial and marine diets respectively (e.g., Arneborg et al., 1999). However, it is important to recognize that these endpoints have great inherent variability (Milner et al., 2004). The terrestrial endpoint, in particular, must incorporate factors such as the $\delta^{13}$C variability within $C_3$ ecosystems, trophic level factors (% terrestrial protein consumed), the extent to which collagen represents dietary protein or dietary total carbon, which can also include carbohydrates and lipids (Howland, 2003; Hedges, 2004; Reynard and Hedges, 2008), nutritional stress (Katzenberg and Lovell, 1999), and uncertainties associated with physiological fractionation factors as dietary carbon is converted to tissue (Barnes et al., 2007). In lower latitude areas or economies that include the introduction of $C_4$ domesticates such as sorghum or sugarcane, untangling a dietary signal based on $\delta^{13}$C values requires assessment of this $C_4$ component as well. In turn, the marine $\delta^{13}$C signal is affected by variability in isotopic composition of the specific marine taxa consumed (e.g., fish, crustaceans, shellfish) as well as environmental contexts within the marine realm (e.g., nearshore, deep water pelagic or benthic, littoral) (Richards and Hedges, 1999). These marine factors also vary geographically and temporally, requiring the development of local endpoints (Yoneda et al., 2002; Ascough et al., 2005; Richards et al., 2006). As such, mixing models yield at best rough approximations of marine/terrestrial dietary sources.

Consequently, $^{14}$C date corrections based on calculations of marine dietary contributions vary considerably, depending on the specific endpoints used and assumptions made concerning the inherent variability. An important consideration in selecting minimum detectable levels of marine dietary intake is that because estimations of an isotopic difference of 1‰ correspond to a roughly 10% change in marine consumption, an uncertainty of $\pm$1‰ in endpoints can yield a range of up to 20% difference in the estimated marine component of the diet (Ambrose, 1993; Hedges, 2004). This uncertainty alone can translate to ages >100 years younger than uncorrected dates. Relatively higher $\delta^{13}$C values, such as $-17$ or $-18$‰, which may indicate a diet of 45% marine resources, can require chronologic corrections on the order of 200 years for late medieval samples. For this reason, in this study we employ corrections that take into account the great degree of variability associated with endpoints when considering radiocarbon dates.

Nitrogen ($\delta^{15}$N) isotopic values of bone collagen have also been utilized to assess the contribution of marine components to the diet (Schwarcz et al., 1985; Walker and DeNiro, 1986; White and Schwarcz, 1989; van der Merwe et al., 1993; Richards and Mellars, 1998; Bayliss et al., 2004). Average bone collagen $\delta^{15}$N values of humans whose dietary protein is estimated to be almost exclusively derived from marine sources (based in part on $\delta^{13}$C values $\geq -14$‰) range from 14.5‰ $\pm$ 1.3‰ to 20.3‰ $\pm$ 0.6‰. For terrestrial diets, they typically range from 4 to 10‰, reflecting varying trophic levels of dietary protein (plant vs. meat) (Richards and Hedges, 1999). Mixing models have been proposed (Schwarcz et al., 1985; Ambrose, 1993), but translating $\delta^{15}$N values into precise percentages of marine versus terrestrial resources use is problematic without comprehensive reference information on the isotopic composition of the local food web. Thus, while we appreciate that $\delta^{15}$N values reflect marine contribution to the diet, since there is no reliable way to incorporate them into date corrections as of yet, we do not use them in this study.

In addition to the marine reservoir effect, it has recently been demonstrated that riverine or freshwater dietary items can also contribute 'old carbon' that affects radiocarbon dates. Aquatic dietary contributions are primarily detected through the $\delta^{15}$N signature of bone collagen (Cook et al., 2002). Because aquatic systems have longer food chains than terrestrial ones, the $\delta^{15}$N values of aquatic species are substantially enriched (Schoeninger and DeNiro, 1984). Accompanying $\delta^{13}$C values that are comparable to and occasionally more negative than those in terrestrial food webs also indicate a freshwater dietary contribution. This is because carbon in these systems can be derived from local geologic sources (Richards et al., 2001). Based on these general trends, simple linear relationships have been suggested to link $\delta^{15}$N values to aquatic food intake and correct for age offsets (Richards and Hedges, 1999; Cook et al., 2001), with $\delta^{15}$N values of 8 and 17‰ reflecting terrestrial and aquatic endpoints, respectively. However, the extent to which a freshwater reservoir effect alters the radiocarbon dates appears to be highly variable, making it difficult to "correct" for (Lillie et al., 2009). Again, we are cognizant that the aquatic effect may result in inaccurate radiocarbon dates, but because there is no straightforward way to correct for it we do not attempt to do so in this study.

As should be clear from this discussion, reconstructing the diet of populations consuming variable combinations of marine and aquatic resources, with the goal of quantifying a potential reservoir effect, remains a challenge. It ultimately requires an intimate understanding of the biochemical cycling of isotopes within and between the various systems involved. Ideally, reservoir corrections would be based on isotopic analyses ($\delta^{13}$C and $\delta^{15}$N) and any corroborating or supporting paleodietary evidence of potential dietary items sampled from large numbers of individuals with associated fauna from a specific location at a specific time (e.g., Müldner and Richards, 2005, 2007). Typically however, these sorts of contextual data are not available. Political, socioeconomic, cultural, and mobility factors further compromise attempts to precisely assess the proportion of marine or freshwater aquatic items in the diet. In short, as the contingencies inherent in interpreting radiocarbon dates are better understood (Higham et al., 2006), it is increasingly apparent that generating accurate and precise dates can be difficult, particularly when a precise time period, such as the late 15th century, is being investigated. Despite these difficulties, it remains critical to attempt to incorporate reservoir effects into radiocarbon dates in populations with access to marine or freshwater dietary items, and ultimately an estimate (with inherent uncertainty) of a marine/aquatic component is required to generate chronologic ranges based on radiocarbon dates.

***Criteria for a pre-Columbian date.*** Recognizing the strengths and limitations of each method discussed, we consider dates for skeletal material generated through multiple, independent lines of evidence to be the most robust. However, because it is often impossible to apply multiple dating techniques, in our criteria a direct radiocarbon date, performed on bone collagen and adequately calibrated for potential reservoir effects, for which the entire 95% confidence interval falls before 1493, constitutes the minimum level of proof necessary for assigning an individual to the pre-Columbian period.

## METHODS

### Overview of review process: Selection and evaluation

The papers reviewed are published reports of pre-Columbian treponemal disease from the Old World (Europe, Africa, Asia, and Australia) written in the 20th and 21st centuries. They were identified through search engines (e.g., Web of Science/ISI Citation Indices, PubMed, and Google Scholar) and the bibliographies of other published reports; a complete list of the works reviewed can be found in Table 1. Our search criteria excluded cases reported only in the "gray literature," i.e., works that are unpublished or not available through conventional routes, because there is no simple, thorough, and unbiased way to search for them. The possibility of overlooking a credible case appears relatively small, however. As Hodges and Schermer (2005) note, because of the popularity and controversy associated with the antiquity of treponemal disease, cases are commonly presented in mainstream journals. Journal articles, book chapters, and other published works were included. When the reports were not written in English, they were translated into English before evaluation. In some reports, the authors themselves did not claim a diagnosis of treponemal disease or that an assigned pre-Columbian date was definitive. However, if their work was cited as evidence of pre-Columbian treponemal disease by others, it was included in the review, since at this point it became pertinent to the debate. When such works were included, both the position of the author of the case and those who cited their work was noted (Table 1). Papers in which cases were assigned to a period prior to western contact, but not prior to 1493, were not included. This is because it is well established that western diseases frequently spread far ahead of western individuals, via intermediary contacts such as trading partners (Crosby, 1972; Ramenofsky, 1989; Hiscock, 2008). Thus, the precontact disease-scape is not an acceptable proxy for the pre-Columbian disease-scape.

Each paper was read by the first three authors and systematically evaluated according to standardized criteria (Table 2). When a report included descriptions of several skeletons from a single archaeological skeletal sample, each individual was ranked separately. The score for the entire archaeological site was then assigned based on the individual with the highest scores. When papers presented scanty, absent, or ambiguous information relevant to diagnosis and dating, we contacted authors and/or site excavators in an attempt to obtain additional details. Additionally, when photos of the reported lesions were not included, we contacted authors in an attempt to obtain photographs. After separate evaluation, discrepancies in the ratings were collectively discussed, but disagreements in scoring were expected and retained when the authors felt their original score was warranted.

### Evaluation criteria

For the purpose of this review, diagnostic and chronological criteria for evaluating treponemal cases were devised from published biomedical, paleopathological, geochronological, and archaeological literature, as described in the background section of this article. Powell and Cook (2005a) created a set of criteria to evaluate New World treponemal cases, and other researchers have developed diagnostic objectives to evaluate other cases of treponemal disease (e.g., Cole and Waldron, 2011; Waldron, 2009). However, no comprehensive, standardized criteria exist for evaluating the diagnostic and chronological certainty of skeletal evidence for treponemal disease, so we describe how our system was devised in the following section.

***Diagnostic criteria.*** As already discussed, our diagnostic criteria, presented in Table 2, mirror Hackett's (1976) standards for diagnosing treponematosis in dry bone. Following Hackett and Powell and Cook (2005a), macroscopic lesions were divided into those consistent, suggestive of and specific to treponemal disease.[4] As stated previously, no attempt was made to distinguish between the three treponemal variants in the reported cases. When they were included, images of histological sections were also evaluated, according to Schultz's (1994, 2001) criteria, though such lesions were considered only consistent with treponemal disease, following Weston (2009). The same is true of several lesion types that have been employed in other studies as diagnostic for treponemal disease (e.g., Rothschild and Rothschild, 1995; Waldron, 2009). For example, because the specificity of tibial bowing and periosteal reactions to treponemal disease has been challenged (Hackett, 1976; Webb, 1995), we ranked both indicators as consistent with treponemal disease. As discussed in the background, inflammation frequently provokes periosteal deposition in treponemal disease. However, periosteal deposition can also be caused by trauma, growth, inflammation due to non-treponemal causes, and other infectious processes (Ragsdale et al., 1981; Ragsdale, 1993; Adler, 2000; Richardson, 2001) and in the absence of other diagnostic lesions, cannot be distinguished from that caused by treponemal disease. Thus it is not useful in differential diagnosis (see Cook and Powell, 2005; Weston, 2008). Finally, as treponemal disease is systemic, the involvement of multiple elements in a skeleton was given greater weight than that of a single element.

Diagnostic criteria for congenital syphilis were derived from multiple studies, including Jaffe (1972), Hillson et al. (1998), Ortner (2003), and Fiumara and Lessel (1970). Lesions were divided into those consistent with, suggestive of, and highly suggestive of congenital

[4]In this article, we use the term "certain" in reference to cases that meet our strictest criteria. We do so to convey that these specimens bear lesions that are specific to treponemal disease using the most rigorous evidence available (i.e., Hackett, 1976). We recognize, however, that researchers can virtually never take for granted that something in science is truly certain, and it is possible that future studies will show that even these lesions are found, very rarely, in connection with non-treponemal conditions.

