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Old World tuberculosis: Evidence from human remains with a review of current research and future prospects

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S U M M A R Y

The evidence for TB in archaeological human remains for the Old World is reviewed in published and some unpublished sources. The evidence of Pott's disease was considered specific for TB, with other bone changes, such as rib lesions, as non-specific. Limitations of the data are discussed. Most evidence for TB comes from skeletons from the northern hemisphere, particularly in Europe in the late Medieval period (12^{th}-16th centuries AD), but there is early evidence in the Near/Middle East and Egypt. Many parts of Africa, Asia and Australasia have very little or no evidence. aDNA analysis has provided data on species and strains of the *Mycobacterium tuberculosis* complex organisms affecting people in the past. The extant data suggest the first epidemiological transition (Neolithic agriculture and permanent settlements) led to an increase in TB, with later increases in urban environments of the late Medieval period. A number of causative factors were at play. Future research, particularly using biomolecular analysis, has the potential to further contribute to our understanding of the origin and evolution of TB, thus merging the disciplines of palaeopathology and evolutionary medicine.

1. Introduction

It was only 25 years ago that Smith was seen to say that 'Tuberculosis is now a conquered disease in the British Isles and the rest of the industrialised world' [1], but it was not long before the World Health Organization had declared tuberculosis (TB) to be a global emergency (1993). TB remains with the world today in both developed and developing countries, it infects a third of the world's population, and in 2012 around 8.6 million people developed TB and 1.3 million died [2]. In the UK, a recent report has highlighted that data there indicate that all sectors of society are affected, that it is an urban disease, and East London was TB capital in the Western world with a higher rate than India [3]. TB has affected the human population for thousands of years and yet it has not been possible to eradicate it today for a variety of reasons. These include the increasing resistance to antibiotics, susceptibility of human immunodeficiency virus compromised people, especially in Africa, increasing poverty, extensive human migration, and specific occupations that predispose people.

Studies of the palaeopathological evidence for TB in skeletons and mummies from archaeological sites have provided a deep time perspective on TB's origin evolution and history through research since the early 20th century [4]. This provides an extended view of the lived experiences of populations with TB which can be used to understand the problem today, and perhaps be used to plan for the future. Indeed, as a disease of the poor, it was apparently common among those living in poverty in the past and, logically, eliminating poverty in the world today could help to control this disease. A more recent development, especially as a result of the sequencing of the TB genome, is the analysis of ancient DNA of the TB bacteria. This is allowing a more nuanced view of TB to be developed, with data indicating the species and the genotypes (strains) of the bacteria that people suffered in the past. Comparing genotypes between past and present populations may in the future provide an opportunity to re-evaluate the reasons for antibiotic resistance, by helping to understand the factors that can lead to mutation of the subtypes and consequent resistance.

This paper aims to take a broad overview of the evidence for TB in archaeological human remains in the Old World by collating the data published to date. It will also review the diagnostic criteria used by palaeopathologists to identify TB, the contributions of biomolecular analysis, the limitations of the data, and future prospects. In such a short review, it is not possible to consider the evidence in great detail, and therefore the reader is referred to further information detailed in the reference section.

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2. Materials and methods

2.1. Materials

The evidence for disease diagnosed in archaeological human remains is to be found both in published and unpublished outlets. However, much data from archaeological contexts are located in what is termed "the grey literature", or unpublished resources, thus making tracking down of evidence challenging. The data for TB in this paper is mainly based on published literature, although recognising the fact that some data may be invisible in unpublished sources. Indeed unpublished data abound in the discipline of archaeology due to many reasons (e.g. almost 40% of health data collated from over 300 cemetery sites in past Britain were unpublished) [5]. Most archaeological data, from pottery to buildings and human remains, are uncovered as a result of "developed-led funded" archaeology in advance of modern building projects; due to pressures of time and money, much data are simply not brought forward to publication. It is likely that this situation applies to most parts of the world. Scholars also do not necessarily publish in outlets that appear in database searches, such as PubMed or Medline, some data are simply never published, and not all scholars necessarily, for many reasons, access research that is written in languages other than english. However, there are now some facilities in archaeology where "grey literature" does appear and can be accessed (e.g. Archaeology Data Service: http://archaeologydataservice.ac.uk/; Archaeological Investigations Project: http://csweb.bournemouth.ac.uk/aip/aipintro.htm; OASIS or Online Access to the Index of Archaeolological Excavations; http://oasis.ac.uk/; accessed October 2013), assuming that scholars with relevant data actively seek to ensure they "engage" with these outlets. Therefore, the data that are used for this paper cannot be viewed as all encompassing, and of course the pattern may change as more data is collected and published, especially in parts of the world where palaeopathology as a discipline is developing or has yet to develop [6].

