Pre-Columbian Treponemal Disease From 14th Century AD Safed, Israel, and Implications for the Medieval Eastern Mediterranean

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ABSTRACT  In 1912, 68 medieval crania were excavated from a cave at Safed in the eastern Mediterranean and brought to the United Kingdom. It is only recently that these skulls have been studied for evidence of disease. One adult individual demonstrates multiple lesions of the cranial vault, compatible with treponematosis. Radiocarbon dating suggests the year of death to be between 1290–1420 AD. This range equates to the mamluk period, just after the crusades. This is the oldest dated case of treponematosis in the Middle East, and the first to confirm its presence there before the epidemiologically important transatlantic voyage of Christopher Columbus. The finding has significant implications for our understanding of the introduction of the disease to the Middle East and of the medieval diagnosis of ulcerating skin conditions by medical practitioners in the Mediterranean world. Am J Phys Anthropol 121:117–124, 2003. © 2003 Wiley-Liss, Inc.

The epidemiology and spread of treponemal disease remain of particular interest to those researching the evolution of disease in humans. For many years, the archaeological evidence suggested a New World origin for the treponematoses (Baker and Armelagos, 1988). Many early cases of human skeletal remains with characteristic lesions had been identified there, some dating back to over 3000 BC (Brothwell and Burleigh, 1975). In contrast, the evidence for its presence in the Old World prior to the 15th and 16th century transatlantic sea voyages was controversial. However, recent years have seen the excavation of a significant number of pre-Columbian cases of treponemal disease from Old World sites. Examples from across Europe date back to Greek and Roman times (Blondiaux et al., 1994; Henneberg and Henneberg, 1994; Mays et al., 2002; Pálfi et al., 1992; Roberts, 1994; Stirland, 1991). In the Pacific, treponemal disease has been identified in pre-European contact populations as early as the 9th century AD (Brothwell, 1976; Trembly, 1996).

While treponemes as a group seem to have been present on several continents even 1,000 years ago, it is by no means clear when, where, and how the clinical forms of treponematosis recognized today developed. Pinta is a skin disease of humid tropical climates, but the other forms all affect bone and so may be detected in archaeological specimens. In the 20th century, yaws was noted to be prevalent in humid tropical climates, bejel (endemic syphilis) was found in arid climates, and venereal syphilis was found worldwide in communities in contact with developed societies (Grin, 1952; Hudson, 1958; Perine et al., 1984). Yaws and bejel are transmitted in childhood from nonsexual physical contact with ulcerated lesions on the skin and mouth, while venereal syphilis is transmitted in adulthood during sexual activity or transplacentally as congenital syphilis (Chulay, 2000; Tramont, 2000). These conditions may cause rashes and ulceration of the skin, destruction of the nose, and a range of bony changes such as anterior bowing of the tibia.

The earliest cases of treponemal disease so far identified in the Middle East date from the 17th–18th centuries and are thought to have been due to bejel (Goldstein et al., 1976; Hershkovitz et al., 1994). These authors suggested that treponematosis came to Israel with the migration of Bedouin tribes at that time. Any cases found to date earlier than this time would greatly alter our views of when and how the disease was introduced to the region. The purpose of this paper is to demonstrate if trepone-
mal disease was in fact present in the Middle East from a much earlier date. Any evidence for the presence of treponematosis in the region by the medieval period would also mean that we would have to re-evaluate not only the method of spread into the region but also the interpretation of ulcerating skin diseases described in medieval medical texts written in the Middle East.

THE SAMPLE

The 68 skulls under study are held in the Duckworth Laboratory at the University of Cambridge (Cambridge, UK). Original records show that they were deposited there in 1912. A hand-drawn map (Fig. 1) and entry note stated that the skulls were from a cave near the town of Safed, to the northwest of the Sea of Galilee (now in Israel). It appears that the postcranial remains were left in situ. This may well be due to the interest in craniometry that was common in the 19th and early 20th centuries. The excavators of the Safed site believed that the remains were of crusaders who had been killed in the sack of the town by Islamic troops. However, no evidence for this assertion was given, no excavation report is available, and no other finds are known. In fact, it is only the hand-drawn map that allows even an approximate location for the remains, and the exact site is unknown today. Interestingly, there is a 12th-century crusader manuscript that mentions that Christians from Safed were buried in the nearby cave church of Tobias (Michelant and Raynaud, 1882). However, without finding the cave of Tobias, it is not possible to say for sure if this was the one from which these skulls came.