*TABLE 1. The reported cases of Old World, pre-Columbian treponemal disease examined in this study: descriptions and scores*

| Site name | Country | Scores[a] | | | Description[b] | Peer-reviewed[c] | Photos available | References |
|---|---|---|---|---|---|---|---|---|
| | | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | | | | |
| **Africa** | | | | | | | | |
| Helouan | Egypt | 2 | 1 | 0 | Isolated tibia with periosteal reactions and a uniform, smooth surface. Individual dated to the 1st dynasty, **presumably based on features of the tomb**. | N/A | | Hussein (1949) |
| El Kurrew | Egypt | 0 | 5 | 0 | N3913: Individual with *caries sicca* (Stages 4–6), erosive lesions, periosteal reactions, and joint involvement on multiple postcranial elements. Individual dated to AD 300–700. **No methodological details provided for the date**. | | X | Ortner (2003) |
| Koobi Fora | Kenya | 5 | 1 | 0 | KNM-ER 1808: Individual with periosteal reactions on multiple postcranial elements, with clearly defined divisions between pathological bone and original cortex. KNM-ER 737: Periosteal reaction on an isolated humerus. Site dated by K-Ar dating, and specimens morphologically identified as *H. erectus*. | X | | Rothschild, Hershkovitz, and Rothschild (1995) |
| Mapungubwe | South Africa | 2 | 1 | 0 | A1732: Individual with periosteal reactions on multiple postcranial elements. Site dated to AD 1000–1300; individual dated by associated artifacts (beads and pottery). | X | X | Steyn and Henneberg (1995) |
| Qubbet el Hawa | Egypt | 2 | 1 | 0 | 103/150/ESK: Individual with medullary narrowing and periosteal reactions on multiple lower postcranial elements. Site dated to c. 4500 YBP; individual dated by associated coffin chamber. | | X | Rösing (1990) |
| Semna South | Sudan | 0 | 1 | 0 | Multiple individuals with tibial bowing (sabre shins), "very minimal" frontal bone scarring. **Cranium thus does not display *caries sicca* (any stages).** Bilateral periosteal reactions on multiple lower postcranial elements. Site dated to 200 BC–500 AD, **with no methodological details provided or given in the cited reference**. | X | | Rothschild and Rothschild (1996) supplemented by Merbs (2009) |
| **Asia and Australia** | | | | | | | | |
| Agripalle | India | 2 | 4 | 0 | Isolated cranium with ulceration, erosion, periosteal reactions, osteitis, stellate scars, and facial and nasopalatine involvement. **Cranium thus displays *caries sicca* (stages 4–6)**. Site dated to 1st–2nd c. BC; individual dated by associated ceramics, iron artifacts, and grave type. | X | X | Rao, Vasulu, and Rector Babu (1996) |
| Ahatelashan | China | 1 | 1 | 0 | Isolated tibia with sclerotic periosteal reactions, substantial expansions, and medullary narrowing. Site dated to 500 BC–150 AD, **possibly based on ceramic evidence**. | X | X | Suzuki, Matsushita, and Han (2005) |

*TABLE 1. (Continued)*

| Site name | Country | Scores[a] | | | Description[b] | Peer-reviewed[c] | Photos available | References |
|---|---|---|---|---|---|---|---|---|
| | | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | | | | |
| Bhimbetka | India | 1 | 1 | 0 | BTK-III-F-16: Isolated cranium with "crater-like depressed" area on parietal. **Cranium thus does not display *caries sicca* (any stages).** Site and individual dated to Iron Age period, **presumably based on tools found at site**. | N/A | X | Kennedy (1990) |
| Blue site | Tinian | 0 | 5 | 0 | Burial 2: Individual with lesions on multiple elements: cranium with "crater-like," porous lesions on the frontal bone, one with sclerosis; multiple destructive and porous lesions on the parietals; and a pit on zygomatic bone. **Cranium thus displays *caries sicca* (stages 4–6)**. Periosteal reactions, medullary narrowing, pitting, cavitations, and a possible sinus on multiple postcranial elements. Site dated from prehistoric period to c. AD 1200 (Latte period) by archaeological features (latte stones); individual dated using radiocarbon dating of a seashell from a refuse dump associated with the house that the burial was recovered from. | X | X | Stewart and Spoehr (1967) |
| Hyatt hotel site | Guam | 3 | 1 | 0 | Nine individuals with periosteal reactions, localized expansive nodes, or diaphyseal expansions on multiple postcranial elements. Specimens are dated to the Latte period, which spans AD 1493, **with methodological details unspecified**. | X | | Stodder (1997) |
| | | | | | Eight individuals reported with "unequivocal yaws," and two with "equivocal yaws." Frontal lesions on undisclosed individuals are reported as "indistinguishable" from "*caries sicca*." **These terms are not defined, and no further description or photos of the cases were provided or available from the author. As such, there is insufficient evidence for an independent diagnosis of *caries sicca* (any stages)**. Eight of these individuals were radiocarbon dated to AD 1200–1521 (Latte period) and one to AD 815 ± 170. **The 95% confidence interval for the date, adjusted for marine signature, is not provided, nor is any other information about the date, and the accession codes and/or pathological status of the skeletons dated are not specified**. | X | | Trembly (1996) |

TABLE 1. (Continued)

| Site name | Country | Scores[a]: Dating | Scores[a]: Diagnosis: Acquired Treponemal Disease | Scores[a]: Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
|---|---|---|---|---|---|---|---|---|
| Inamgaon | India | 2 | 1 | 0 | INM-196: Isolated cranium with single porous, "cratered," depression on the occipital. Possible depressed fracture or osteolytic lesion **(with no endocranial involvement). Cranium thus does not display *caries sicca* (any stages)**. Site dated by stratigraphic and cultural evidence to 1700–700 BC; individual dated to 1400–700 BC by grave type and associated ceramics and house floor plan. | X | X<br>X | Lukacs et al. (1986)<br>Lukacs and Walimbe (1984) |
| Iznik, Roman Ampitheatre | Turkey | 1 | 3 | 3 | ITK'90 56/6: Individual with lesions on multiple elements: cranium with Hutchinson's incisor **(i.e., notch present on one incisor; highly suggestive lesion),** mulberry molar **(suggestive lesion)**, darkened enamel; facial involvement and destruction, sclerosis on the vault, and a lesion resembling a radial scar on the frontal bone. **This radial scar appears consistent with a vascular impression or taphonomic damage.** Tibial bowing (sabre tibia), dactylitis, osteitis, periosteal reactions, and gummatous and non-gummatous osteomyelitis with sclerosis on multiple postcranial elements. Diaphyseal thinning also reported. Individual dated to AD 1222–1254 stratigraphically and by unassociated *in situ* artifacts (coins, etc.). | X | X | Erdal (2006) |
| Leo palace hotel site | Guam | 1 | 1 | 0 | Burial 19: Individual with bone changes attributable to treponemal disease (e.g., periosteal reaction, gummatous osteitis, and cloacae) observed on left distal tibia. Site dated to AD 1000–1400, based on radiocarbon dates obtained from charcoal at the site. Ceramic evidence indicates a date of between AD 800 and 1300, while radiocarbon dates from shells at the site, uncorrected for marine signature, indicate a date of between AD 600–1300. | X | | Pietrusewsky, Douglas, and Ikehara-Quebral (1997) supplemented by Davis, Tomonari-Tuggle, and Wickler (1992) |
| Safed cave | Israel | 3 | 4 | 0 | SK 5111: Isolated cranium with multiple lesions on the parietal bones, including a depression with rolled edges and a stellate lesion. **Cranium thus displays *caries sicca* (stages 4–6).** Site is medieval; individual radiocarbon dated (revised date) to AD 1424–1479 with 95.4% confidence, without adjustment for the marine signature; **AD 1424–1953 with adjustment (Table 3).** | X | X | Mitchell (2003, 2009) |

*TABLE 1. (Continued)*

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| Shangsunja | China | 1 | 1 | 0 | M-981: Individual with osteomyelitis: sclerotic periosteal reactions with plaques and expansions on multiple postcranial elements. Site dated to 500 BC–150 AD, **possibly based on ceramic evidence.** | X | X | Suzuki, Matsushita, and Han (2005) |
| Shuozhou City, Burial Site M59 | China | 2 | 2 | 0 | Case 3: Isolated femur* with "tumor-like" enlargements, isolated plaques, and "worm bitten" corrosion. **Thus displays coarsely striated, rugose, and pitted expansions on a long bone.** Site dated to Han Dynasty (202 BC–220 AD); individual dated to Han Dynasty because of its presence in tomb from that era. (*potentially unassociated with any other skeletal elements from the site) | X | X | Zhang (1994) |
| Tell Gubba, Himrin Basin | Iraq | 1 | 3 | 0 | IR.8: Individual with circumferential expansion, "crater-like" pits, medullary narrowing, and osteitis on multiple postcranial elements. **Thus displays striated and pitted expansions on multiple elements**.<br>IR.19: Individual with discoloration and pitting, coarse striation, circumferential expansion, and medullary narrowing on multiple postcranial elements. Discoloration and pitting on the cranium. **Thus displays coarsely striated and pitted expansions on multiple elements. Cranium displays *caries sicca* (stages 1–3)**. Site dated from the Samarra period (6th millennium BC) to the Islamic period (ending 13th–14th c. AD); individuals stratigraphically dated to the Islamic period. | X | X | Wada, Ikeda, and Suzuki (1987) |
| Wan Fu Gong, Dongshan County | China | 0 | 4 | 0 | Case 2: Isolated cranium with "worm eaten appearance" **(i.e., extensive irregular traces of gummatous destruction)**, corrosion **and possible lytic pits** on the vault—**thus displaying *caries sicca* (stages 4–6)**, as well as resorption of the anterior nasal spine. Individual reported to be "dated back to the Song Dynasty" (AD 960–1279), **no methodological details given**. | X | X | Zhang (1994) |

TABLE 1. (Continued)

