Dental crown morphology variations associated with congenital syphilis and their importance in paleopathological diagnosis

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Abstract

Background

Standardized methods to diagnose syphilis in skeletal remains have been established, however, they are not efficient due to the lack of a full set of skeletal manifestations in many individuals, and changes similar to syphilis, occurring in other infections. Similar issues arise for congenital syphilis. Dental and skeletal manifestations do not occur in all cases, and dental signs also vary. It is well documented that mercury was used to treat congenital syphilis before 1943, however, the effects of mercuric treatments on dental formation have not been considered as diagnostic signs. Thus, individuals who do not demonstrate typical dental stigmata have been dismissed as possible cases of congenital syphilis. This thesis investigates dental malformations in cases of congenital syphilis to determine the range of possible dental signs of congenital syphilis, and mercuric treatments. Determining the effects of mercuric treatments on tooth crown development would establish a method for a diagnosis of congenital syphilis based on a full range of abnormalities.

Methods

The criteria to determine dental signs of congenital syphilis were based on the standard developed by modern scholars and on own study of 19th century descriptions and illustrations of patients. To determine dental signs of mercuric treatments, descriptions and illustrations of teeth of congenital syphilis patients treated with mercury by 19th century physicians were used. These are the first and only observations made of dental signs attributed to congenital syphilitic treatments.

Dental criteria were applied in a survey of remains of 259 individuals from several skeletal collections: the Wellcome Museum of Anatomy and Pathology, London, St Mary's cemetery, South Australia, Smithsonian Institute, Washington DC, and the Cleveland Museum of Natural History, Cleveland, Ohio. Dental traits attributed to congenital syphilis (Hutchinson's incisor, Moon's, and Fournier's molars, and canines with sharp groove-like hypoplastic defects on the tip) and its treatments were recorded. In cases where it was permitted, levels of mercury were tested for using portable x-ray fluorescence (pXRF). Furthermore, paleopathological cases from the literature with high quality dental images were used. A history of the use of mercury to treat

congenital syphilis and syphilis in the United States and Europe was explored based on government reports and the literature.

Results

Congenital syphilis and mercury affect similar kinds of permanent teeth, (incisors, first molars, and canines) due to tooth development times. However, mercury and congenital syphilis affect odontogenesis and amelogenesis differently resulting in distinct malformations exhibiting individual variation. The range of variation has been established and illustrated. Levels of mercury detected in hard tissues do not prove nor disprove the use of mercury as a form of treatment of congenital syphilis due to mercury turnover in the body.

Conclusion

Variation beyond the classical models of congenital syphilitic teeth occurs. Dental signs produced by mercury should be considered when making a differential diagnosis of congenital syphilis. This is the first study to consider the use of dental signs associated with congenital syphilitic treatments in a paleopathological context which could help elucidate controversial cases of the disease and shed some light on its origins.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of The University of Adelaide and where applicable, any partner institution responsible for the joint award of this degree.

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Research Contribution

Peer-reviewed Publications

Ioannou S., Hunt D., Henneberg M. 2017. Five Cases of Dental Anomalies Attributable to Congenital Syphilis from Early 20th Century American Anatomical Collections. *Dental Anthropology*. 30(1):25-37.

Ioannou S., Henneberg M. 2016. A rare case of congenital syphilis and a supernumerary fourth molar in an early 20th century African American woman. *Dental Anthropology*. 29(1): 41-47.

Ioannou S., Henneberg M., Henneberg R. & Anson T. J. 2015. Diagnosis of mercurial teeth in a possible case of congenital syphilis and tuberculosis in a 19th century child skeleton. *Journal of Anthropology* 2015: 1-11. 10.1155/2015/103842.

Ioannou S., Sassani S., Henneberg M. & Henneberg R. J. 2015. Diagnosing congenital syphilis using Hutchinson's method: Differentiating between syphilitic, mercurial, and syphilitic-mercurial dental defects. *American Journal of Physical Anthropology*. 10.1002/ajpa.22924.

Submitted Publications

Ioannou S., Henneberg M. 2017. Lack of dental signs and bony changes in syphilitic individuals in the Hamann-Todd Skeletal Collection possibly due to effective mercuric treatments. *Anthropological Review*. Article Reference Number: AR_80040417 Submitted 22 July 2017.

Ioannou S., Henneberg RJ., Henneberg M. 2017. Presence of dental signs of the congenital syphilis in Pre-modern specimens. *Archives of Oral Biology*. Article Reference Number: AOB-D-17-00502 Submitted: 29 August 2017.

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Conference Presentations

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Ioannou, **S**, Sassani, S, Henneberg, M, Henneberg, R.J. (2014). Diagnosing congenital syphilis using Hutchinson's method: Syphilitic versus mercurial vs syphilitic-mercurial teeth, (**Podium**). Australasian Society for Human Biology (ASHB), 28th Annual Conference 10th-13th December, Adelaide, SA.

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Thesis Style and Layout

This format of this thesis is “Thesis by Publication”. The chapters are in the following order: Chapter 1: Introduction, discusses the general background, aims and importance of this doctoral study. The methodology of each study is discussed in each research article. Chapters 2, 3, 4, 5, 6, and 7 are the results of original research in the form of six research articles, four of which have been published in peer-reviewed journals, and two which have been submitted for publication in peer-reviewed journals. Each result chapter is prefaced with a ‘Statement of Authorship’, which details the contribution of each author. The purpose and objective of each research article is outlined before each article. The layout and format of each research article is in accordance with the journal requirements (i.e. US or British spelling, different reference style etc.), therefore, formatting may vary between articles. Chapter 8 provides an overall summary/discussion, drawing upon the findings of each publication, how the findings have contributed to the current body of work and describes what further investigations could be conducted. Appendices contain data that were collected for research articles.

