

# On the Origin of American Tuberculosis

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**After more than a century of debate, it is now firmly established that tuberculosis existed in the New World before the arrival of Columbus. What is not yet known is how or when, exactly, the infection reached the Americas, how it spread from one continent to the other, and whether the pre-Columbian infection was caused by *Mycobacterium tuberculosis* or *Mycobacterium bovis*.**

Just north of Merida, capital city of the Mexican state of Yucatan, there exist the decayed remnants of a Maya town known as Dzibilchaltun, which flourished during that culture's classical period (250–900 C.E.). The most prominent structure in the partially restored archeological site is the Temple of the Seven Dolls, so named because of 7 terra-cotta figurines discovered inside it at the time of its excavation during the latter part of the 20th century. These anthropomorphic figurines, seemingly modeled after deformed or diseased individuals, appear to have been placed as offerings below the temple floor during postclassical times (i.e., 900–1521 C.E.), long after the building's original construction [1, 2]. At least 1 shows an acutely kyphotic upper back, of the kind most often due to Pott disease in underdeveloped areas of the globe (figure 1). If the figurine depicts the actual physical appearance of a pre-Columbian Mayan subject, it not only raises the possibility that the individual had advanced tuberculosis of the spine, but it also implies that tuberculosis existed in Mayan society—and therefore, in Mesoamerica—well before the arrival of Columbus. But did tuberculosis antedate Columbus there, and if so, precisely when and how did it reach that region during its spread through the Americas?

Spinal abnormalities similar to the one exhibited by the Dzibilchaltun figurine abound in indigenous American iconography [3]. Such deformities are present in numerous depictions of humans uncovered at population centers that flourished in North America, South America, Central America, and the Caribbean during the second half of the first millennium C.E. In a limited survey of figurines currently residing in the Museo Popol-Vuh in Guatemala that depict a multitude of pre-Columbian, Mayan themes and activities, Daniel [4] found possible gibbositities in 10% of the figurines from 2 sites, but none in figurines from a third site. Although the figurines that exhibited gibbous deformities might have represented Pott disease, it is also possible that they depict persons with other causes of acute dorsal kyphosis. Thus, at best, they constitute only circumstantial evidence of tuberculosis in pre-Columbian Mesoamerica.

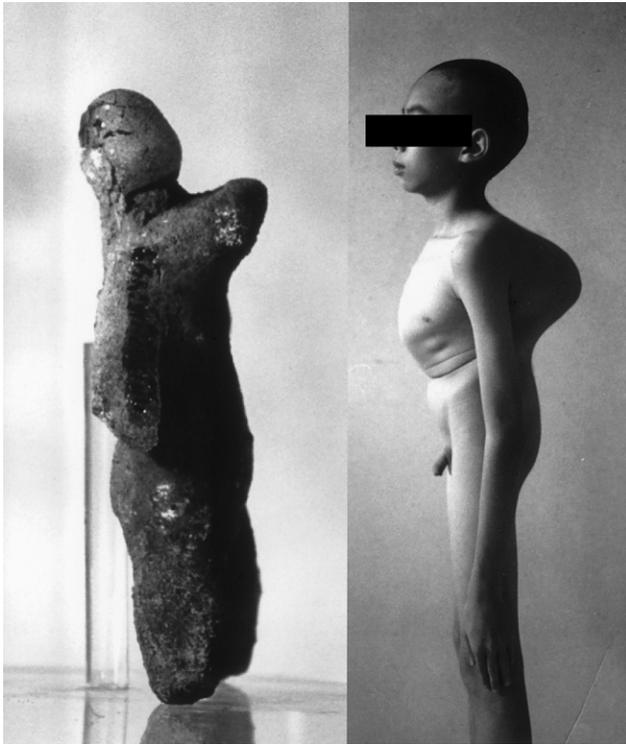
Although instructive, these terra-cotta figurines (and also paintings, drawings, carvings, and the like) depict diseases according to the artistic conventions of the day and may be more indicative of cultural expression than clinical reality. Moreover, they may be prone to distortions arising from the tendency of artists to depict only the most common or most horrifying diseases of their day [5, 6]. For this reason, although visual representations are useful in documenting, with varying degrees of certainty, the existence of some diseases, in the absence of written records, they provide no meaningful inferences about either the incidence or prevalence of disease. Unfortunately, neither the indigenous peoples of America nor the early explorers and settlers of the New World (among whom there were virtually