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| **Europe** | | | | | | | | |
| Apple Down, West Sussex | England | 2 | 3 | 0 | SK 152: Individual with lytic erosion and pitting on the frontal bone of the crania, with perforation and penetration to the endrocranial surface (*caries sicca*, stages 1–3). Crania also exhibits extensive **(likely unrelated)** periosteal reactions on the endocranial surface, and on the palate, maxilla, and mandible. Periosteal reactions, expansions, and regions of "irregular variation in thickness" of periosteal new bone, reported as "suggestive" of gummata, on multiple postcranial elements, including ribs and thoracic vertebrae. Site dated to late 5th/ early 6th c. AD to 17th c. AD using grave goods; individual dated to early-mid 6th c. AD by presence of early Anglo Saxon grave goods. | X | X | Cole and Waldron (2011) |
| Ardenne, Normandy | France | 0 | 5 | 0 | SK62: Individual with *caries sicca* **(stages 4–6)** on the frontal and parietal bones and periosteal appositions on the maxillae and zygomatic bones of the cranium; femorae **(with pitting and periosteal reactions)** and left tibia display necrosis. **(Right tibia also exhibits periosteal lesions.)** Individual dated to 13th c. AD on the basis of associated stylistic markers. However, radiocarbon dated to AD 1467–1641, uncorrected for marine signature. | | X | Blondiaux (2008, 2010) |
| Arles, Roman Cemetery | France | 0 | 4 | 0 | Isolated cranial fragment with *caries sicca* (**stages 4–6)** and nasopalatine destruction. Recovered from pre-15th c. archaeological site, but radiocarbon dated to AD 1480–1663 (post-15th c. deposition reported as most "reasonable"), without adjustment for marine signature **(Table 3)**. | X | X | Mafart et al. (1993)<br>Mafart et al. (1998) |
| Bajkara | Kazakhstan | 0 | 2 | 0 | Kurgan 1, Grave 1, SK1: Individual with sclerosis, medullary narrowing, exostoses, periosteal reactions, enlargement, and grenzstreifen on the left femur and right tibia (tibia also displays grenzstreifen and a "worm-eaten" appearance). **Thus pitted, coarsely striated expansions on a long bone**. Sequestration, an involucrum, fistulae, and necrosis on a single rib. Individual possibly dated to early Sarmation period (2nd–1st c. BC). **No methodological details provided for the date.** | | X | Schultz, Schmidt-Schultz, and Wolf (2003) |

*TABLE 1. (Continued)*

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| Blackfriars, Gloucester | England | 1 | 5 | 0 | SK77: Individual with multiple stellate and destructive gummatous lesions and nasopalatine destruction on the cranium. **Cranium thus displays *caries sicca* (stages 4–6).** Possible osteomyelitis, osteoproliferative and destructive lesions, and joint destruction on multiple postcranial elements. Burials at site dated to AD 1246–1538 by historical records; individual stratigraphically dated to early to mid 16th c. **and radiocarbon dated to AD 1438–1635, with adjustment for marine signature (Table 3)**. | | X | Roberts (1994) supplement-ed by Ortner (2003), and Roberts (2009) |
| Cappenberg Stift Church | Germany | 3 | 1 | 0 | Individual with periosteal reactions, grenzstreifen, and medullary sclerosis on multiple postcranial elements. Individual identified as Count Gottfried von Cappenberg (AD 1097–1127) by historical material and radiocarbon dated to the 8th–12th c. AD, **with no 95% CI or other information on radiocarbon date provided.** | X | X | Kuhnen et al. (1999) |
| Castle Mound, Huntingdon | England | 1 | 0 | 0 | Sk HC017: Periosteal deposition and medullary encroachment on multiple lower postcranial elements. Site dated to 8th to 17th c. AD; **individual radiocarbon dated to AD 1020–1270, with adjustment for the marine signature (Table 3).** | X | X | Mays et al. (in press) |
| Costebelle Hyère | France | 2 | 1 | 1 | Fetus (“Cristobal”): individual with periosteal appositions, localized sheathed calcifications, and osseous resorptions (erosive and lytic lesions) on the cranium and multiple postcranial elements. **Roentogram also revealed possible Wimberger’s sign on the tibiae.**<br>Associated female skeleton: Individual with periosteal appositions on tibiae. Site dated to 2nd to 5th c.; individuals dated to 3rd–4th c. AD by features of associated tomb and artifacts. | X | X<br>X<br>X<br>X<br>X | Pálfi et al (1992)<br>Bérato, Dutour, and Pálfi (1994)<br>Borreani and Brun (1994)<br>Dutour et al. (1994b)<br>Pálfi, Bérato, and Dutour (1994) |
| Czarna Wielka | Poland | 0 | 1 | 0 | SK1: Individual with thickened, porotic cranial vault and “general porotic process” on multiple postcranial elements.<br>SK2: Isolated tibia with periosteal reactions, medullary narrowing and partial obliteration (chronic osteitis), and osteolytic foci. Site dated to 12th to 14th c. AD. **No methodological details provided for the date.** | | X | Gladykowska-Rzeczycka (1994) |

*TABLE 1. (Continued)*

| Site name | Country | Scores[a]: Dating | Scores[a]: Diagnosis: Acquired Treponemal Disease | Scores[a]: Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
|---|---|---|---|---|---|---|---|---|
| Hamage | France | 0 | 0 | 3 | Hamage 1047: Individual with Moon's crenulated hypoplastic defects and Hutchinson's incisors on multiple teeth. Individual dated to the 7th to 8th c. AD. **No methodological details provided for the date.** | | X | Blondiaux (2008) |
| Hull Magistrate's Court | England | 1 | 5 | 0 | HMC94-SK0805: Individual with dactylitis, osteitis, and periosteal reactions on multiple postcranial elements (possible grenzstreifen and polsters on fibula).<br>HMC94-SK0932: Individual with healed *caries sicca* lesions on cranium and osteitis and periosteal reactions on multiple postcranial elements.<br>HMC94-SK1121: Individual with osteitis and periosteal reactions on multiple postcranial elements (grenzstreifen and polsters on fibula).<br>HMC94-SK1216: Individual with "classic" erosive and sclerotic *caries sicca* lesions **(stages 4–6),** nasopalatine destruction, and facial involvement on the cranium; erosive cloacae/sequestrae **(possibly gummatous)**, osteitis, periosteal reactions, and "snail tracks" on multiple postcranial elements (possible grenzstreifen and polsters on tibia).<br>Site dated to AD 1300-1450 by stratigraphy **(details unpublished)**, $^{14}$C radiocarbon dating, and dendrochronology of unassociated coffins. SK1216, the only individual with treponematosis-specific lesions (score = 5), has been radiocarbon dated to AD 1428–1611, unadjusted for the marine signature. **This and other dates from the site are presented in Table 3.** | X | X[d] | von Hunnius et al. (2006) and Roberts (2009) |
| Ipswich Black-friars Friary, Suffolk | England | 0 | 3 | 0 | Ipswich SK 1965: Individual with concentric thickening, periosteal reactions, bone spicules and plaques, and medullary encroachment on multiple postcranial elements. **Thus nodes and finely striate expansions on multiple elements.** Cranium with area of irregular sclerosis and multiple shallow, ovoid or circular depressions with raised rims on the frontal bone. **Cranium thus displays *caries sicca* (stages 1–3).** Individual dated to AD 1440–1620, unadjusted for the marine signature **(Table 3)**. | X | X | Mays, Crane-Kramer, and Bayliss (2003) |
| Isiaslavl | Belarus | 0 | 1 | 0 | Isolated cranium with two shallow depressions and "destroyed" ectocranial surface **(endocranial aspect not described).** Site is dated to AD 1241. **No methodological details provided for the date.** | | X | Rokhlin (1965) |

*TABLE 1. (Continued)*

| Site name | Country | Scores[a]: Dating | Scores[a]: Diagnosis: Acquired Treponemal Disease | Scores[a]: Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
|---|---|---|---|---|---|---|---|---|
| Michelet Necropolis, Lisieux | France | 2 | 0 | 1 | Sepulchre 128: Adult male with massive lytic lesion and periosteal apposition on the frontal as well as plaques and grooves on both parietals of the skull. Periosteal apposition is also present on both tibiae. | | X | Blondiaux and Alduc-Le Bagousse (1994) |
| | | | | | SK653: Neonate with periosteal appositions and fine, sheathing hyperostosis on multiple long bones (associated adult female skeleton displays no pathologies). | N/A | X | Alduc-Le Bagousse and Blondiaux (2001) |
| | | | | | SK 223: Infant with periosteal appositions on the cranium; osteitis, fine, sheathing hyperostosis, and periosteal appositions on multiple postcranial elements; and radiologically visible "hyperlight" tibial metaphyses **(possible Wimberger's sign)**. Individuals dated to the mid and late 4th c. AD, respectively, based on associated artifacts and features of the graves. | | | |
| Pantanello Necropolis, Metaponto | Italy | 1 | 1 | 1 | T22: Crania with naso-maxillary deformation (e.g., pitting, remodeling or periosteal deposition). | | X | Henneberg, Henneberg, and Carter (1992) |
| | | | | | T53: Individual with saber shins: "bent appearance," cortical thickening, and medullary involvement on the tibiae. | | X | Henneberg and Henneberg (1994) |
| | | | | | T99: Cranium with erosion suggestive of 'worm eaten' destruction from gummatous ulcers. **Cranium thus does not display *caries sicca* (any stages).** | | X | Henneberg and Henneberg (1998) |
| | | | | | T151: Juvenile with bilateral periosteal reactions on the femoral metaphyses. | | | |
| | | | | | T236: Cranium with erosion suggestive of 'worm eaten' destruction from gummatous ulcers. **Cranium thus does not display *caries sicca* (any stages).** | | | |
| | | | | | T240: Cranium with erosion suggestive of 'worm eaten' destruction from gummatous ulcers and naso-maxillary deformation. **Cranium thus does not display *caries sicca* (any stages).** | | | |
| | | | | | T276: Individual with saber shins—"bent appearance" and cortical thickening—with medullary involvement on the tibiae. | | | |
| | | | | | T306: Juvenile with pitting and crenulation of occlusal surface of 1$^{st}$ molar resembling "mulberry (Moon's) molars." | | | |
| | | | | | T320: Juvenile with a thickened tibial cortex (saber shin) and hypoplastic defects on several incisors and premolars. The incisors also bear narrowed crowns and on one, a slight occlusal notch. **Related images show no evidence of crown narrowing.** | | | |
| | | | | | T192: Neonate with osteochondritis described as grossly and radiologically visible **(no images provided)**. Multiple individuals display both sclerotic thickening and saber tibiae; 25% ($N$ = 12) exhibit multiple lesions. | | | |
| | | | | | *The Hennebergs note that poor preservation prevented definitive diagnosis in cases of cranial thickening presented as caries sicca.* Site dated to 580–250 BC. **Individuals may have been dated by unassociated artifacts and features.** | | | |

TABLE 1. (Continued)

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| Rostov Velikiy | Russia | 0 | 1 | 0 | Case no. 1: Individual with clustered pits and superficial cavitation on the frontal bone **Cranium thus does not display *caries sicca* (any stages).** Proliferation, periosteal reactions, medullary obliteration, and pitting on multiple postcranial elements. Case no. 2: "Massive" periosteal reactions, medullary obliteration, and periosteal proliferation on an isolated tibia and fibula. Site dated to the mid 16th c. AD by historical records and a solitary coin, **but cited as pre-Columbian by Erdal (2006).** | X | X | Buzhilova (1999) |
| St. Helen-on-the-Walls Cemetery, York | England | 3 | 4 | 0 | SK5556: Isolated calvarium with widespread ulceration of the frontal and parietal bones. Mays (1998) specifies radial scarring on the frontal bone. **Cranium thus displays *caries sicca* (stages 4–6).** Site dated to AD 1020–1550; **individual radiocarbon dated (revised date) to AD 1426–1486 with 95.4% confidence, without adjustment for the marine signature; AD 1421–1669, adjusted for marine signature (Table 3).** | | X | Dawes and Magilton (1980) supplemented by Mays (1998) and Chamberlain (2011) |
| St. Idzis Church, Wroclaw | Poland | 0 | 5 | 0 | Grave 1: Individual with cranium displaying extensive "defects" on the ectocranial surface, sclerotic and lytic areas visible radiologically. Possible endocranial involvement. **Cranium thus displays *caries sicca* (stages 4–6).** Hyperplasias, "creative changes," polsters, and defects, resembling those on the skull, present on a femur and tibia. Site dated to 14th to 15th c. AD. **No methodological details provided for the date.** | X | X | Gladykowska-Rzeczycka (2003) |