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List of Abbreviations

Abbreviation	**Full Description**
AI	*Amelogenesis imperfecta*
CS	Congenital syphilis
TB	Tuberculosis

Chapter One

INTRODUCTION

What is Syphilis?

Syphilis is a disease that is caused by a small spirochete bacterium known as *Treponema pallidum*. The disease is typically transmitted through sexual contact, although it can also be transmitted by anybodily fluid contact and via the placenta from an infected mother to the fetus while she is in the most infectious stages of the disease, secondary or early tertiary stage. The disease transferred to the fetus is known as congenital syphilis.

The knowledge of syphilis

The origins of venereal syphilis, and how it spread throughout the old world is largely based upon written evidence, most notably the works of Rodrigo Ruy Diaz de Isla (1539), and Hieronymus Fracastoro in 1530 (Claiborne, 1911). The first recorded European epidemic coincides with Christopher Columbus's return from the New World in 1493.

However, there is evidence that supports multiple theories of the origins of the disease. There are two sources that these conflicting theories are based upon, historical documents and archaeological remains. The theories that have been put forth include the pre-Columbian, post-Columbian and Unitarian theory. The pre-Columbian theory states that syphilis was present in the Old World but in a mild form, unrecognizable till the epidemic in 1496 (Buret, 1891; Holcomb, 1935; Cockburn, 1961), the disease was confused with other diseases particularly "venereal leprosy" (Buret, 1891; Holcomb, 1935; Hudson, 1961), until a more virulent form of the disease was introduced to the Old World by Columbus, facilitating its recognition and descriptions in the literature (El-Najjar, 1979). The post-Columbian theory argues that Christopher Columbus's crews introduced syphilis to the Old World after their voyage to the New World in 1493 (Diaz de Ysla, 1539; Claiborne, 1911; Harrison, 1959; Goff, 1967; Crosby Jr, 1969; Baker et al., 1988; Harper et al., 2011). The Unitarian theory suggests that four diseases: venereal syphilis, yaws, pinta and bejel were the result of infections with the same bacterium *Treponema*, varying due to environmental conditions (Hackett, 1963; Hudson, 1963; Hudson, 1965a; Hudson, 1965b; Aristone 2011). Another hypothesis suggests that syphilis originated in Africa (Manson, 1903).

While the post-Columbian theory has been the most agreed upon due to descriptions of the disease surfacing in Europe only after the 15th century, this topic continues to draw attention and debate.

Importance of paleopathological specimens

Paleopathological specimens are used to determine the origin of syphilis, and according to those who side with the post-Columbian theory, have to meet certain criteria in order to be accepted and given a differential diagnosis of syphilis or congenital syphilis. The criterion that specimens must meet is to display diagnostic characteristics that are specific to that disease (Armelagos et al., 2012; Hackett, 1975). However, the diagnosis of syphilis in ancient human remains is difficult. Typically, the primary and secondary stages of the disease do not affect or leave any signs on hard tissues of the body. In rare cases, bone lesions can occur in the form of periosteal reactions in the primary stage (Reynolds and Wasserman, 1942; Dismukes et al., 1976; Ehrlich and Kricun, 1976; Hansen et al., 1984), as well as osteitis and narrowing of the medullary cavity in the secondary stage (Steinbock, 1976; Ortner, 2003). Cranial vault destruction is also rare as most bony changes occur in the tertiary stages. Bony changes have been found in about 1/3 of patients (Steinbock, 1976), or between 2% and 13% (Rothschild 2005), including periosteal reactions, osteitis, and osteomyelitis. While various bones can be affected including the ribs, and shafts of the long bones, scapulae and sternum, it is only during the tertiary stage, in severe cases, that diagnostic signs of the disease may develop. These diagnostic signs include "*caries sicca*", sclerosis and pitting on the outer table of the cranial vault resulting from accumulation of stellate scarring (Hackett, 1975; Steinbock, 1976), and nodes/tissue expansions with superficial cavitation in the long bones (Hackett, 1975). These are the only bony lesions considered to be pathognomonic signs for syphilis. However, in cases where these diagnostic changes are not present, differential diagnosis can be difficult. Isolated lesions of the skull vault and on long bones may be produced by other diseases (Rothschild and Heathcote, 1993; Holloway et al., 2011; Holloway et al., 2013). Therefore, differential diagnosis of a particular set of skeletal remains cannot always distinguish changes caused by syphilis, tuberculosis and other diseases. The lack of skeletal evidence of syphilis in a "text book form", with full set of well developed bony changes comprising diagnostic criteria on one skeleton, in European individuals

predating the 15th century has also led to these earlier reported as syphilis being considered as “controversial cases”.