Most of the crania are incomplete and are comprised of either facial elements with a frontal bone, or just the cranial vault. Three individuals were immature, and the remaining 65 were adults. Although the absence of postcranial elements made the determination of sex difficult, using standard criteria (Ferembach et al., 1980; Novotný et al., 1993), only three of the adults were indeterminate.

Of the 62 sexable individuals, 37 (60%) were identified as probable females and 25 (40%) were probable males. The cranial size and shape of this sample are compatible with a Mediterranean phenotype (Novotný et al., 1993). It is not known if the skulls represent all those individuals interred in the cemetery, a truly random sample from a larger series, or a sample selected for a particular reason. However, none of the lesions described here were recorded in the notes written about the remains in 1912, although great detail was recorded on aspects of natural variation, such as skull shape and suture pattern. It seems most likely that if the samples are a nonrandom selection, then factors such as the completeness of the skull or the proximity of the remains to the soil surface would have been more likely sources of bias than the prevalence of pathological conditions.

One adult cranium in the population under investigation is of particular interest due to the presence of cranial vault lesions. The skull (code 5111) is comprised of the right and left parietal bones and part of the occipital bone (Figs. 2–4). In consequence, it was not possible to assign sex to this individual. Unfortunately, a hole was noted in the left parietal bone which had the appearance of periexcavation damage from a trowel or similar implement (Fig. 4). Some postmortem erosion of the left parietal bone is also present inferiorly and posteriorly, with flaking and crumbling of the external cortex, and this prevents the study of lesions in those areas. Macroscopic and radiological analysis was undertaken. In view of the uncertain provenance of the remains, accelerator mass spectrometry (AMS) radiocarbon dating was performed at the Oxford University Radiocarbon Accelerator Unit (Oxford, UK). The analysis provided a date of 1290–1420 AD with 95.4% confidence. This range would place the remains in the mamluk period (1249–1517 AD), just after the Crusades (Ashtor, 1976).
DESCRIPTION OF REMAINS

Individual 5111 demonstrates multiple lesions of the outer table of the parietal bones. On the right parietal bone there are several distinct lesions (Fig. 2), but two of these are particularly prominent (Fig. 3). These are located in the posterior and middle parts of the bones. The posterior lesion abuts, though does not cross, the lambdoid suture. It is 3 × 3 cm, and round in shape. The surface is comprised of smooth, cortical bone suggesting a healed pathological process. The margins are rolled inwards towards the center of the lesion and fine grooves are present, compatible with the presence of small blood vessels. While the floor of the lesion is thin, the central part is raised somewhat relative to the floor of the peripheral parts of this lesion. Nowhere is the floor perforated. The inner table shows no evidence of pitting on the endocranial surface. The other prominent lesion lies anterior to this first lesion. It is 3 × 2 cm across and stellate in shape, with convexity towards the center of the lesion as a whole. The base of the lesion is thin, and the surface is formed from cortical bone. The inner table of the skull appeared unchanged. A radiograph of the right parietal bone demonstrates several stellate lucent areas with surrounding sclerotic bone (Fig. 5). The posterior part of the left parietal bone is also involved. Unfortunately, this side of the skull is harder to interpret due to the postmortem erosion of the outer table of the bone inferiorly and posteriorly, coupled with a small hole compatible with trowel damage at excavation. However, immediately superior to this trowel hole there is a stellate lesion 2 × 1 cm across, with a raised central nodule 5 mm across. Curving grooves extend anteriorly, superiorly, and posteriorly from this central nodule, being widest at the nodule and tapering to a point more peripherally (Fig. 4). The surface of the lesion is comprised of cortical bone, and the inner table of the skull appears normal. The fine superficial pitting present on the surface of this lesion may be secondary to postmortem erosion.