Data from skeletal remains and preserved mummies were considered for inclusion in this study from all periods of time and all regions of the Old World. This collation of data builds on those published in Roberts and Buikstra [7]. It should be noted that most data derive from skeletal remains because they are the most common type of human remains discovered in archaeology, and bodies are preserved only in special environmental circumstances, such as very cold and dry, or hot arid, conditions.

2.2. Methods

Selection of data for TB to include in this paper required specific criteria to be met. It should be noted that he majority of scholars who study ancient disease in human remains use macroscopic analysis to diagnose TB [8]. This is because this method is the most cost effective, with other methods (histological, radiographic and biomolecular) being out of the reach of most because of lack of availability of expertise and finance, and access to analytical facilities. Thus, it is argued by some that a lack of a biomolecular diagnosis for TB means that there is no "proof" that a person suffered TB. However, the process of diagnosis in human remains is rigorous. Bone formation and destruction, and plotting the distribution pattern of lesions in the skeleton are the first steps towards a differential diagnosis. Following this process, a list of possible differential diagnoses is formulated, and a most likely diagnosis is suggested. While there are challenges to inferring health from the skeleton [9], including the inability to produce absolute frequency rates in the past, other methods also have their limitations. For example, on the face of it, ancient DNA analysis, presents a method that can potentially provide real frequency rates for TB in the past, diagnose TB in people whose remains do not show any evidence, and give nuanced data about the species and strain of TB a person suffered, but the method depends on the preservation of aDNA in human remains, and the data produced being accurate [10].

The bone changes of TB may be specific, or pathognomonic to, TB, or could be non-specific, meaning they could be related to TB but could also be caused by a number of other diseases; only 3–5% of untreated people develop bone damage in their skeleton. This is via haematogenous and lymphatic spread from a primary focus (lungs or gastrointestinal tract), but more often than not it is the spine that is involved. Of course, evidence for TB in antiquity can also be located in documents and art [7]. These data sources are not considered here. The pathognomonic changes are to be found in destructive lesions, with little or no new bone formation; these changes are especially seen in the lower thoracic and lumbar spine. The hip and knee joints can also be affected, but any bone of the body may be involved. The non-specific bone changes may include bone formation on the visceral surfaces of ribs, calcified pleura or granulomatous lung modules, destructive lesions of the bone underlying the skin lesions of lupus vulgaris, bone formation particularly on long bones, as seen in hypertrophic pulmonary osteoarthropathy, tuberculous dactylitis of the short bones of the hands and feet, and bone changes possibly as a result of tuberculous induced meningitis on the endocranium or gastrointestinal tuberculous involvement of the pelvic bones [7]. These non-pathognomonic bone changes can be caused by many other diseases, and should never be used alone to diagnose TB, and neither can they be "proved" to be caused by TB based on biomolecular analysis. When collecting data on tuberculosis from human remains it is important to accurately and consistently use the diagnostic criteria outlined, and when the biological data are interpreted it is vital that available archaeological and historical data are used to understand the patterns seen.

The data to be presented were collected mainly from published sources, and initially assessed for diagnostic accuracy before being used for final interpretations.

3. Results (Figure 1)

The data presented here provide an overview of the general distribution pattern of TB in the Old World both from a geographical and temporal viewpoint. Data for the New World tends to be later in date but are not discussed here, and can be found elsewhere [7,11]. Most of the data considered were from diagnoses of lesions in skeletons from a macroscopic point of view. However, there has been an increase in diagnoses using other methods over time, such as radiography, histology and ancient pathogen DNA analysis, the latter seeing increasing use in the last 20 years. Evidence for tuberculosis in skeletal remains from the Old world is plentiful in Europe but less so for the rest of the area. Apart from North and South America (New World), there is definite evidence in three other continents (of five) of the world (Europe, Africa and Asia); there is possible evidence in Australasia [7], but no evidence in the Antarctic.

The majority of the evidence in the Old World is in Europe, with very few countries having no evidence (e.g. Belgium and Iceland) and some having much (e.g. the UK and Hungary). The definitive evidence in the Old World ranges in latitude from 20° to 70°, and in longitude from 0° to 120°. All evidence is in the Northern Hemisphere. There are many parts of Africa, Asia and Australasia that have no evidence. The earliest dated evidence is from Israel (7250-6160 BC) [12], with early Egyptian (4500 BC) [13], German (5400–4800 BC) [14], Hungarian (5th millennium BC) [15], and Polish and Portuguese "Neolithic" data. However, most skeletal