Lesions of congenital syphilis can also be difficult to identify in skeletal samples as remains of fetuses, infants and children (Fiumara et al., 1952; Fiumara and Lessell, 1970), are not often preserved. In those patients who survive for at least a few years, bone lesions will vary between the early and late stages (Dorne and Zakon, 1935; Dax and Stewart, 1939; Laird, 1950; Fiumara and Lessell, 1970; Fiumara and Lessell, 1983; Armangil, et al., 2009; Basu and Kumar, 2013; Agrawal et al., 2014), and can either be minimal or will heal in approximately 50% to 75% of cases, (Steinbock, 1976), thus, frequencies of skeletal signs are low and do not appear often in skeletal remains (Steinbock, 1976; Rothschild and Rothschild, 1997). Therefore, a diagnosis of the disease can be difficult. Other signs that are considered pathognomonic of the disease are specific dental abnormalities: Hutchinson’s incisors, Moon’s molars, Fournier’s molars and hypoplastic groove like defects on tips of cusps of the canines (Hutchinson, 1859, 1863, 1887, 1909; Moon, 1884; Fournier, 1886; Johnston et al., 1941; Sarnat and Shaw 1942; Fiumara and Lessell, 1970; Hillson et al., 1998; Freiman et al., 2009). These dental abnormalities are thought to occur due to the disruption of odontogenesis which occurs at the time of infancy. While these dental abnormalities are used by researchers for diagnosis, there appears to be confusion in the literature as to what these dental abnormalities look like, the terms used, and their individual variability.

Dental signs observed in patients diagnosed with congenital syphilis

Sir Jonathan Hutchinson, a physician who worked in the 19th century with a vast array of syphilitic patients, described the pathognomonic signs of congenital syphilis (Hutchinson, 1859, 1863, 1887). Henry Moon (1884) and Alfred Fournier (1886) described changes in the first permanent molars in congenital syphilis and discussed Hutchinson’s observations in further detail. These descriptions of congenital syphilitic teeth have been the primary source for clinical (Dorne et al., 1935; Fiumara and Lessell, 1970; Grossmann III, 1977; Liwen and Owczarek, 2012), and paleopathological diagnoses (Jacobi et al., 1992; Hillson et al., 1998, Erdal, 2006; Henneberg and Henneberg, 2006; Gaul and Grossschmidt, 2014). However, there are those who believe defects in the molars are not a characteristic sign of congenital syphilis (Armelagos et al., 2012). This may be due to: (1) approximately 10%-30% of

congenital syphilitic patients display no sign of dental abnormalities (Svejda, 1952; Lipski 1959), and (2) variation in altered tooth morphology of various teeth can occur (Hutchinson, 1859, 1863, 1887).

Syphilitic, mercurial and syphilitic-mercurial teeth

Knowledge of the type of treatments used to combat syphilis and congenital syphilis throughout history has been documented, including natural remedies, chemical compounds and recently penicillin (Hutchinson, 1878, 1887; Moon, 1884; Fournier, 1889, 1898; Claiborne, 1911; Stopford-Taylor et al., 1911; Wardle, 1911; Evans, 1912; Lancet, 1925; Cole and Proctor, 1949; Mahoney et al., 1943; Goldwater, 1972). However, our knowledge of the effects of these treatments on hard tissues of the body has not been explored in depth or applied to paleopathological specimens. Hutchinson, Moon, and Fournier studied congenital syphilitic patients during the 19th century, a time when mercury's use as a treatment for syphilis was widespread. Hutchinson and Moon noticed that dental development was influenced not only by the disease but also by mercurial treatments, and this may have caused confusion among physicians when making a diagnosis of the disease in patients (Hutchinson, 1878; Moon, 1884). Treatments containing mercury were administered in various forms, in combination with other elements and in large quantities (Smith, 1844; Coote, 1847; Hutchinson, 1887). In comparison to what is accepted as safe amounts by health officials today (World Health Organization, 2007), large amounts of mercury were administered, they were toxic, and caused adverse side effects (Weatherill, 1833). It is more than likely that infants and children, who are more sensitive than adults, would experience adverse side effects to developmental processes including odontogenesis and amelogenesis resulting in abnormal tooth morphology.

The effects of mercury have never been considered in the literature when examining paleopathological specimens. As such, a review of Hutchinson, Moon's and Fournier's original works is conducted to establish the differences in tooth morphology between those caused by the disease and those by treatments containing mercury. These original works were obtained by visiting the Royal Society of Medicine in London, and through the University of Adelaide's Special Collection library, and various online digital libraries. These clinical descriptions and illustrations were then applied to pre-and post-Columbian paleopathological specimens in the literature and to various skeletal collections. To facilitate this research, studies of various anatomical collections have

been organized at the Royal College of Surgeons of England (n=14), the Smithsonian Institute in Washington DC (n=38), the Cleveland Museum of Natural History in Cleveland, Ohio (n= 171), and a series of material excavated from St Mary's Cemetery housed at the University of Adelaide (n=36), totaling 259 individuals examined.

Aims and Objectives

This research investigates the variation of dental changes associated with congenital syphilis and its treatments using the original literature and selected specimens. Establishing that there are dental changes associated with treatments of congenital syphilis that are significantly different from those caused by the disease itself, can aid in the diagnosis of specimens that have been disregarded in the past for not displaying "typical" Hutchinson's teeth, and become a new method of diagnosing congenital syphilis. Studying the range of dental abnormalities associated with the disease and its treatments may also contribute to discussions on the origins of syphilis and its evolution.

Written evidence of syphilis

Ancient historical texts are an important source of information about our past. These texts have described events, wars, the rise and fall of empires, the roles and heroics of individuals, nature, medical beliefs and practices, and diseases. These descriptions play an important role in our knowledge and understanding of our past and the evolution of diseases and their treatments.