DISCUSSION

The cranium of this individual possesses multiple lesions that should allow determination of the underlying disease process. In an ideal situation, we would look for supportive evidence from bones of the face and peripheral skeleton. However, the circumstances of the excavation nearly 100 years ago mean...
that this corroborative evidence is not available. Differential diagnosis of lesions of the cranial vault includes treponematoses, depressed fractures, bacterial osteomyelitis, tuberculosis, benign and malignant primary tumors, metastases, hematological malignancy, and postmortem damage (Ortner and Putschar, 1981).

The problem in differentiating depressed fractures and some old, remodelled treponemal lesions was highlighted in past work (Hackett, 1976; Hershkovitz et al., 1994). A number of factors may help distinguish the two conditions. If the inner table of the bone is protruding into the cranial cavity, this is suggestive of a depressed fracture rather than treponematoses. If the shape of the lesion is oval or round with edges concave towards the center when viewed from above, this is compatible with both a depressed fracture and treponematoses. If the shape is stellate, with edges convex towards the center when viewed from above, this is suggestive of treponematoses. The size of the lesion may be helpful, as a large depressed area due to fracture is highly likely to also depress the inner table. If the area is large and the inner table remains intact, then this would be more suggestive of healed treponemal disease from the contiguous series of the caries sicca sequence. While histology is useful in active lesions (Schultz, 1994), its use in old lesions that have healed and remodelled many years before death may be more challenging. Certainly a small, shallow, oval depressed area on the outer table with gently sloping margins and no proliferative bone remains hard to interpret. Hackett (1976) believed that a collection of such lesions on a skull is very suggestive of treponematoses, but not diagnostic. To reliably distinguish all depressed fractures from old, remodelled treponemal lesions with more certainty may require a research project studying skeletal remains in endemic populations where medical records mentioning trauma events are available for each individual.

Differentiation between treponematosis and a range of other conditions affecting the skull is also necessary to identify the underlying pathological process. Osteomyelitis of the skull may follow infection of one of the cranial air sinuses or middle ear, dental disease, or an open skull fracture. The bony lesion is classically comprised of a central sequestrum surrounded by a lytic zone, and then an area of sclerotic response with periosteal new bone peripherally on both inner and outer tables (the involu- crum). Tuberculosis typically gives a solitary lesion which destroys both tables of the skull, with the inner table most affected. There is little or no bony reaction, and the margins of the lesion are irregular and destructive. Neoplasia in bone may be benign or malignant, primary or secondary, and may trigger an osteoblastic, osteolytic or mixed response. The most common neoplastic lesions are due to metastases, which usually spread from carcinomas of organs such as the breast, prostate, thyroid, lung, and kidney. Osteoblastic lesions (such as originate from carcinoma of the prostate) result in an irregular structure of sclerotic new bone formation expanding from the original bone, which has increased density on radiographs. Lytic metastatic lesions (such as originate from carcinoma of the breast) lead to destruction of the bone most pronounced in the diploe, with minimal if any new bone formation. Hematological malignancies such as myeloma and histiocytosis X may also affect the skull. In myeloma, the “pepper pot skull” is affected by multiple punched-out lytic lesions 3–10 mm across. Histiocytosis X may cause larger destructive lesions through both tables of the skull, with geographic contours and little reactive new bone formation. Primary tumors of the skull are less common than metastases from other organs. Osteoblastic lesions range from benign osteoma and hemangioendothelioma to malignant sarcomas, although these are very rare in the skull. Osteolytic primary tumors of the skull include benign dermoid cysts and giant-cell tumors (osteoclastoma), which are typically encased with a thin, periosteal shell of bone (Ortner and Putschar, 1981).