TABLE 1. *(Continued)*

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| St. Margaret's *incombusto*, Magdalen Street, Norwich | England | 1 | 5 | 0 | SK 412: Individual with florid periosteal deposition, remodeling, pitting, rugosity, coarse striations, inflation, and medullary encroachment on multiple postcranial elements, **including dactylitis**.<br>SK68: Individual with healed depressions on the frontal and parietal bones (and a sharp-edged lesion on the frontal; no endocranial involvement), and clustered confluent pits on the maxilla; stellate lesions on the left humerus, right scapula; medullary encroachment and rugose, inflated bone on multiple postcranial elements; "fresh" gummatous lesions on the left femur and tibia.<br>SK 129: Individual with healed radial scars, clustered and confluent pits, and focal superficial and nodular cavitation on the cranium. **Cranium thus displays *caries sicca* (stages 4–6).** Periosteal reactions with medullary encroachment on the fibulae.<br>SK227: Individual with solitary focal superficial cavitation on cranium; periosteal deposition and striated nodes with lytic pitting (superficial cavitation) on multiple postcranial elements.<br>SK305: Individual with healed lesions, active pitting, and serpiginous cavitation on the cranium. **Cranium thus displays *caries sicca* (stages 4–6)**. "Coral-like" periosteal deposition on the right femur, and plaque-like periosteal deposition with perforating lesions on multiple postcranial elements.<br>SK349: Individual with plaques of "coral-like" periosteal deposition on multiple postcranial elements.<br>Site dated to AD 1254–1468 (author notes that burial may have ceased prior to this date; there is no archaeological evidence for burial post-AD 1468). SK412 stratigraphically dated as an "early burial." Individuals radiocarbon dated to AD 1088–1644, unadjusted for marine signature **(Table 3)**. | X | X<br>X | Stirland (1991)<br>Stirland (1994) supplemented by Stirland (2009) and Roberts (2009) |

TABLE 1. (Continued)

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| St. Mary and All Saints Church Churchyard, Rivenhall, Essex | England | 3 | 3 | 0 | Rivenhall SK204: Individual with concentric thickening, periosteal reactions, bone spicules and plaques, pitted and roughened surfaces and medullary encroachment on multiple postcranial elements. **Thus displays coarsely striated and pitted expansions and rugose nodes on multiple elements.** Erosive joint involvement in upper appendages. **Dated to AD 1294–1630, adjusted for the marine signature (Table 3).** | X | X | Mays, Crane-Kramer, and Bayliss (2003) |
| St. Mary Spital, London | England | 4 | 1 | 1 | Juvenile individual with "*caries sicca* associated with congenital syphilis." **This term is not defined, and no further description or photos were provided by the authors. As such, there is insufficient evidence for an independent diagnosis of *caries sicca* (any stages)**. Site dated to AD 1197–1539; **the individual was radiocarbon dated to AD 1217–1444, adjusted for the marine signature (Table 3)**. | | | Sidell et al. (2007) |
| Sarkel's Necropolis | Russia | 0 | 1 | 0 | Multiple individuals with osteitis and periosteal reactions on long bones and crania. Multiple ($N = 20$) cases of "ossified gumma." Single individual with lesions attributed to tabes dorsalis. Site dated to 10th–12th c. AD. **No methodological details provided for the date.** | | X | Rokhlin (1965) |
| Spitalfields Market, London | England | 0 | 4 | 0 | Isolated cranium with "worm-eaten" appearance "typical of syphilitic (gummatous) osteomyelitis" covering the vault and perforations on the frontal bone. **Cranium thus displays *caries sicca* (stages 4–6)**. Site dated to AD 1197–1537 based on historical records. | X | X | Brothwell (1961) supplemented by Morant and Hoadley (1931) |
| Suraz, Lapy district | Poland | 0 | 0 | 0 | Isolated palate **(i.e., palatine process of the maxilla)** with "characteristic" porotic lesion **(possible gangosa).** Site dated to 11th to 14th c. AD. **No methodological details on the date provided.** | | X | Gladkowska-Rzeczycka (1994) |
| Thaon | France | 0 | 5 | 0 | Thaon 108: Individual with *caries sicca* **(stages 4–6)**, thickening, and endocranial reactions on the cranium; osteoperiostitic lesions **and gummata** on the humeri; "intracortical *geodes*," periosteal remodeling and osteitis on the tibiae, with cortical necrosis and sclerosis also present on the right tibia. Dated to 14th c. AD with radiocarbon-dated charcoal found in association with burial. However, skeleton was radiocarbon dated to AD 1446–1635, uncorrected for marine signature **(Table 3).** | | X | Blondiaux (2008, 2010) |

*TABLE 1. (Continued)*

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| Trolla's Chapel, Kintradwell | Scotland | 4 | 0 | 1 | SK 14: Juvenile with "dental pathology typical of congenital syphilis" but "no osteological manifestations present." Roberts (2001), an unpublished supplementary report, describes multiple deep hypoplastic grooves and defects on the incisors and severe hypoplastic defects on the first permanent molars which "resemble" mulberry molars and Hutchinson's incisors. **Individual radiocarbon dated to AD 1040–1280, adjusted for marine signature (Table 3).** | X | | Lelong (2003) supplemented by Roberts (2001) |
| Tuva | Russia | 0 | 0 | 0 | Isolated cranium with "ossified syphilitic gumma." Site dated to 1st c. AD. **No methodological details on the date provided.** | | X | Rokhlin (1965) |
| Uspensky Cathedral, Kievo-Pecherskaja-Lavra | Ukraine | 0 | 5 | 0 | Individual with hyperostosis, destruction, nodular cavitation, radial scars, and osteoporosis on the vault. **Cranium thus displays *caries sicca* (stages 4–6).** Periosteal deposition on the malar and maxillae of the cranium; periosteal deposition on the tibiae and a humerus. Burials at site dated to the end of the 15th c. AD. **No methodological details on the date provided.** | NA | X | Loganovskaja et al. (2000) |
| Waterford | Ireland | 0 | 1 | 0 | E435: B253: Juvenile with periosteal deposition on multiple postcranial elements, slight lateral bowing of the left tibia, sinus formation on the humeri and left femur, and a cyst-like cavity on the left scapula. On the cranium: a small indentation from a cyst-like formation on the frontal, an oval lesion on the mandible, and a circular lesion on a maxillary sinus. Individual radiocarbon dated to AD 1438–1635, unadjusted for marine signature, **but cited as pre-Columbian by Roberts (1994) and Erdal (2006).** | | X<br>X | Power (1992)<br>Hurley, Scully, and McCutcheon (1997) |

TABLE 1. *(Continued)*

| | | Scores[a] | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Site name | Country | Dating | Diagnosis: Acquired Treponemal Disease | Diagnosis: Congenital Syphilis | Description[b] | Peer-reviewed[c] | Photos available | References |
| Whithorn | Scotland | 0 | 4 | 1 | Isolated cranium with "typical *caries sicca*" **(stages 4–6)** and two unassociated permanent 1st molars with severe hypoplastic defects on the occlusal surfaces, categorized as "mulberry molars." **No available images or detailed description;** authors note that both teeth are likely from the same individual, recovered from disarticulated remains.<br>Hill 1997: Disarticulated remains dated to 11th c. AD to 1510 AD.<br>Cardy 1997: *Same* disarticulated remains dated to 6th c. -1450 AD, with the majority dated to AD 1300–1450.<br>**This specimen radiocarbon dated to AD 1459–1644, unadjusted for the marine signature (Table 3).** | | X | Hill (1997) supplemented by Cardy (1997), Lunt and Watt (1997), Roberts (2009) |
| Zabaikal'e | Russia | 0 | 1 | 0 | Isolated tibia with bilateral periosteal reactions (saber shin). Individual dated to Bronze Age. **No methodological details on the date provided**. | | X | Rokhlin (1965) |

[a] Scores from all reviewers were identical unless otherwise indicated.
[b] Comments in bold belong to the authors of this article.
[c] N/A indicates that the information was not available.
[d] Photos are of microscopic features only.

*TABLE 2. Scoring criteria employed*

| Category | Score | Criteria |
|---|---|---|
| Dating | 0 | Ambiguous date provided or date includes post-1493 period. |
| | 1 | Dating based on stratigraphy, artifacts found in other graves, or stylistic markers on artifacts not associated with the skeletal remains in question. |
| | 2 | Dating based on artifacts found in close approximation to the skeletal remains in question or features of the grave that predate the 15th century. |
| | 3 | Radiocarbon date based on bone collagen in which 1493 falls outside the 95% confidence interval, but $\delta^{13}$C values are not available or marine contribution to diet was not incorporated into the corrected date. |
| | 4 | Radiocarbon date based on bone collagen in which 1493 falls outside the 95% confidence interval, after marine contribution to diet has been taken into account. |
| | 5 | Radiocarbon date based on bone collagen in which 1493 falls outside the 95% confidence interval after marine contribution to diet has been taken into account, and archeological context—of the type described in category 2—supports the date; or morphological characteristics of the bone indicate it belongs to another hominid species, such as *Homo erectus,* with supporting K/Ar dates. |
| Diagnosis: Acquired treponemal disease | 0 | Lesions consistent with a nontreponemal process (e.g., taphonomic process, noninfectious etiology, etc.). |
| | 1 | Lesions consistent with treponemal disease on one or more skeletal elements (periostitis, tibial pseudo-bowing, polsters, grenzlinie). |
| | 2 | Lesions suggestive of treponemal disease on a single element [Hackett's (1976) *on trial* characteristics: Finely striated nodes and expansions; coarsely striated and pitted expansions; and rugose nodes and expansions on long bones]; or Stage 1–3 *caries sicca* lesions (clustered pits, confluent pits, focal superficial cavitation). |
| | 3 | Lesions suggestive of treponemal disease on multiple skeletal elements. |
| | 4 | Lesions specific to treponemal disease [Hackett's (1976) diagnostic criteria: Stage 4–6 *caries sicca* lesions (serpiginous cavitation, nodular cavitation, and *caries sicca)* or nodes/expansions with superficial cavitations on long bones] on a single skeletal element. |
| | 5 | Lesions specific to treponemal disease found on multiple skeletal elements or in the presence of lesions suggestive of treponemal disease on other skeletal elements |
| Diagnosis: Congenital syphilis | 0 | Lesions consistent with a nontreponemal process (e.g., taphonomic process, noninfectious etiology, etc.) |
| | 1 | Lesions consistent with congenital syphilis (periostitis, high palatal arch, disproportionate maxillae and mandible, true tibial bowing). |
| | 2 | Lesions suggestive of congenital syphilis (Parrot's/Higoumenakia sign, flared scapulae, Fournier's/Mulberry molar). |
| | 3 | Lesions highly suggestive of congenital syphilis (Wimberger's sign, notched and tapering (Hutchinson's) incisors, Moon's molars). |

infection. As discussed in the background, there are no diagnostic indicators whose specificity to congenital syphilis have been rigorously demonstrated. However, lesions that frequently occur in other conditions, such as tibial bowing, received lower rank, whereas lesions, including Wimberger's sign and Hutchinson's incisors, that appear to occur primarily in congenital syphilis were ranked more highly.