Written evidence is an important source regarding the origins of syphilis. There is very little known definitive evidence in the ancient texts describing possible signs and symptoms of syphilis to suggest it was present during antiquity. Therefore, a search of the ancient literature was conducted in the works of authors with medical or scientific interests for signs and symptoms that may be interpreted as syphilis. Specific works that were read included: Hippocrates' 'Works', vol. I, III, VI and V, Herodotus' '*Histories*', Galen's 'Method of Medicine', books 1-4, 5-9, 10-14, Pliny the Elder's '*Natural History*', and Aristotles' '*Minor Works*'. All books were Loeb editions. Keywords were put into search engines: Perseus: www.tufts.edu, and TLG (Thesaurus Linguae Graecae): www.irvine.edu for translations. The search strategy involved using key terms separately and in combination. While there were various mentions in

the literature, there was not enough evidence to consider that they are unquestionable signs of syphilis or related to syphilis. Therefore, this thesis relies on dental evidence.

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Chapter 2

ARTICLE 1:

Diagnosing congenital syphilis using Hutchinson's method: differentiating between syphilitic, mercurial and syphilitic-mercurial dental defects

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Contribution to the Paper	- Thought of idea for paper and its significance to literature. - Conducted all research. - Wrote paper. - Created images for paper.
Overall percentage (%)	65%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Purpose of Published Article

Congenital syphilis produces skeletal and dental manifestations. However, these manifestations do not occur in all individuals which can be problematic when considering a differential diagnosis of congenital syphilis. All paleopathological cases in the literature consider skeletal and dental manifestations caused by congenital syphilis itself. As discussed in the introduction, the use of mercury to treat congenital syphilis is well known, and while its effects on dental development have been documented and illustrated, they have never been considered or used in the differential diagnosis of the disease in paleopathology. Therefore, the purpose of this article is to investigate the types of dental abnormalities observed in untreated and treated individuals with congenital syphilis to broaden our understanding of the types of defects associated with congenital syphilis and introduce a new category to consider when making a differential diagnosis of congenital syphilis.

Research Aims:

- To investigate the types of dental abnormalities that are associated with congenital syphilis and its treatments (mercury)

- To determine whether there are significant differences between dental abnormalities produced by congenital syphilis and treatments containing mercury in order to establish a new method to diagnose congenital syphilis.

Abstract

Objectives: This study focuses on the dental abnormalities observed by Sir Jonathan Hutchinson, Henry Moon and Alfred Fournier in patients with congenital syphilis and in those treated with mercury, in order to define alterations in dental morphology attributable to each of these causes. These definitions are applied to reported paleopathological cases, exploring various etiologies behind the defects, in order to aid in the diagnosis of congenital syphilis.

Methods: Original works were examined for descriptions of dental abnormalities in congenital syphilis and in mercurial treatments. These descriptions were compared to dentitions of paleopathological cases (n = 4) demonstrating abnormalities attributed to congenital syphilis.

Results: Distinct morphological differences were recognized between congenital syphilitic teeth and teeth affected by mercury. Mercury produces a pronounced deficiency in enamel of incisors, canines and first permanent molars that become rugged and pitted, and of dirty grey honeycombed appearance. Mercury-induced dental changes are evident in three out of four cases studied here. In one case, only syphilitic changes were present.

Discussion: Dental changes in congenital syphilis range from no visible signs to those beyond the classical models of Hutchinson, Moon and Fournier. Treatment of neonates and infants with mercury produces additional changes. Signs of disease and treatment with mercury on teeth may occur together; permanent incisors, first molars and canines, are typically affected, premolars and second/third molars are usually spared. Signs of treatment with mercury might be the only evidence of the occurrence of the disease as mercury was rarely used to treat other diseases.

Congenital syphilis is an infectious disease caused by the transmission of *Treponema pallidum* from the syphilitic mother to the fetus during pregnancy or delivery. This form of the disease produces specific changes to the hard tissues of the body and it is these changes that can aid in a differential diagnosis. There are two stages of congenital syphilis; early, occurring at birth and during infancy, and late with signs and symptoms of the disease occurring usually after two years of age. Lesions vary between the two stages. Periosteal reactions, metaphysitis and osteomyelitis occur in the early stages (Rosen and Solomon, 1976; Rasool and Govender, 1989) while cranial gummatous lesions, frontal bossing, a high arch palate, destruction of the nasal bridge, sternoclavicular thickening and tibial bowing (sabre shin) appear in the late stage (Laird, 1950; Fiumara and Lessell, 1970; 1983; Frangos et al., 2011). Specific dental abnormalities are the most characteristic signs of the disease. These include Hutchinson's crescentic notched incisors or screwdriver incisors (Hutchinson, 1887), Moon's dome shaped molars (Moon, 1884) and Fournier's multiple noduled molars (Fournier, 1884). The crowns of the permanent central incisors and first molars form around the time of birth (Ubelaker, 1999) thus, they can be affected by the disease much earlier on than the other teeth. However, these dental abnormalities do not occur in all congenital syphilitic cases. Some authors state that only 10-30% of infected individuals display dental abnormalities (Švejda, 1952; Lipski and Przylipiak, 1959), while others state that abnormalities occur in 60% (Hillson, 1996) and 65% of individuals (Goens et al., 1994). It is obvious that dental signs of congenital syphilis do not occur in all cases and show individual variation.