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**Figure 1.** *Left*, Mayan terra-cotta figurine from the postclassical period (900–1521 c.e.) discovered inside the Temple of the Seven Dolls at the Dzibilchaltun archeological site in Yucatan, Mexico (photograph provided by and published with the permission of D. Trejo, Museo del Pueblo Maya de Dzibilchaltun, Instituto Nacional de Antropología e Historia). *Right*, Gibbous deformity of a child with advanced Pott disease attended by one of the authors (P.A.M.) in the late 1960s, shown for comparison.

no medical observers) appear to have kept written medical records.

To date, the earliest primary evidence of American tuberculosis has come from mummified remains from the first millennium c.e. recovered at the coastal site of Caserones in the Atacama desert of northern Chile. In 1981, Allison et al. [7] reported finding acid-fast bacilli in cavitory pulmonary lesions in 2 mummies recovered from the site and in the healed ghon complex of a third. Numerous other archeological sites in the Americas have yielded evidence (primarily skeletal) of 1 or more additional pre-Columbian cases of tuberculosis, the heaviest concentrations of which exist in South America and in North America, north of Mexico (figure 2) [3]. Only isolated examples of probable skeletal tuberculosis have been discovered in western Mexico and the Central Highlands [3, 8–10]. Of the datable diseased remains found thus far, all have been traced to the second millennium c.e. In Mesoamerica, virtually no convincing skeletal evidence of tuberculosis has been found, in spite of the region's large concentrations of people during the 2 millennia before European contact. In the Mayan area in particular, with its large (albeit deteriorated) skeletal record, not

a single pre-Columbian case of likely Pott disease or other skeletal evidence of tuberculosis has been found.

Why evidence of tuberculosis has yet to be found in pre-Columbian Mesoamerica is a mystery. The region's climate could be in part responsible, in that it is not one conducive to the preservation of skeletal remains; yet, hundreds of remains have been recovered from ancient Teotihuacán, where an estimated 150,000–200,000 people once lived, and none exhibit evidence of tuberculosis [11, 12]. Similarly, of the >700 remains uncovered in the Copan pocket of the Mayan realm of the classic period (circa 250–900 c.e.), not one shows the distinctive abnormalities of skeletal tuberculosis [12, 13].

It is also possible that the stressors with which the Mayans had to contend caused those with tuberculosis to die of the infection before invasion of bone had had time to occur. This, too, seems unlikely, because considerable evidence of skeletal tuberculosis has been detected among the indigenous peoples of eastern North America who lived under no less stressful conditions [3].

One other possible reason why classic Pott disease may yet be detected in the remains of pre-Columbian Mayan subjects concerns the manner in which the remains of certain deformed subjects were disposed. Depictions of hunchbacks and dwarfs in painted Mayan ceramics suggest that they enjoyed special status as shamans endowed with the capacity to guide the souls of deceased nobles into the underworld [14]. If so, their remains might simply have been interred away from main burial sites in places not yet discovered.

Although proof of the existence of tuberculosis in pre-Columbian Mesoamerica is presently lacking, the recent demonstration of mycobacterial DNA by PCR amplification of specimens from ancient human tissues recovered from sites elsewhere in the Americas removes any doubt that the infection was already endemic to the New World before the European entrada. PCR amplification was first used successfully in such demonstrations in the early 1990s to examine a subpleural nodule in a middle-aged woman who lived ~1000 years ago in the vicinity of the Chiribaya Alta site in South America. With use of the nested PCR technique of Eisenach et al. [15, 16], Salo et al. [17] isolated a 97 base-pair (bp) segment of the IS6110 specific for the *Mycobacterium tuberculosis* complex. When digested with the restriction enzyme *Sal* I, the 97-bp unit separated into anticipated 42-bp and 55-bp segments, and when the PCR product and 9 clones were directly sequenced, the *M. tuberculosis* attribution was confirmed. Three other archeological sites have yielded similar evidence of ancient *M. tuberculosis* complex DNA, 2 in eastern North America (Uxbridge and Schild) and 1 in South America (SR1) [3]. In each of the examinations, attribution of ancient DNA has been based on extraction and amplification of IS6110. Because this particular insertion sequence is shared by the 5 closely related strains that