Postmortem damage may be difficult to differentiate from some lesions on the skeleton, and certainly erosion of the outer table of some areas of the left side of the skull did occur. Water, tree roots, insects, and the weight of overlying soil can all lead to alteration in bone shape or surface characteristics. However, bone can only ever be lost by this process, so that any excess bone present is likely to be formed during life as a consequence of the disease process. Furthermore, postmortem erosion that leads to a depression on the bone surface causes the deeper structures in the bone to become visible, such as the diploe in the skull. We would not expect to find a smooth layer of cortical bone over areas of deep postmortem erosion, and such a layer again suggests that healing of the lesion occurred during the lifetime of the individual.

The cranial lesions of treponemal disease may be described with the eight pathological stages in the caries sicca sequence first described by Hackett (1975, 1976, 1981, 1983). The eight stages are further divided into three sections, termed the initial series, the discrete series, and the contiguous series. Lesions of the initial series progress either to the discrete series if small, or to the contiguous series if covering a large area of the skull. The initial series is comprised of the first two caries sicca stages, and is believed to occur in the early development of all lesions. Stage 1 is clustered pits. This is a well-defined, round area 10–15 mm across, with pits 1 mm in diameter. There is a zone of increased bone density around each cluster. The outer table is heavily involved, but there are few or no changes on the inner table. The frontal and parietal bones are most commonly involved, but individual lesions tend to avoid crossing sutures. Stage 2 is confluent clustered pits. The pits in the outer table increase in size and coalesce. This may lead to a central erosion, or leave a centrally pitted plug of bone surrounded by
With further healing, the nodules enlarge to 5–10 nodules about 5 mm across. Stage 8 is caries sicca. Margins become rounded, and there is formation of nodular cavitation. In the healing phase, a rim of new bone forms around the lesion. The margins appear rolled and may be finely grooved by small blood vessels. In early stages, the raised rim may be pitted. The rolled margins give a stellate shape to the lesion, with edges convex to the center of the lesion. Adjacent circumvallate cavities may sometimes fuse to create arabesque shapes. Stage 5 is radial scarring. Continued healing covers the walls and base of the cavity with new bone until only a shallow depression remains. Initially there is a radial pattern of thin wavy lines, surrounded by the rimmed margin. With remodelling the rimmed margin flattens, but the depression remains for life. The contiguous series is formed by peripheral extension of the initial series (stages 1 and 2) to lead to larger areas of change in the skull. Despite the fact that its stages are numbered 6–8 in the caries sicca sequence, it is not a progression from stages 3 to 5 (the discrete series). Stage 6 is serpiginous cavitation. Here an irregular confluence of clustered pits covers an area up to 10 cm across. This leads to snake-like cavities which have sharp irregular margins with concave walls, and the floor is formed by the diploe. Stage 7 is nodular cavitation. As healing proceeds, the sharp margins become rounded, and there is formation of nodules about 5 mm across. Stage 8 is caries sicca. With further healing, the nodules enlarge to 5–10 mm across, and this encroaches on the spaces separating them. When the nodules touch, this leaves stellate depressions between them. The inner table may also be thickened. In large areas of skull involvement there may be caries sicca centrally, nodular cavitation more peripherally, and serpiginous cavitation at the edges, suggesting the progression of the lesion as it spreads outwards. Sequestra may be present in any stage of the caries sicca sequence, but are not diagnostic of treponemal disease.

A comparison of the lesions noted on the Safed material with those in our differential diagnosis allows the underlying disease process to become clear. The lesions on both the right and left parietal are not destructive or lytic, so that neoplasm and tuberculosis would not be the cause. Furthermore, the lesions are multiple and involve the outer table and diploe rather than the single lesion principally affecting the inner table which is characteristic of tuberculosis. There are no sequestra, involucra, clacae, or periosteal new bone, so osteomyelitis is very unlikely. While the lesions are associated with cortical new bone formation, the shape together with the presence of central depressed areas on the right parietal preclude a diagnosis of benign tumor. The rolled margins, stellate shape, and intact inner table of each lesion argue against depressed fractures. The smooth cortical bone, even at the base of these lesions on the right parietal, makes postmortem erosion very unlikely as a cause. Postmortem damage is present on the inferior and posterior aspects of the left parietal, but neither the destructive loss of the outer table commonly caused by water damage nor the hole due to the excavation trowel could explain the raised central nodule surrounded by circumferentially radiating grooves with intact cortical bone (Fig. 4).