Hutchinson, Moon and Fournier's descriptions of congenital syphilitic teeth have been the primary source for clinical (Fiumara and Lessell, 1970; 1983; Grossman III, 1977; Liwén and Owczarek, 2012) and paleopathological studies (Henneberg et al., 1992; Jacobi et al., 1992; Hillson et al., 1998; Erdal, 2006; Henneberg and Henneberg, 1994; 2006; Gaul and Grossschmidt, 2014). Although the original descriptions appear clear with illustrated diagrams, there still seems to be confusion in the literature about what these teeth actually look like and there are those who believe that particular defects in the molars are not characteristic signs of congenital syphilis (Armelagos et al., 2012).

In the past, little attention has been paid to the effects of the treatment of syphilis on developing teeth, even though knowledge of the types of treatments used to combat syphilis and congenital syphilis throughout history have been documented.

The treatments ranged from natural remedies such as the stem from a guaiac tree (Claiborne, 1911) to chemical compounds such as arsenic and more recently penicillin (Hutchinson, 1878, 1887, 1909; Claiborne, 1911; Stopford-Taylor et al., 1911; Evans, 1912; Mahoney et al., 1943; Cole and Proctor, 1949). However, the effects of these treatments on hard tissues of the body have not been explored in depth and are poorly understood.

One of the most popular treatments for skin diseases, including syphilis, in ancient medicine was mercury (Norn et al., 2008; Beers and Mousavi, 2013). Its persistent use in ointments for ulcers dates back to 2,000 years in Chinese, Egyptian, Greek and Arabian medicine (Buret, 1891; Norn et al., 2008). The Persian physician Abu Ali al Hussein is thought to have used mercury for syphilis in the 11th century (Di Cicco, 2014). With the epidemic appearance of venereal syphilis in Europe at the end of the 15th century and beginning of the 16th century, mercury ointments and solutions were immediately employed (Claiborne, 1911).

By the 19th century, mercury was widely recommended as the main treatment for syphilis and was commonly used despite often horrible side effects including death (Weatherill, 1833). By the 20th century, the occasional use of mercury to treat other diseases was also in practice. For example, in one US naval hospital in the early 20th century, attempts were made to treat tuberculosis (Wright, 1908). The use of mercury to treat leprosy was ineffective (Neve, 1889; Charteris, 1890) and in 500 cases of skin infections, treatment with mercury produced mixed results (Byrne, 1947).

Hutchinson, Moon and Fournier all studied patients with congenital syphilis during the 19th century, when treatment with mercury was widespread. Mercury was given to mothers during pregnancy (Hutchinson, 1887; Sheill, 1910) and to children in infancy (Hutchinson, 1878). It was administered in various forms including calomel teething powders, ointments, pills (Smith, 1844; Coote, 1847; Hutchinson, 1887) and injections (Lambkin, 1909). Doses of the treatment varied from two grains of solution (Warner, 1881) up to approximately 10 grains of calomel ointment (Cornbleet et al., 1939) for infants (Hutchinson, 1887). A grain was a unit of mass measurement used by English apothecaries equal to 64.79891 mg (Connor, 1987). In 2001, the United States Environment Protection Agency estimated a maximum acceptable daily exposure to mercury, as 0.001 mg per kilogram of body weight before any adverse side effects appeared (United States Environment Protection Agency, 2001). Therefore, a child with a weight of 10 kg should not be treated with more than 0.01

mg of mercury in order to avoid any health problems. The levels of mercury in treatments used during the 19th century and described by Hutchinson exceeded this acceptable safety limit by a significant degree. Two grains of mercuric solution equaled 129.6 mg. Hence, developmental problems due to the effects of mercury in these children might be expected. However, no immediate clinical signs of poisoning were described in children taking two grains of mercury, while skin lesions healed and disappeared (Warner, 1881). Clinical complications in the form of abnormalities in the development of permanent teeth were only noted in infants given 10 grains of mercury or 648.0 mg (Hutchinson, 1887).

Hutchinson (1887) and Moon (1884) both commented that the variety of dental defects caused by the combination of syphilis and treatment with mercury, or treatment with mercury alone, provided challenges in the diagnosis of syphilis. This difficulty in making the diagnosis may also be the case among paleopathologists (Erdal, 2006; Gaul and Grossschmidt, 2014). While many have been aware that mercury was used for treatments in the past (Steinbock, 1976; Roberts and Manchester, 1995), the potential impact of such treatments on the identification and description of dental stigmata associated with congenital syphilis in paleopathological cases has not been considered. In adult cases of syphilis, Ortner (2003) suggested that the treatment with mercury may have exacerbated the severity and extent of skeletal lesions. Aufderheide and Rodriguez-Martin (1998) mentioned that mercuric treatments used in adults with syphilis made teeth brittle and accelerated their attrition. Mercury also affected the gingiva, resulting in periosteal new bone growth on the mandible and maxilla, necrosis and tooth loss (Thoma, 1944). None of these authors mentioned the influence of mercury on the formation of the dental enamel.

Using Hutchinson, Moon and Fournier's descriptions, this article outlines the set of changes seen in congenital syphilitic teeth, the effects of mercury on dental enamel formation, and the appearance of teeth affected by both syphilis and the treatment of mercury. As only 30% of individuals with congenital syphilis develop dental stigmata (Švejda, 1952; Lipski and Przylipiak, 1959), some skeletons with congenital syphilis may only display signs of treatment with mercury without further evidence of the disease. Hence, the teeth of individuals suffering from congenital syphilis may display three types of anomalies: 1) primary effects of syphilis on developing enamel and morphology of the teeth (Fiumara and Lessell, 1970; 1983; Liwén and Owczarek, 2012); 2) dental anomalies resulting from the effects of mercury

alone; 3) a combination of the effects of syphilis and mercury on developing dentition. Each type of change will be discussed in detail to aid in future paleopathological diagnoses.

