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Editorial Open Access

The Possible Origins of Tuberculosis in South America

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Editorial

Tuberculosis is one of the most widespread bacterial diseases on the planet. It is an infection that has plagued humans for over millennia. One line of bioarchaeological research is concerned with the origins and spread of the disease (phylogeography). A new research study within this field indicates that the origin of the disease in the South American continent is attributable to transmission from seals and sea lions, rather than from people [1]. This finding re-opens a longstanding debate as to whether tuberculosis originated from a bovine source and proceeded to infect humans, which infers a specific historical trajectory relating to the domestication of animals, or whether the pathogen is considerably older and developed in tandem with the first humans.

Tuberculosis is a widespread infectious disease caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis*. The symptoms of infection consist of a chronic cough with blood-tinged sputum, fever, night sweats, and weight loss. Tuberculosis is closely linked to both overcrowding and malnutrition; *argumentum a fortiori* the disease is regarded as one of the principal diseases of poverty [2].

As well as being a current concern, tuberculosis is also an ancient disease; skeletal remains show prehistoric humans (4000 BC) had tuberculosis, additionally tubercular decay in the spines of Egyptian mummies dating from 3000-2400 BC have been reported [3]. Despite the long lineage, there is no scientific consensus on the origins of the disease. One of the earliest detections of *M. tuberculosis* is in the remains of bison that date to around 17,000 years ago [4]. Whether tuberculosis originated in bovine species and was then transferred to the human population remains a matter of conjecture. An alternative evidence strand is that tuberculosis diverged from a common ancestor [5]. The new research considered here takes a divergent path from the bovine argument, although the presence of a mammalian vector remains.

The conclusion that tuberculosis reached South America from pinnipeds is drawn from an analysis of tuberculosis DNA recovered from three 1,000 to 1,300 year old Peruvian skeletons. Whilst the existence of tuberculosis in the pre-Columbian Americas is controversial, not least because the morphology of the lesion is not specific, the organism is culturally non-viable in ancient tissues, and non-pathogenic soil mycobacteria can contaminate buried bodies, a paper by Salvo et al. found specific evidence for the pre-Columbian presence of human tuberculosis in the so-termed "New World" [6].

The analysis by Bos and colleagues indicates that the genetic remnants of the strain of *Mycobacterium tuberculosis* recovered from these ancient bones does not match the strain of the bacterium thought to have been introduced to the continent by the European explorers from the time of Columbus [1]. Instead, the strain isolated closely resembles a type that infects seals found in the Southern Hemisphere.

This discovery can be incorporated into an alternate narrative to the one conventionally associated with the epidemiology of tuberculosis. Many scientists have long thought that *Mycobacterium tuberculosis*, originated in cattle as *M. bovis*. The bacterium then became a human associated disease after dairy cows were domesticated. Linking to the research on the Columbian skeletons, domestic cows were introduced into the Americas with the European conquerors and settlers [7]. The link between tuberculosis and European explorers is supported by historical research that indicates tuberculosis experienced a 25-fold expansion worldwide in the 17th century; this was an era when human populations underwent considerable growth and is coincidental to when European exploration of Africa, the Americas, Asia and Oceania was at its peak.

The alternate argument, which Bos' paper tallies with, is that tuberculosis was introduced to the South American continent pre-contact with Europe as a result of sea mammals transmitting the disease to humans from across the ocean. There is support to this hypothesis from some earlier research findings [8].

Taking a step backwards, comparative genomics of modern isolates suggests that *M. tuberculosis* followed human dispersals out of Africa during the Pleistocene epoch (around 70,000 years ago) [9]. Incidences of the disease then expanded as a consequence of increases in human population density during the Neolithic period. This diaspora is thought to have triggered the global spread of the disease.

That there was a common origin of tuberculosis has been shown in previous studies. Brooch et al. examined the distribution of twenty variable regions in the genomes of the tubercle bacilli in a study that examined 100 strains of *Mycobacterium tuberculosis*, *Mycobacterium africanum*, *Mycobacterium canettii*, *Mycobacterium microti*, and *Mycobacterium bovis* [10]. This analysis found that the majority of these polymorphisms did not occur independently in the different strains of the *M. tuberculosis* complex. Instead, the data suggests that these resulted from ancient, irreversible genetic events in common progenitor strains. Moreover, based on the presence or absence of an *M. tuberculosis* specific deletion (TbD1), the researchers discovered that *M. tuberculosis* strains can be divided into ancestral and "modern" strains, the latter comprising representatives of major epidemics like the Beijing, Haarlem, and African *M. tuberculosis* clusters.

The study also revealed that successive loss of DNA was identified for an evolutionary lineage represented by *M. africanum*, *M. microti*, and *M. bovis* that diverged from the progenitor of the present *M. tuberculosis* strains. This observation infers that the common ancestor of the tubercle bacilli resembled *M. tuberculosis* that it was probably an established human pathogen.

Thereafter, how tuberculosis moved from Europe to other regions in the world presents a challenging line of inquiry. The popular historical story is to pin the responsibility onto explorers like Christopher

Columbus [11]. The overview presented here offers a challenge to that assumption. In keeping with the African point-of-origin, it could have been that seals and sea lions contracted the disease from a host animal from Africa and swam across the Atlantic to South America. The mammals were then possibly eaten by coastal people who were themselves then infected and spread the bacteria to others.

Consideration of the biogeography of tuberculosis is not only of historical interest. New methods for controlling tuberculosis are urgently needed as incidences of global cases increase (globally, tuberculosis is the second most common cause of death from infectious disease, after those as a result of HIV infection). *M tuberculosis* has a clonal genetic population structure that is geographically constrained and strain-specific differences in virulence and immunogenicity conform to a global phylogeography. If researchers can successfully develop a strain selection framework, based on rphylogenetic markers, this will allow for the development of new tools for tuberculosis control.

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