***Dating criteria.*** Our dating criteria (Table 2) were based on published reports of the accuracy, reliability, and margins of error for different dating methods (see Schiffer, 1986; Higham et al., 2006). Higher scores were given to cases that had been dated using associated artifacts and features, direct radiocarbon dating of skeletal remains that incorporated a consideration of the marine reservoir effect into the corrected date, and those that employed multiple lines of evidence. Conversely, ambiguous dates, or those that demonstrably overlapped with the late 15th century, as well as dates based on stratigraphy or unassociated artifacts, were given lower scores. We included and evaluated unpublished data from radiocarbon dating reports for a number of the reviewed cases.

Radiocarbon date ranges were calculated using the OxCal (v.4.1) program (https://c14.arch.ox.ac.uk/oxcal/OxCalPlot.html) and adjusted for marine contributions to the diet, based on $\delta^{13}$C values, whenever sufficient data was available (Table 3). As discussed earlier, a simple linear mixing model using endpoints of −21‰ and −12‰ (representing exclusive terrestrial and marine signals, respectively) was used to estimate the marine dietary component. These endpoints have been developed and utilized in northwest Europe (Arneborg et al., 1999). Incorporating the marine reservoir effect, Table 3 presents two radiocarbon age ranges: one in which just the estimated marine dietary percentage was entered into the OxCal program and the other incorporating the percentage as well as a ±20% uncertainty. As discussed earlier, the uncertainty in the endpoints conservatively reflects the variability inherent in both terrestrial $C_3$ ecosystems and marine sources and the difficulty in unequivocally determining precise endpoints for any linear mixing model. We acknowledge that simple linear mixing models cannot adequately account for the complexity inherent in these sorts of paleodietary analyses. For example, as information on 100% terrestrial and marine dietary endpoints for $\delta^{15}$N is not available in the published literature for the pre-Columbian Old World, we did not attempt to incorporate nitrogen isotopic values into the adjusted dates. Similarly, due to the current lack of understanding regarding the extent to which the freshwater component of a diet alters radiocarbon dates, we did not attempt to use $\delta^{15}$N values to correct reported dates for freshwater reservoir effects, though we recognize their potential importance.

## RESULTS AND DISCUSSION

### Overview

The 54 papers analyzed dealt with 50 archaeological sites: 6 from Africa, 13 from Asia and Australia, and 31

*TABLE 3. Radiocarbon dates of specimens reviewed in this study: Unadjusted and adjusted for marine signature*

| Specimen | Location | Lab ID (Year) | Uncalibrated date (YBP) | Collagen $\delta^{13}C$ (‰) | Nitrogen $\delta^{15}N$ (‰) | delta R (local deviations from the global average R(t))[a] | Estimated % marine carbon in diet[b] | Radiocarbon date uncorrected for marine signature, 95% CI, (AD) | Radiocarbon date corrected for marine component, 95% CI, (AD) | Radiocarbon date corrected for marine component assuming ±20% uncertainty,[c] 95% CI, (AD) | Reference |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Old World individuals with a certain diagnosis of treponemal disease (Score > 4)** | | | | | | | | | | | |
| Ardenne 62 | Ardenne, France | Lyon-6497 (2010) | 340 ± 35 | N/A[d] | – | −31 ± 56 | 0 | 1,467–1,641 | N/A | N/A | Blondiaux (2010) |
| Arles Cranium | Bouches-du-Rhône, Arles, France | OxA-5316 (1996) | 305 ± 40 | −18.2 | – | 23 ± 71 | 31.1 | 1,473–1,659 | 1,651–1,954 | 1,520–1,954 | Mafart et al. (1998) |
| Gloucester 77 | Blackfriars, Gloucester, UK | OxA-4875 (1994) | 385 ± 45 | −22.8 | – | −20 ± 36 | 0.0 | 1,438–1,635 | N/A | N/A | Roberts (2009) |
| Hull 1216 | Hull Magistrate's Court, Hull, Humberside, UK | OxA-9478 (2000) | 549 ± 33 | −18.5 | 13.4 | −33 ± 90 | 27.8 | 1,310–1,435 | 1,408–1,611 | 1,313–1,645 | |
| | | OxA-12037 (2003) | 425 ± 25 | −18.1 | – | −33 ± 90 | 32.2 | 1,428–1,611 | 1,492–1,657 | 1436–1806 | |
| Norwich 68 | Church of St. Margaret Fyebriggate, Magdalen St, Norwich, UK | OxA-4872 (1994) | 355 ± 50 | −21.6 | – | −33 ± 90 | 0.0 | 1,451–1,641 | N/A | N/A | |
| Norwich 129 | | OxA-4871 (1994) | 465 ± 50 | −20.1 | – | −33 ± 90 | 10.0 | 1,321–1,621 | 1,411–1,633 | 1,315–1,654 | |
| Norwich 227 | | OxA-4941 (1994) | 435 ± 60 | −19.9 | – | −33 ± 90 | 12.2 | 1,402–1,635 | 1,434–1,640 | 1,320–1,795 | |
| Safed 5111 | Safed, Israel | OxA-10107 (2001) | 595 ± 40 | −18.5 | – | 57 ± 101 | 18.8 | 1,294–1,414 | 1,327–1,614 | 1,283–1,625 | Mitchell (2003) |
| | | OxA-19360 (2007) | 438 ± 24 | −18.3 | – | 57 ± 101 | 30.0 | 1,424–1,479 | 1,495–1,660 | 1,424–1,953 | Mitchell (2009) |
| St. Helen-on-the-Walls 5556 | Church of St. Helen-on-the-wall, York, UK | HAR-6887 (1986) | 680 ± 80 | −21.3 | – | N/A | 0.0 | 1,197–1,419 | N/A | N/A | Mays (1998) |
| | | OxA-24162 (2011) | 434 ± 24 | −19.2 | – | N/A | 20.0 | 1,426–1,486 | 1,457–1,633 | 1,421–1,669 | Chamberlain (2011) |
| Thaon 118 | Thaon, France | Lyon-6496 (2010) | 370 ± 35 | N/A[d] | – | −31 ± 56 | 0.0 | 1,446–1,635 | N/A | N/A | Blondiaux (2010) |
| Whithorn cranium | Whithorn, Scotland, UK | OxA-4873 (1994) | 350 ± 45 | −22.5 | – | N/A | 0.0 | 1,459–1,644 | N/A | N/A | Roberts (2009) |
| **Old World individuals with an uncertain diagnosis of treponemal disease (Score < 4)** | | | | | | | | | | | |
| Castle Mound HC017 | Castle Mound, UK | SUERC-19641 | 955 ± 30 | −19.2 | 12.5 | −31 ± 56 | 20.0 | 1,022–1,155 | 1,046–1,217 | 1,020–1,270 | Mays et al. (in press) |
| Hull 932 | Hull Magistrate's Court site, Hull, Humberside, UK | OxA-12073 (2003) | 461 ± 23 | −17.8 | – | −33 ± 90 | 35.6 | 1,410–1,475 | 1,478–1,647 | 1,421–1,801 | Roberts (2009) |
| Hull 1121 | | OxA-12034 (2003) | 398 ± 27 | −18.1 | – | −33 ± 90 | 32.2 | 1,435–1,625 | 1,497–1,671 | 1,442–1,952 | |
| Ipswich 1965 | Ipswich Blackfriars Dominican Friary, Ipswich, UK | UB-3202 | 380 ± 18 | −19.3 | 16.1 | −20 ± 36 | 18.9 | 1,440–1,620 | 1,518–1,647 | 1,436–1,803 | Mays, Crane-Kramer, and Bayliss (2003) |
| Norwich 412 | Church of St. Margaret Fyebriggate, Magdalen St, Norwich, UK | OxA-5123 (1994) | 955 ± 31 | −18.1 | – | −33 ± 90 | 32.2 | 1,022–1,156 | 1,052–1,270 | 1,025–1,290 | Stirland (2009) |
| Rivenhall 204 | St. Mary and All Saints Church, Rivenhall, UK | To-8315 | 550 ± 60 | −19.5 | 12.9 | −33 ± 90 | 16.7 | 1,295–1,445 | 1,303–1,618 | 1,294–1,630 | Mays, Crane-Kramer, and Bayliss (2003) |
| St. Mary Spital 28460 | London, UK | UB-4594 | 709 ± 19 | −19.8 | – | 50 ± 31 | 13.3 | 1,265–1,298 | 1,285–1,390 | 1,217–1,444 | Sidell et al. (2007) |
| St. Trolla's Chapel 14 | Kintradwell House, Sutherland, Brora, Scotland, UK | AA-45S73 | 840 ± 40 | −22.3 | – | N/A | 0.0 | 1,040–1,280 | N/A | N/A | Lelong (2003) |
| Waterford E435: B253 | Waterford, Ireland, UK | OXA-4876 | 385 ± 45 | −20.9 | – | –59 ± 41 | 1.1 | 1,438–1,635 | 1,440–1,635 | 1,410–1,665 | Housley (1997) |
| **New World individuals with a certain diagnosis of treponemal disease (Score > 4)** | | | | | | | | | | | |
| Specimen DgRw 199 7.5-8.0S:1 | Gabriola Island, British Columbia | TO1145 (1988) | 2,760 ± 60 | −13.8[e] | – | 440 ± 50 | 80.0 | 1,049–805 BC | 368–16 BC | 719 BC–235 AD | Skinner (1994) |
| Burial 360, Boardwalk Site | Prince Rupert Harbour, British Columbia | S01735 (1979) | 2,510 ± 90 | −13.8[e] | – | 265 ± 80 | 80.0 | 805–407 BC | 347 BC–196 AD | 409 BC–380 AD | Cybulski (1990, 2010) |
| Specimen 458-22 A-ICNMHN | Aguzuque, Colombia | GrN 12930 (1985) | 4,030 ± 40 | −20.3 | – | −16 ± 30 | 8.1 | 2,836–2,467 BC | 2,830–2,457 BC | 2,865–2,298 BC | Coreal Urrego (1990), Deenen (2010) |

[a] Delta R was calculated by averaging marine sampling sites in geographic proximity to the archeological site using the CHRONO Marine Reservoir Database (accessed through Oxcal). In cases where no sites were nearby, which occurred only in the UK, the average value of −33 ± 90 yrs for UK coastal waters was used (Barrett et al. 2004).
[b] Calculated using linear mixing model of $\delta^{13}C$ collagen with terrestrial dietary endpoint of −21‰ and a marine dietary endpoint of −12‰ (Phillips and Gregg, 2001).
[c] In cases where the % marine carbon in the diet was estimated to be 0, an assumption of no uncertainty was made. In some cases, the algorithm used to correct radiocarbon dates with 20% uncertainty in the percentage of marine carbon in the diet gave a timespan that slightly predated the uncorrected date.
[d] It was not possible to obtain $\delta^{13}C$ values from the laboratory that dated these specimens. Because even the uncorrected 95% CI overlapped 1493, no correction was attempted in these cases.
[e] A $\delta^{13}C$ value was not available for this specimen, so the average for the region was used in our corrections.

from Europe. The publication dates ranged from 1949 to 2011. The reports were published in Chinese, English, French, German, Russian, and Ukrainian; over 30% of the papers were in a language other than English. Over half of the papers were in peer-reviewed publications (56%), and most reports were accompanied by photos (81%). Scores for diagnoses and dating are recorded in Table 1, as well as a description of the pathology for each specimen. For those cases wherein the diagnosis or pre-Columbian status of a case described in an article differed from our findings for the same specimen, our rationale for the score assigned is provided in bold face in Table 1, following the published diagnosis and date.