MATERIALS AND METHODS

The original works of Jonathan Hutchinson (1863; 1874; 1878; 1887; 1888; 1909; 1914), Henry Moon (1877; 1884) and Alfred Fournier (1884; 1886) were examined for descriptions of pathognomonic signs of congenital syphilis observed in patients. These included characteristics associated with the disease including Hutchinson's incisors, Moon's molars and Fournier's molars and the differences between congenital syphilitic teeth and teeth of patients treated with mercury. Original works were obtained through the University of Adelaide's Special Collection library, the Royal Society of Medicine in London and through the online digital library (www.archive.org). Four previously published cases of congenital syphilis were selected as all were given a differential diagnosis of congenital syphilis. Re-examination of the dental defects was carried out using the developed criteria to test whether these three types of changes could be recognized, and whether these children had undergone treatment for their disease.

The first case is an 8 to10 year old child (B70) from St Mary's Church cemetery, Adelaide, South Australia. The cemetery was in use from 1846 to the early 20th century (Anson, 2004; Ioannou et al., 2015). The second case is a 6-year-old (±24 months) child excavated from the cemetery of 'Neuer Schottenfriedhof' in Vienna, Austria, in use between 1765 and 1784 (Gaul and Grossschmidt, 2014). The third, specimen RCSOM/D 33.633, held in the Odontological Collection at the Royal College of Surgeons of England since 1943, consists of two molars from a 9-year-old male child previously studied by Hillson et al. (1998). The final case is a 15-year-old subadult (ITK'90 56/6) dating back to the 13th century (1222–1254) and excavated in the Iznik district of Bursa, Turkey (Erdal, 2006).

Syphilitic versus mercurial teeth versus syphilitic-mercurial teeth

While most clinicians were uncertain as to the direct cause of changes on teeth in patients with syphilis, Hutchinson (1887) recognized that there were distinct morphological differences between syphilitic teeth and teeth of patients treated with mercury. The term "mercurial teeth" was first used by Hutchinson in his original book (Hutchinson, 1878, p.53). He deemed that the presentations of mercurial teeth were so

distinct that dentition affected by syphilis or treatment with mercury or both, was worthy of classification (Hutchinson, 1878, 1909). However, Hutchinson (1909) was well aware that there were limitations in determining how much variation seen in clinical cases was due to syphilis or mercury and in particular cases due to both. The following descriptions of syphilitic, mercurial and syphilitic-mercurial teeth provide a set of diagnostic criteria that should be used in the assessment of paleopathological cases.

***Syphilitic teeth*.** Teeth of patients with congenital syphilis were recognized to be the result of abnormal tooth development. The characteristic sign of congenital syphilis are Hutchinson's incisors, specifically the maxillary central incisors are considered to be pathognomonic. A typical presentation has symmetrically affected maxillary permanent central incisors. The presentation of syphilitic incisors includes a peg-like or screwdriver appearance (Hutchinson, 1878, 1909; Fournier, 1884; Švejda, 1952). These teeth were later described as "pumpkin seed" in shape (Jacobi et al., 1992; Hillson et al., 1998). Their unusual morphology and smaller than usual 'dwarfed' size often means they do not make contact with the lateral incisors and appear to slant towards one another (Hutchinson, 1909). Most typically, these incisors have a crescent-shaped notch resulting from thinned enamel along the incisal edge (Hutchinson, 1887). There is a spectrum of variability of this notch, from a barely noticeable divot, to wide and deep semi-circular crescents that penetrate markedly into the dentine (Švejda, 1952). Evidence of this variation is noted in Hutchinson's (1888) drawings of the teeth of patients with congenital syphilis (Fig. 1). The only consistent element to this notch across all presentations is that it is present at the point where the central mamelon would normally develop (Hutchinson, 1887; 1888; Švejda, 1952). This pattern corroborates Moon's (1877) postulation that the syphilitic incisor morphology is directly related to the poor development of the central mamelon during dental development. Syphilologist Alfred Fournier (1884) has discussed the presentation of this central notch and said that it was primarily seen in younger patients (under the age of thirty years) whose teeth were not worn or lost. The notched appearance of the central incisors is commonly lost due to diet and attrition, thus eradicating this pathognomonic indicator from observation (Fournier, 1884).

There is uncertainty regarding the presence of the notch on the lateral incisors of patients with congenital syphilis (Fournier, 1884). Several case studies, however, including Hutchinson's (1878, 1887), have noted the appearance of a notch on the maxillary lateral incisors, mandibular lateral incisors and mandibular central incisors. An unusual incisal appearance of the canines including a flat edge (Fournier, 1884) and a deep crescentic notch (Hutchinson, 1887) have also been noted. Other varieties of syphilitic incisors include a saw-like incisal edges with multiple spines and tubercles, which are frail and easily chipped (Fournier, 1884).

The first permanent molars are also typically affected in congenital syphilis. Two varieties have been described; Moon's molar and Fournier's molar. Moon's molar is described as 'exceedingly prone to be smaller and more dome-shaped than usual' (Fig. 2) (Moon, 1877, p.241) while Fournier's molar is described as having several large nodules and tubercles on the occlusal surface (Fig. 3) (Hillson et al., 1998). Fournier's molar image (Fig. 3) is from his original work "La Syphilis Hereditaire Tardive" (Fournier, 1886, p. 84).