While each of these nontreponemal conditions may lead to destructive changes to the cranial vault, none give the characteristic stellate scars and caries sicca pattern on healing which enables a diagnosis of treponematosi. This is likely to be a consequence of the underlying pathology. The cranial lesions of treponemal disease are a result of an oblitative inflammatory arteritis leading to ischemia and necrosis of the outer cortex (Hackett, 1981). Healing of the gummatous osteitis results in characteristic thickened nodules of cortical bone not found in these other conditions. In consequence, the lesions described in this individual are most compatible with a diagnosis of treponemal disease. The posterior lesion on the right parietal bone has characteristics of healing circumvallate cavitation (stage 4). It has rolled margins, grooves from small blood vessels, and a thin, well-corticated floor. The lesion anterior to this has rolled margins, a thin, well-corticated floor, and a stellate shape which is also suggestive of circumvallate cavitation (stage 4). Radiographs confirm the diagnosis by demonstrating several stellate lucent areas with surrounding sclerotic bone (Fig. 5), identical to the appearance of healed lesions in modern clinical treponemal cases (Swiader et al., 1994; Palmer and Reeder, 2001). The stellate lesion immediately superior to the trowel hole on the left parietal bone has the appearance characteristic of a limited area of caries sicca (stage 8). The central nodule is abutted by nodules of healing bone that leave a radiating pattern of grooves between them (Fig. 4). All three of these lesions are diagnostic of treponemal disease, following the criteria proposed by Hackett (1976). Past research on cases of bejel noted the presence of healed crater-like lesions on the skull vault without the proliferative new bone of caries sicca, similar in appearance to depressed fractures (Hershkovitz et al., 1994; Mays et al., 2002). It has been suggested that in populations where treponematosi is endemic, a significant proportion of these lesions may be secondary to treponematosi rather than trauma (Hackett, 1976, p. 58). In the 65 adults from this series, 3 more cases (all female) exhibited these ambiguous healed, depressed lesions on the frontal bone. The fact that many crania are incomplete may mean that further cases were not
identified, as the pathological portions of the skull were not recovered.

It has become increasingly clear that identifying the form of treponemal disease from the physical examination of a particular set of skeletal remains is often impossible. Although attempts have been made to such a differentiation at a population level (Rothschild and Rothschild, 1994), many researchers feel that a reliable method has still to be developed (Heathcote et al., 1998). In the future, it is possible that advances in ancient DNA analysis may allow differentiation between each form, but at present the oldest skeletal remains in which treponemal aDNA has been satisfactorily identified are only 200 years old (Kolman et al., 1999). However, since bejeel is the form currently present in the Middle East, it seems plausible that this may have been the form present at Safed in the 14th century. Identifying the community from which these remains came is difficult. While crusader textual sources confirm that Christians from Safed were buried in the nearby cave church of St. Tobias (Michelant and Raynaud, 1882), the carbon-dating result is not from the time of the crusades (1096–1291). The individual appears to have died after the crusaders lost control of Safed to the Muslims in 1266 (Kennedy, 1994), and therefore comes from the mamuluk period. One possibility is that the local Christian community from Safed continued to bury their dead over the following centuries in the same cave church as was used during the crusader occupation. Another is that this cave may represent a completely different cemetery, and therefore may have been the burial ground for any religious group.