**Figure 2.** Map of the Western Hemisphere indicating locations at which pre-Columbian human remains exhibiting evidence of tuberculosis (TB) have been found. Adapted from [1].

constitute the *M. tuberculosis* complex (*M. tuberculosis*, *Mycobacterium bovis*, *Mycobacterium bovis* BCG, *Mycobacterium africanum*, and *Mycobacterium microti*), the specific strain within the *M. tuberculosis* complex infecting these ancient tissues is uncertain. Thus, after >1 century of debate, PCR methods have finally firmly established the presence—but not yet the complete identity—of mycobacterial infection prevalent among pre-Columbian Americans.

Although recent evidence indicates that *M. tuberculosis* predated *M. bovis* in the Old World [18–20], some authorities believe that *M. bovis*, which has a predilection for human bones and lymph nodes, was responsible for the pre-Columbian cases of New World tuberculosis, rather than *M. tuberculosis* [4, 21]. If this were so, human tuberculosis in the Americas likely would have consisted initially only of sporadic infections, because *M. bovis* is rarely transmitted via an airborne route and is not readily spread from human to human. Moreover, until the advent of *M. tuberculosis*, the infection would have been one largely confined to its principal animal reservoir, cattle, which,

although domesticated in the eastern Mediterranean basin ~7000–9000 years ago (some believe even earlier in Africa), did not reach the New World until imported by the Spanish during the 16th century C.E. [22]. Given that bovine tuberculosis has been detected in modern llamas and wild bison, their ancestors might have transported tuberculosis to the New World across the Bering land bridge before it sank below the Arctic Sea. However, because neither animal is a natural host for *M. bovis*, it is more likely that the original cases of American tuberculosis were *M. tuberculosis* infections transported to the new land not by animals, but by infected humans.

Thus, several critical questions concerning the origin and spread of American tuberculosis remain unanswered. Which strain of the *M. tuberculosis* complex was responsible for the mycobacterial infections of pre-Columbian Americans? Was it *M. tuberculosis*, or was it, as some have speculated, *M. bovis*? If tuberculosis reached the New World well before the European entrada, exactly when did it do so and in what manner? Did it evolve on the primitive continent of Gondwanaland to be

transported throughout the globe by continental drift? Or was it carried to the new world by nomadic peoples (or perhaps animals) across the Bering land bridge, or across the Ocean Sea by ancient Polynesian mariners? Why have we not found archeological evidence of tuberculosis in pre-Columbian Mesoamerica, in spite of ample depictions of lesions consistent with such illness and an abundance of direct skeletal evidence of the infection in both North and South America? Is it because the Mayans believed that hunchbacks had shamanistic callings as guides for the souls of nobles into the underworld and, therefore, accorded their remains special treatment that has prevented their discovery by modern day archeologists? Or because climatic conditions in Mesoamerica tend to be less hospitable to the preservation of ancient remains, compared with more northern or more southern climes? Or is it simply a consequence of selective collection and retention of remains by archeologists and/or the limited number of systematic collections thus far surveyed by physical anthropologists [23]? Whatever the answers to these questions, it is clear that, as we look to the future for ever more-effective methods of preventing, diagnosing, and treating tuberculosis and for additional insights into the mechanisms underlying the success of this most mysterious of pathogens in causing human disease, we can also look to the past and find questions about the origins and spread of tuberculosis that are no less interesting or daunting.

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