Morphological characteristics of Moon's molar and Fournier's molar have been seen in both clinical and paleopathological cases (Henneberg and Henneberg, 1994, 1998; Hillson et al., 1998; Chowdhary et al., 2014). However, confusion persists as to whether or not these two anatomical varieties are one and the same (Hillson et al., 1998). Moon's molars may resemble those described by Fiumara and Lessell (1970) who call them "mulberry molars", while Fournier's molars resemble the descriptions provided by Mayes et al. (2009). The term "mulberry molar" appears to have been used first by Karnosh (1926). This author provided the following description: "the most common deformity produced is referred to as the mulberry molar of Fournier or Moon" (Karnosh, 1926, p. 33). The "mulberry molar" term is used when the cusps of the first permanent molar are reduced in size and crowded together, thus, resembling the mulberry fruit. Examples of mulberry molars are provided by Curtin (2005), Freiman et al. (2009), Mayes et al. (2009), Nystrom (2011) and Chowdhary et al. (2014).

Strict categorization of the many individual anatomical variations is a difficult task. It would perhaps be more prudent to view the presentation of individual syphilitic teeth as a spectrum, which is dependent upon the timing of infection and its interference with dental development (Karnosh, 1926; Švejda, 1952). Assignment of

individual teeth as Hutchinson's incisors, Moon's or Fournier's molars should be made with caution.

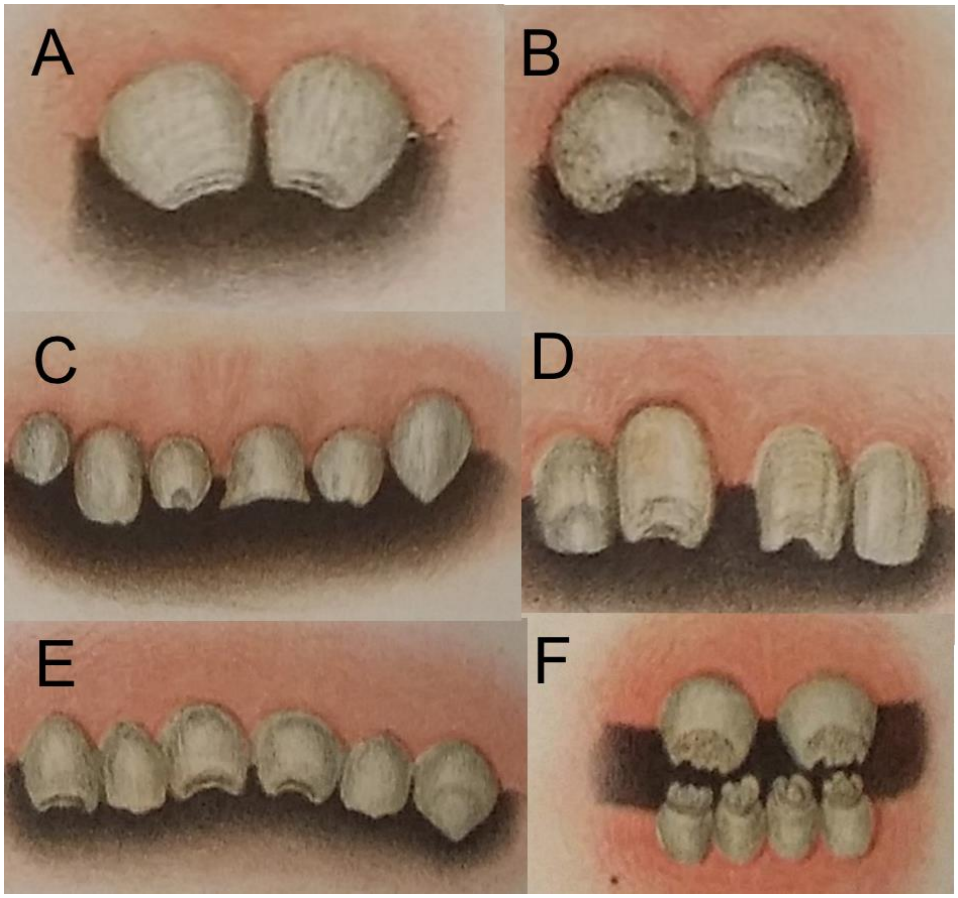

Figure 1. Variations of congenital syphilitic teeth. Hutchinson, (1888) p.10: Plate XLII, Items IV (A) I (B) II (C) VII (D) VIII (E) IX (F)

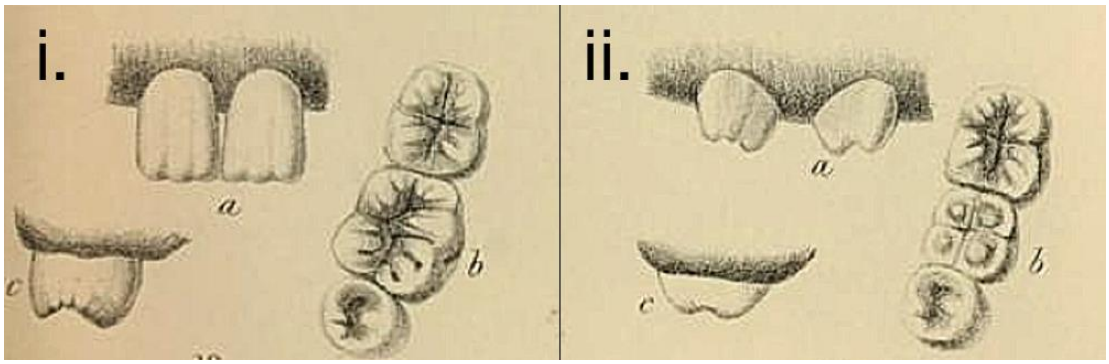

Figure 2. (i) Normal teeth (ii) syphilitic teeth as seen by Moon (1877; p. 224), Plate IV, Items 12 (i) 13 (ii).