The significance of this discovery at the widest level is that it can be regarded as further support for the presence of treponemal disease in the pre-Columbian Old World. This is the first pre-Columbian evidence from the Middle East, and as such helps to clarify the pattern of disease epidemiology in the past. With this evidence, it seems that previous suggestions as to how the disease reached the region that is now Israel will have to be revised. The dating of past cases of treponematosis in Israel (17th–18th century) coincided with the migration of certain Bedouin tribes, and it was thought that the disease was introduced to the region by them (Hershkovitz et al., 1994). However, the evidence here shows that treponematosis must have been present there since the 14th century at the very least, and makes other methods of disease spread more likely. The lack of evidence from earlier periods may be interpreted in a number of ways. It is possible that treponemal disease was present in this region but in a form that did not result in sufficiently classic bony involvement for positive identification by paleopathologists today. Examples of such cases for which treponematosis should now be included in the differential diagnosis include long bone periostosis noted in the remains of children from 12th century Tel Jezreel, Israel and Al-Wu‘ayra castle in Jordan (Mitchell, 1994; Rose et al., 1998). Another alternative is that the disease might have been very rare in earlier periods, and so by chance was not found in those individuals studied by archaeologists. A further option is that treponematosis may have been introduced into the area shortly before the 14th century. The role of pilgrimage both by Muslims to Mecca and Christians to Jerusalem at the time of the crusades has been discussed as a potential method of treponemal disease spread in the region (Hudson, 1963). However, at the time of the article by Hudson (1963), such suggestions were merely hypotheses, as there was little evidence that the organism was present in the Middle East in the medieval period. Safed was a provincial capital under the Mamlukes and the major trading center for over 200 settlements (Bosworth et al., 1995). The many merchants and caravans of camels converging on the city would have provided ample opportunity for the spread of disease from other regions. While there is not enough evidence at present to say for sure exactly when and how treponemal disease did reach the eastern Mediterranean, these findings do show that it was present there at least by the 14th century. Consequently, past arguments based on historical sources should now be reevaluated in the light of this archaeological evidence.

The likelihood that treponemal disease was present in this region in the medieval period raises many questions as to the diagnosis of disease at that time. Medieval medical texts from the Mediterranean region do not describe as a distinct condition the group of symptoms that modern readers would interpret to be treponematosis (Bos, 1997; Campbell and Colton, 1955). This is despite the fact that signs of treponematosis such as skin ulceration and destruction of the nose must have been highly visible to others in the population. A number of authors have argued that treponemal disease may have been confused with other ulcerating conditions such as leprosy in some regions during the medieval period, and that both conditions were perhaps regarded as the same disease (Hudson, 1961; Mitchell, 2000a). An inability to differentiate the two diseases at that time is plausible, as both conditions may cause ulceration of the skin, destruction of the nose, and bony changes in the lower legs. Not everyone agrees with this hypothesis (Demaitre, 1985; Baker and Armelagos, 1988), since excavation of a limited number of leprosaria in northern Europe has only rarely found skeletally diagnosable cases of treponematosis (Møller-Christensen, 1978; Manchester and Roberts, 1989). However, there is no reason to assume that evidence from northern Europe should be applicable to the Middle East with its different climate, social attitudes, religions, and medical practices. Those deciding who should be classed as having leprosy in medieval Denmark may have been using very different criteria from those making the same decisions in the Middle East. A diagnosis of “leprosy” was socially very important in Christian
communities, as people regarded as having the disease often had to leave their families and live apart from society, as advocated in the Bible (Richards, 1977; Mitchell, 2000b). There is evidence for other diseases to have been grouped under the umbrella term of “leprosy” in the past. Psoriatic arthritis shares a number of similarities with leprosy, as they both cause skin lesions and deformity in the hands and feet. Research in the Byzantine monasteries of the Judean Desert suggests that, at least in the 6th century AD, psoriatic arthritis may well have been in the group of diseases regarded as “leprosy” (Zias and Mitchell, 1996). Until such time as the excavation of leprosaria cemeteries in the Middle East gives a definitive answer, it seems sensible to keep an open mind to the possibility that the ulcers from treponematosis and leprosy may not have been distinguishable by eastern medical practitioners.

Further discovery of cases of treponematosis in early human skeletal remains will continue to improve our understanding of the paleoepidemiology of this important group of diseases, and will allow us to track their spread around the ancient world. Such cases not only have major implications for paleopathologists working on the evolution and epidemiology of disease in the past, but are also vital to the medical historian attempting to understand how our ancestors viewed disease and attempted to treat it.

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LITERATURE CITED


Hackett CJ. 1976. Diagnostic criteria of syphilis, yaws and treponarid (treponematoses) and of some other diseases in dry bones. Berlin: Springer-Verlag.