## Diagnoses

The scores assigned in the diagnostic category ranged from 0 (lesions consistent with a cause other than treponemal disease) to 5 (lesions specific to treponemal disease present, with multiple elements in a single skeleton affected). Full descriptions of the pathologies reported for each case, using standardized terminology (e.g., "periosteal reactions"), are listed in Table 1. We found that nondiagnostic lesions, such as systemic and localized subperiosteal reactions, continue to be equated with treponemal disease even in relatively recent studies. Twenty-two percent of papers on Old World, pre-Columbian treponemal disease published in the last 20 years made a diagnosis of treponemal disease based primarily upon the presence of periosteal reactions. This occurred despite a long-running recognition in paleopathology that these reactions have multiple etiologies and should be interpreted cautiously (see Brothwell and Sandison, 1967; Hackett, 1976; Ortner and Putschar, 1981, 1985; Ortner, 2003; Cook and Powell, 2005; Weston, 2008). Thirty-three percent of the articles reviewed described diagnostic lesions, however. These certain cases came from France (Mafart et al., 1998; Blondiaux, 2008), England (Brothwell, 1961; Dawes and Magilton, 1980; Roberts, 1994; Stirland, 1994, 2009; von Hunnius et al., 2006), Scotland (Hill, 1997), Poland (Gladykowska-Rzeczycka et al., 2003), Ukraine (Loganovskaja et al., 2000), Egypt (Ortner, 2003), India (Rao et al., 1996), Tinian (Stewart and Spoehr, 1967), Israel (Mitchell, 2003), and China (Zhang, 1994).

Of the eight reported cases of possible congenital infection, only two, Erdal's (2006) presentation of a case from Anatolia and Blondiaux's (2008) presentation of a case from Hamage, France provided strong evidence for congenital syphilis. These cases both garnered a 3, the highest score possible in this article for a report of congenital syphilis, though the lesions are not necessarily specific to this disease, as discussed above. While the report of a specimen with congenital syphilis from Costebelle, France was much publicized, its diagnosis has been questioned (Skinner, 1994; Rothschild and Rothschild, 1997).

## Dating

Despite the importance of securely dated cases in the debate over the origins of treponemal disease, the methods used to assign time periods to each case were not described in many of the papers. Dates and dating methodologies for each case are listed in Table 1. In contrast to providing a clear differential diagnosis, which the vast majority of authors did, 39% of the articles did not describe the dating methods used in any detail. In some cases, it was possible to surmise how dating was performed even though the methods were not explicitly discussed; in other cases, this was not possible due to vague descriptions and our inability to obtain additional information. Only 6% ($n$ = 3) of the articles reviewed described specimens that were securely dated to the pre-Columbian period, with scores of 4 or 5.

The problems imposed by vague descriptions of dating methods are best illustrated by the primary publication, von Hunnius et al. (2006), on four specimens recovered from the Hull Magistrate's Court site, in Hull, England. In the article, von Hunnius et al. described the date range associated with the cases as pre-Columbian, based on $^{14}$C radiocarbon dates (which the authors duly stated were problematic because of the marine reservoir effect), dendrochronology, and stratigraphic data. Dendrochonological analysis of coffins recovered from the site did provide a date range of AD 1340 to 1369 (Miller, 2000; von Hunnius et al., 2006). However, these coffins were not found in association with, or even within the same strata, as the reported cases and consequently have no pertinent temporal relationship (Evans, 2000; Evans, 2007). A description of the stratigraphic context for these individuals has yet to be published. Instead, radiocarbon dates for the skeletons, discussed in previous papers but presented here for the first time, unadjusted and adjusted for the marine signature, all overlap 1493 by a wide margin (Table 3). Thus, despite extensive media attention (Salt, 2002), no evidence has yet been published that suggests that these burials are pre-Columbian.

As indicated by the Hull results, radiocarbon dating has played a useful role in the debate over the antiquity of treponemal remains, as it can be used to confirm or refute dating based upon other lines of evidence. A number of more striking examples exist among the specimens reviewed. For example, a cranium with a certain diagnosis (score = 4) of treponemal disease was uncovered in a Roman-era cemetery in Arles (Mafart, 1993; see Table 1). This skull represented a compelling case of pre-Columbian treponemal disease based on archeological evidence, but radiocarbon dating demonstrated that the skull was, in fact, from more recent times. The results corresponded to a confidence interval, uncorrected for marine signature, indicating a 68.2% probability that the sample dated from between AD 1518 and 1588 and 30% probability that it dated from between AD 1625 and 1653 (Mafart et al., 1998). With the marine signature taken into account, the 95% confidence interval stretches as late as the 20th century (Table 3). Similarly, another individual with a certain diagnosis was identified in Ardenne, Normandy, buried under a door dated to the 13th century AD (Blondiaux, 2010). The archaeological context was once again deceiving, as a radiocarbon date demonstrated that the individual came from the 15th–17th centuries AD (Blondiaux, 2010). Finally, in perhaps the most surprising example of a misleading archaeological context, a skeleton from Thaon, Normandy (Blondiaux, 2010) with a certain diagnosis was found with a jar of perfume. Charcoal from the perfume jar was radiocarbon dated to AD 1258–1375. However, direct dating of the skeleton itself demonstrated that it was from the 15th–17th centuries

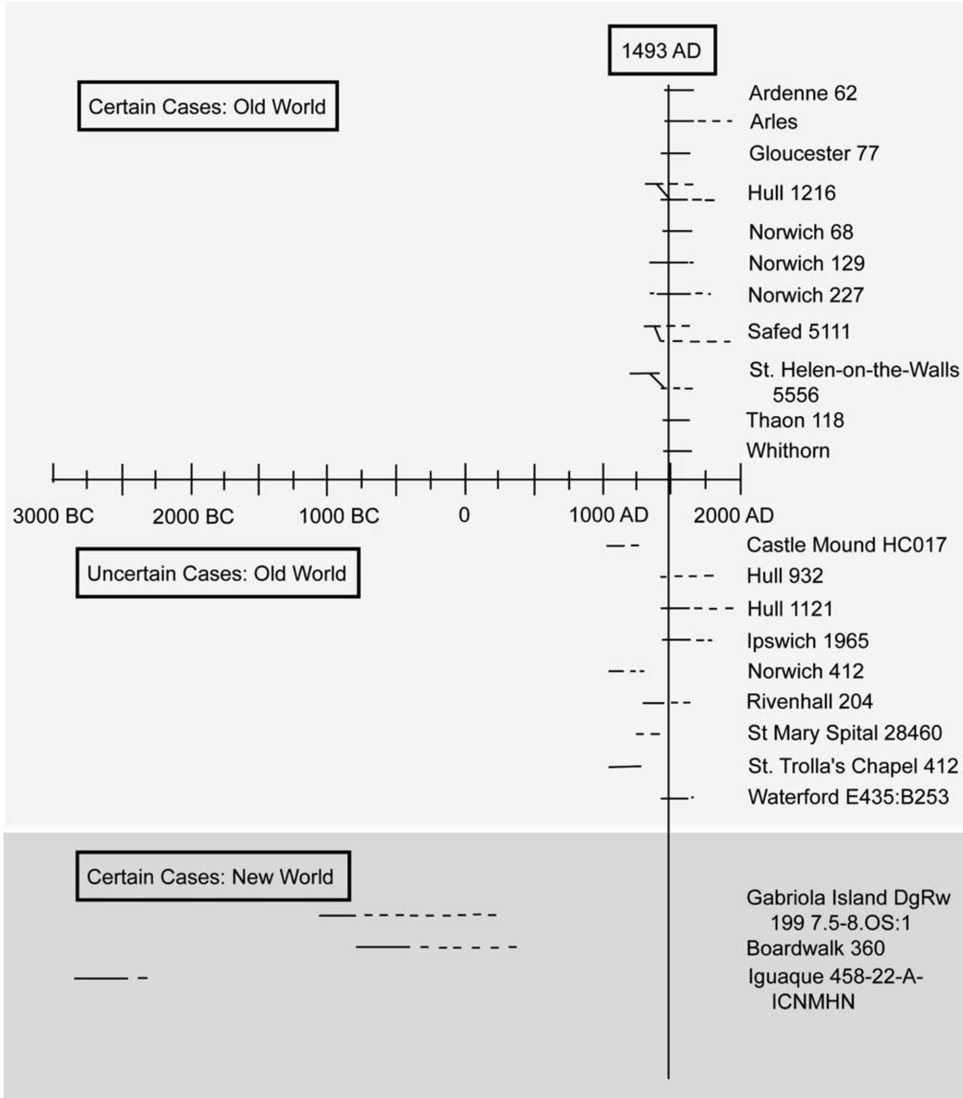


**Fig. 1.** A timeline showing the radiocarbon dates for reported pre-Columbian Old World and New World cases of treponemal disease demonstrates that the earliest Old World cases with a certain diagnosis (score ≥4) cluster tightly around the year 1493. This contrasts with both Old World cases with an uncertain diagnosis and New World cases with a certain diagnosis, which include specimens that can be securely dated to much older periods. The solid lines represent 95% confidence intervals for the radiocarbon dates, unadjusted for the marine signature. The dashed lines indicated the range of dates that must be considered after adjusting for the marine signature. Freshwater reservoir effects and some other sources of uncertainty were not incorporated into the adjustments, as described in the text.

AD (Blondiaux, 2010). These cases demonstrate the importance of using stringent dating criteria when evaluating reports of pre-Columbian treponemal disease; radiocarbon dating of bone collagen has proved invaluable.

Radiocarbon dating also has important limitations, however. It is well established that it is important to adjust for the marine reservoir effect when interpreting radiocarbon dates. The effect of the marine reservoir, as can be seen in Figure 1, is that the possible range of dates associated with an individual often becomes much larger and includes more recent time periods. However, only 4 of the 12 papers that included information on radiocarbon dates discussed the effect of the marine reservoir (Mays et al., 2003; von Hunnius et al., 2006; Sidell et al., 2007; Mays et al., in press). Some authors cited radiocarbon dates in their papers but did not provide the basic information needed to assess the certainty of the $^{14}$C results, such as the sample IDs identifying the laboratory facility at which they had been analyzed, the year of analysis, the calibrated and uncalibrated dates, and the $\delta^{13}$C value needed to estimate marine contributions to the diet (e.g., Trembly, 1996; Kuhnen et al., 1999; von Hunnius et al., 2006). Thus, due to the omission of critical data, the reported radiocarbon dates did not contribute to the certainty of dating in these cases, although this information is now available here for the specimens from the Hull Magistrate's Court site (Table 3).

Although we did not attempt to use isotopic nitrogen values to adjust dates for the effects of marine or freshwater reservoirs, the relatively enriched $\delta^{15}$N values reported for some individuals (Table 3) suggest substantial consumption of marine or aquatic dietary proteins. $\delta^{15}$N values were reported for only four individuals, but the values given are consistent with diets in which ~ 60–100% of consumed protein was derived from aquatic resources. Thus, we are left with a problematic situation: the radiocarbon dates of many of these individuals require adjustment, in light of the marine and freshwater components of their diet, but our current state of knowledge prevents us from using $\delta^{15}$N values to accurately quantify the effects of both marine and freshwater reservoir effects. However, our current inability to utilize $\delta^{15}$N values to adjust dates to account for reservoir effects should not prevent readers from considering the fact that, in many cases, a great degree of uncertainty remains but cannot be incorporated into the 95% confidence interval we calculated, even after adjusting for the marine reservoir effect using $\delta^{13}$C values.

Another limitation stemming from uncertainty not captured in the 95% confidence interval for radiocarbon dates is evident in Figure 1. Three individuals with certain (score $\geq$4) diagnoses of treponemal disease were radiocarbon dated twice. In the case of SK5111, an isolated cranium recovered from Safed, Israel, the first date placed the cranium between AD 1294 and 1414, the second between AD 1424 and 1479. After adjustment, the later, more accurate date spans from AD 1495 to 1660 or AD 1424 to 1953 (assuming 20% uncertainty in the dietary marine percentage). In the case of HMC94-SK1216 from Hull, the first, unadjusted date indicated that the individual died before Columbus's journey, between AD 1310 and 1435, while the later, unadjusted date stretched from AD 1428 to 1611. Adjusted, with uncertainty, the latter date extends to AD 1806 (see Table 3). Finally, St. Helen-on-the-Walls 5556, an isolated cranium from the UK, was initially radiocarbon dated to AD 1197–1419. A second date yielded a later estimate: AD 1426–1486; once adjusted for the marine signature, the latter interval reaches AD 1669. For all three individuals, the radiocarbon date obtained first gave a range that was much earlier than the date that was obtained subsequently. Adjusting for the marine signature helped to minimize the difference in date ranges indicated by independent measurements, except for the case of the St. Helen-on-the-Walls cranium, which initially did not appear to have a substantial marine dietary contribution. These cases illustrate the difficulty encountered in using radiocarbon dates to assign individuals to a very narrow historical window. The difference in dates in the Safed case appears to have been due to laboratory contamination that was subsequently detected and corrected (Mitchell, 2009). However, undetected sources of uncertainty may also cause relatively slight shifts in the range of dates obtained for an individual, shifts that are nevertheless problematic in interpreting the data in terms of historical debates such as this one. The problem of multiple dates that are statistically different is especially common in samples with low collagen yield, although it can also occur in samples with high collagen (Weber et al., 2005). For this reason, when obtaining an accurate radiocarbon date for a sample is especially important, as is the case for many of the individuals reviewed in this article who appear to have died very near AD 1493, we recommend that collagen yield be assessed, dates be adjusted for the marine signature, and multiple dates be obtained, so that a reasonable time span can be established.

## Synthesis of diagnosis and dating

The relatively large collection of specimens with radiocarbon dates allows us to test the Columbian hypothesis in a novel way. If this hypothesis is correct, all skeletons with certain diagnoses of syphilis should date to the period after 1493. As discussed in the background and methods, we made no attempt to differentiate between lesions caused by syphilis and those caused by the nonvenereal variants, due to a lack of evidence-based criteria with which to do so. However, an absence of treponemal disease in the Old World prior to Columbus's return necessitates an absence of syphilis. Because it is unavoidable that a certain amount of error enters into dating, under the Columbian hypothesis one would predict that a small number of specimens with definite treponemal lesions would be mistakenly dated to pre-Columbian times. Radiocarbon dates should show that these specimens cluster within the time period surrounding 1493, since the error in most dates will be reasonably small. If a radiocarbon date falls much earlier than 1493, it would have to belong to a specimen with ambiguous lesions, since very large errors in dating are unlikely. Alternately, if treponemal disease existed in the Old World long before 1493, one would expect radiocarbon dates for the definite cases to show a wide distribution, occurring much earlier than 1493, as they do in the New World (Fig. 1).

There were eleven cases that met our criteria for a certain diagnosis of treponemal disease that also had accompanying radiocarbon dates (Tables 1 and 3, Fig. 1). A definite trend, consistent with the predictions of the Columbian hypothesis, is present in Figure 1; the cases with certain diagnoses have confidence intervals that both cluster around and overlap AD 1493. In other words, these 11 individuals represent the earliest definite cases of treponemal disease yet discovered in the Old World, and their radiocarbon dates indicate that they lived in a relatively short time period surrounding 1493. We argue that rather than representing evidence of pre-Columbian treponemal disease, these cases actually provide support for the Columbian hypothesis. As expected if the Columbian hypothesis is correct, only cases with an uncertain diagnosis of treponemal disease—in other words, cases whose lesions could be attributed to other conditions—could be radiocarbon dated to earlier periods.

Several reports described cases of treponemal disease that appeared to be certain (score $\geq$4), but which did not provide strong evidence of a pre-Columbian date. In these cases, radiocarbon dating may help clarify their age and thus contribute to the debate about treponemal disease's antiquity. Such reports included skeletal remains from Agripalle, India (Rao et al., 1996), the Blue Site, Tinian (Stewart and Spoehr, 1967), Dongshan County, China (Zhang, 1994), Uspensky Cathedral in Kiev, Ukraine (Loganovskaja et al., 2000), Spitalfields Market in London (Brothwell, 1961), St. Idzis, Poland (Gladykowska-Rzeczycka et al., 2003), and El Kurrew, Egypt (Ortner, 2003; see Table 1). Although radiocarbon dating may be of limited utility in the cases that date from the time period immediately surrounding 1493 for the reasons described above, it should easily confirm the cases thought to be much older (e.g., those from Agripalle, Dongshan County, and El Kurrew).

## Possible explanations for the lack of treponemal disease in the pre-Columbian Old World

Our evaluation indicates that there is not a single published case from the Old World that can be confidently diagnosed as treponemal and that has a radiocarbon date that places it firmly in the pre-Columbian period. The trope that absence of evidence is not the same as evidence of absence will be invoked by some. While it is true that a working hypothesis may be falsified at any time, at what point does the absence of skeletal evidence of pre-Columbian treponemal disease in the Old World become compelling? After all, the best proof of a theory is failure to disprove it, and we find that despite intense research interest, credible evidence disproving the Columbian Hypothesis is lacking. Here, we discuss some of the rationales for the scarcity of evidence of Old World treponemal disease that have been raised in the past.

Roberts (1994) has argued that the relative infrequency of skeletal involvement in treponemal disease may lead to a low number of recognizable cases in the archaeological record. Even in the pre-Columbian New World, where a nonvenereal treponematosis was likely endemic, diagnostic cases are fairly uncommon (Hutchinson and Richman, 2006). Ortner et al. (1992) have suggested that diagnostic pre-Columbian Old World cases could logically be just as scarce. As such, is it possible that cases of treponemal disease are present in the pre-Columbian Old World and have been overlooked due to their scarcity? This appears to be a valid hypothesis for some regions. Skeletal evidence from vast expanses of sub-Saharan Africa and Asia has not yet been well studied or thoroughly reported (Larsen, 1997, 2002; Kennedy, 2000; Meyer et al., 2002). Treponemal cases in these regions may have been overlooked, not yet recovered and recognized, or been lost to poor preservation. However, in other regions, such as Europe and North Africa, tens of thousands of skeletons have been examined. In Egypt, an estimated 25,000 skeletons had been examined for pathologies by the early 20th century (Steinbock, 1976). Similarly, though systematic analysis of skeletons did not begin in England until the 1990s, an estimated 50,000 skeletons have been examined for pathologies in that country alone (Roberts, 2002). From all of these bones, no securely dated, diagnostic cases of pre-Columbian treponemal infection have yet been published. In contrast to the dearth of treponemal cases, bones bearing the marks of other diseases, such as leprosy and tuberculosis, are plentiful in the pre-Columbian time period (Pálfi et al., 1999; Roberts et al., 2002; Roberts et al., 2009). Skeletons from the post-1493 period are another matter. After the return of Columbus, certain evidence of treponemal disease begins to appear immediately (e.g., Jankauskas, 1994; Boulter et al., 1998); therefore, researchers who argue that pre-Columbian cases of osseous treponemal disease are too rare to detect must explain why the prevalence of specific lesions would have changed immediately at the end of the 15th century.

Similarly, some investigators have argued that the availability of training, funding, and of researchers interested in documenting treponemal disease may play a pivotal role in the scarcity of pre-Columbian, Old World treponemal cases. For example, Roberts (1994), Vasulu (1994), and Becker (1988) have argued that the advanced paleopathological training, adequate funding, and emphasis on diagnostics (e.g., Ortner and Putschar, 1985; Aufderheide and Rodrìguez-Martìn, 1998; Ortner, 2003) in North America in the past could be partially responsible for the hemispheric asymmetry in published cases. We argue, instead, that the radiocarbon-dated cases with certain diagnoses (scores $\geq$4) in this article indicate that researchers in the Old World have done an excellent job at identifying some of the earliest cases of treponemal disease; it appears, however, that these earliest cases may simply date to the post-1493 period. As for the arguments discussed above, those who assert that lack of personnel, interest, or training is to blame for the absence of Pre-Columbian cases must explain the ability of researchers to identify cases in the period immediately after 1493 and to identify traces of other infectious diseases, such as leprosy and tuberculosis, before this date. In a recent summary of the results thus far from the Global History of Health Project, which has systematically studied over 12,000 European skeletons, it was stated that while all "probable treponemal disease cases" were confined to the high middle ages or later, tuberculosis was found to be common as early as classical antiquity, and leprosy cases could be found in the early middle ages (Roberts et al., 2009; p 223). These findings do not seem compatible with a deficit of researcher training or attention to treponemal disease in the Old World.

Another issue that has been raised deals with demographic patterns in the pre-Columbian Old World. Because tertiary stage treponemal infection can take years to develop, it has been argued that lower life expectancies in the past may have cut many infections short and prevented the development of diagnostic skeletal lesions (Watts, 1997). Again, however, there is no evidence of a widespread demographic shift towards higher life expectancies in the Old World in the late 15th century that could explain the considerable evidence of treponemal disease found in many regions in the period immediately after 1493 (e.g., Suzuki, 1984; Jankauskas, 1994; Boulter et al., 1998; Lynnerup and Rhee, 2010; WORD database 2010). Widespread, sustained increases in longevity instead occurred among many Old World populations in the 19th and 20th centuries (Wrigley and Schofield, 1981; Steckel and Floud, 1997; Steckel, 1999).

Finally, several researchers have argued that, in the United Kingdom in particular, pre-Columbian individuals suffering from syphilis may have been grouped with leprosy sufferers in hospitals and public institutions (Stirland, 1991; Roberts, 1994). This lumping of diagnostic categories could explain why syphilis was not recognized as a disease prior to the end of the 15th century; it would also predict that skeletons with evidence of treponemal disease would be found in leprosy hospital cemeteries. As only a few hospital cemeteries in the UK have been excavated and studied (Roberts, 2007; White, 2009), pre-Columbian treponemal cases could be languishing there, unrecognized. Do existing data support this hypothesis, though? Historical evidence indicates that late medieval medical practitioners in many regions were able to discriminate between leprosy and syphilis immediately, as the disease spread across Europe in the 1490s and early 1500s (see Mitchell, 2003; McGough, 2005).[5] In Italy, for example, physicians and chroniclers compared syphilis and leprosy for classificatory purposes, but their writings, as well as contemporary mortality and hospital records, indicate widespread recognition of a new disease and uniformly clear, rigorous clinical differentiation between the two conditions as syphilis

[5]While a thorough discussion of the emergence of diagnostic criteria for syphilis is beyond the scope of this article, Oriel (1994) and Harris (1996) provide an in-depth discussion of this topic.


**Fig. 2.** Maps depicting **A**) all reported cases of pre-Columbian treponemal disease in the Old World; **B**) those cases with a certain diagnosis (score ≥4); and **C**) those cases with both a certain diagnosis (score ≥4) and a radiocarbon date with a 95% CI interval that ends before 1493, after adjusting for the marine signature (dating score ≥4).

spread through each community in the 1490s (Arrizabalaga et al., 1997; Carmichael, 1990). Historical records indicate the same level of diagnostic clarity in contemporary France, Scotland, and England (Foa, 1990; Quétel, 1990). It is unclear why, then, the same practitioners would have been unable to separate the two diseases prior to the 1490s. In addition, excavations of pre-Columbian leprosy hospital cemeteries have not produced any cases of treponematosis to date (Møller-Christensen, 1969; Crane-Kramer, 2002). While future excavations and analyses of medieval hospital cemeteries will further illuminate this issue, as of yet the hypothesis that syphilis was routinely misdiagnosed as leprosy prior to the 1490s has little empirical support.

In sum, after reviewing the current evidence on the subject, we agree that certain areas of the world need to be studied more before the book on the history of treponemal disease in the Old World can be closed. Vast areas of Asia and Sub-Saharan Africa have been relatively neglected, in some cases largely due to the lack of well-preserved human remains to study. Increasing attention by researchers to sites in little-studied areas may shed light on the history of this infection in human populations worldwide. The same cannot be stated of Europe and the Mediterranean, however. In these regions, large numbers of skeletons have been studied but have not yielded a single convincing case of treponemal disease that dates to the period before 1493. Moreover, skeletal samples that span 1493 demonstrate that cases with certain diagnoses start to appear immediately after this date. For example, we find, as did Jankauskas (1994), that in Rokhlin's extensive studies of Russian individuals before and after this period, the first certain diagnoses (scores ≥4) did not appear until after 1493 (Rokhlin and Rubasheva, 1938; Rokhlin, 1965). The absence of certain cases of treponemal disease before 1493 and its frequent presence after that year has also been noted in Lithuania, Latvia (Jankauskas, 1994), and Japan (Suzuki, 1984). In Naestvad, Denmark, where six hundred and fifty individuals dating from 400 to 700 YBP were studied, the earliest treponemal case dated to between AD 1500 and 1550 (Møller-Christensen, 1978). In Hungary, too, in a large series in which the majority of skeletons were dated to before the 14th century AD, the first cases of treponemal disease were found in individuals dated broadly to the 14th–17th centuries, although tuberculosis was plentiful throughout the period studied, consistent with a post-1493 origin for syphilis (Marcsik, 1994). We argue that the scarcity of evidence immediately prior to 1493 and the relative wealth of evidence immediately after this date, in sample after sample, support the hypothesis that treponemal infection arrived in Europe and the Mediterranean with the return of Columbus and his crew.

## CONCLUSION

Using rigorous criteria to assess the diagnosis and dating of reported cases of pre-Columbian treponemal disease, criteria similar to those proposed by other researchers in the past (e.g., Skinner, 1994), we find that the evidence remains consistent with a scenario in which treponemal disease in Europe and the Mediterranean appeared after 1493. Figure 2 shows the geographical distribution of a) all sites evaluated in this study, b) all sites yielding cases with certain treponemal diagnoses (score ≥4), and c) all sites yielding cases with certain diagnoses and radiocarbon dates which, when adjusted for the marine signature, place them in the pre-Columbian period (both scores ≥4). The number of sites in the last category is zero; though many certain cases of treponemal disease were reviewed in this article, the dates remain problematic in all of them.

This situation contrasts with that found in the pre-Columbian New World. Radiocarbon dating and other types of destructive analysis of indigenous human remains recovered from the New World is often not possible or advisable because of NAGPRA (Native American Graves Protection and Repatriation Act) and other social, ethical, and political concerns (Mihesuah, 2000; O'Rourke et al., 2005; Cassman, 2007; Walker, 2008). Because of this and the fact that the antiquity of treponemal disease in the New World is not nearly as controversial, specimens are usually only dated indirectly, using stratigraphy, artifacts, or radiocarbon dating of associated organic materials. Even so, specimens bearing diagnostic signs of treponemal disease have been radiocarbon dated to periods well before 1493. In contrast to the situation in the Old World, these dates do not cluster near the late 15th century AD (Fig. 1). Instead, they span a period dating back to 3000 BC, as one would predict if the disease were actually present thousands of years before AD 1493. The fact that multiple New World specimens meet our criteria, in spite of the harsh climate towards radiocarbon dating in this part of the world, demonstrates that we have not set the bar for proof too high and that we can reasonably expect cases from the Old World to yield 95% confidence intervals that exclude

1493. In fact, the New World cases meet even more stringent criteria for radiocarbon dating, as their 99.7%, or $3\sigma$, confidence intervals exclude AD 1493 as well. Since, given enough reports, roughly 1 in every 20 skeletons dating from the early post-Columbian period will appear to be pre-Columbian due to chance alone when evaluated using 95% confidence intervals, applying the 99.7% confidence interval criterion to putative cases should be considered in future studies.

One of our major findings is that considerable problems with presentation prevent researchers from easily assessing the validity of reports and unnecessarily complicate the debate over the origin and antiquity of syphilis. When presenting a possible case of pre-Columbian treponemal disease, a detailed and accurate description of the case and its date are essential. The overwhelming majority of investigators appreciate the profound importance of documenting lesions using standardized terminology and diagnostic criteria (see Ortner, 1994; Cook and Powell, 2005; Powell and Cook, 2005b; Waldron, 2009). Only this approach opens cases to independent evaluation by other researchers, allows the comparison of cases from different regions and time periods (Roberts, 1994), and advances paleopathology as a scientific field. However, some authors whose works were reviewed here did not describe the pathologies of the case and presented only a classification of a lesion [for example, indicating that skeletons display "*caries sicca*" without providing supporting imagery or description of the lesions (e.g., Trembly, 1996; Sidell et al., 2007)]. Much more common is the lack of information about dating. Nearly 40% of the articles did not provide enough information about the employed dating methods for the reader to be able to assess whether the pre-Columbian date reported was secure. Seven of the 21 articles that did not provide sufficient documentation appeared in peer-reviewed journals.

We found another common problem to be the use of nonspecific indicators to diagnose treponemal disease. It is discouraging that some investigators continue to diagnose treponemal disease based on nonspecific lesions such as periosteal reactions, despite abundant evidence that such lesions occur in many other conditions (e.g., Hackett, 1976; Cook and Powell, 2005; Weston, 2008). It is even more discouraging that eight of the ten articles published in the last 20 years which diagnosed treponemal disease based primarily on these lesions appeared in peer-reviewed journals.

We suggest that all future reports of pre-Columbian disease meet certain basic requirements. The first is a diagnosis based on standardized criteria and lesions specific for treponemal disease and presented using descriptive, standardized terminology (e.g., Brothwell, 1981; Buikstra and Ubelaker, 1994; Ortner, 2003; Brickley and McKinley, 2004). Cases should be presented with a cautious, thorough differential diagnosis (e.g., Mays et al., 2003), particularly when inconclusive evidence, such as systemic periosteal reactions, is being assessed. Ideally, cases should also be accompanied by high-resolution photographs. Although it is not always possible to obtain permission to photograph specimens or space to include pictures in a publication, it is unlikely that unphotographed specimens will meet the burden of proof required by this controversial subject. The second criterion for publication is a standardized presentation of the evidence that places the find securely in the pre-Columbian era. Such evidence should be described clearly and thoroughly and should be confirmed using radiocarbon dating, with a full presentation of supporting data and a discussion of reservoir effects. If researchers adhere to these guidelines, the debate over treponemal disease's origins should progress more rapidly. In addition, we encourage the publication of negative results (i.e., large skeletal samples in which no evidence of treponemal infection is present) as well as new and ongoing collaborations between researchers, to create regional and national databases of skeletal collections and enlarge those already established (e.g., WORD database). Only in this way can researchers develop a clear picture of the geographic and temporal distribution of treponemal disease throughout human history.

In this analysis, following 23 years after Baker and Armelagos's (1988) comprehensive review, we report that there is still no secure evidence of treponemal infection in the pre-Columbian Old World. These results are consistent with genetic data that suggest syphilis, or a progenitor, arose in the New World; however, they are inconsistent with evidence from the same study that the nonvenereal treponemes have an ancient history in the Old World (Harper et al., 2008a,b; contra Mulligan et al., 2008). Problems with diagnosis and dating persist despite the best efforts of researchers, and it is through the ready sharing of research findings from multiple sites that progress in paleopathology is made. As in epidemiological studies of modern populations, isolated findings mean little until they are confirmed by identifying patterns across multiple, diverse samples. We eagerly await the forthcoming publication of the findings of large population-level studies of Old World skeletal samples (e.g., Roberts et al., 2009; Connell et al., in press; McIntyre et al., in preparation), and we are enthusiastic to learn what the next 20 years will reveal about the syphilis enigma.

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