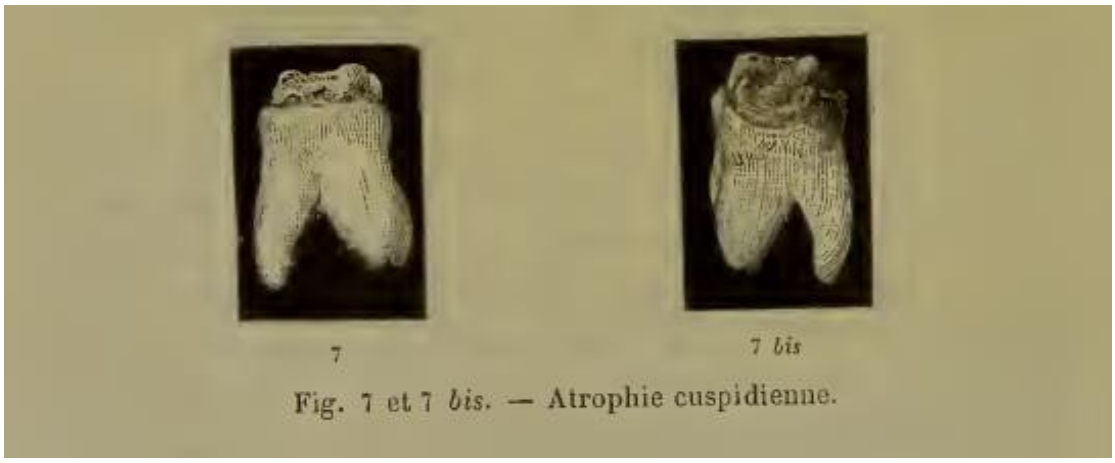

Fig. 7 et 7 *bis*. — Atrophie cuspidienne.

Figure 3. Fournier's molars. Fournier, (1886; p. 84), Figure 7.

Mercurial teeth. In comparison to the effect of syphilis on teeth, treatments with mercury produce stronger distinct enamel defects and to a lesser degree, affect the dentine (Fig. 4). These changes have been primarily described in the permanent dentition, and affecting pairs of teeth symmetrically (Hutchinson, 1887). In the diagnosis of mercurial teeth, the first permanent molars of the maxilla and mandible are considered pathognomonic (Hutchinson, 1878). Hutchinson (1909), while aware of Moon's molar, makes it clear in his descriptions that damage to teeth caused by mercury is a completely separate entity – one that primarily affects the enamel surface and when severe, the dentine. The damage to the tooth inflicted by mercury was not relegated to a small area, as with syphilis, but to large expanses of deficient enamel that was rugged and pitted, ultimately producing an appearance of a dirty grey honeycombed tooth (Fig. 4A,C) (Hutchinson, 1878, 1887, 1909). Large areas of enamel could also be entirely missing, particularly on occlusal surfaces, where 'dentine grows through, presenting a number of discolored tubercles or spines' (Fig. 4A) (Hutchinson, 1878, p. 54). Moon (1884) also observed the same phenomenon in that mercury acted injuriously on enamel, labeling molars as 'honeycombed' or 'rocky'. Moon (1884) explained that in mercurial teeth, if the pitting in the enamel was superficial, no color change may be observed but if the pitting was deeper, it presented as multiple black points into the dentine. Moon illustrated the series of progressively more pronounced changes ranging from normal, to syphilitic, to mercurial, and to syphilitic-mercurial teeth to highlight the distinct changes (Fig. 5). In many cases, the transition from a normal to mercury-affected tooth was sudden and well-demarcated

(Fig. 4A), similar to a linear hypoplastic line, which begins at the same point on all the affected teeth (Hutchinson, 1878). Typically, the normal appearance of the enamel structure would be towards the cervical aspect of the crown and the portion affected by mercury would be towards the occlusal aspect (Hutchinson, 1878) – this is evident in Hutchinson's drawings (Fig. 4). Since the occlusal and incisal portions of the dentition develop within the first 2 years of life, the causes of these changes had to have occurred at this age. Furthermore, to illustrate the extensive damage mercury produced in the dentition, both Moon (1877) and Hutchinson (1878) made reference to multiple cases of congenital syphilis where the enamel was 'wholly perfect' when there was no case history of mercury treatment. According to Hutchinson (1887), syphilis and treatment with mercury each produce specific changes that can be distinguished from each other. Syphilitic changes were of a lesser extent and were also consistent in their location, while changes due to mercury primarily affect the enamel and were more extensive and varied.

Hutchinson (1878) also observed the effect of mercury on the incisors and canines. In maxillary incisors and canines there was a severe hypoplastic linear defect separating the lower (closer to the tip) part of the crown from the rest of the crown. The enamel below that line, closer to the tip, was deficient and unevenly formed. Similar changes occurred on mandibular teeth (Fig. 4B). This however, was variable amongst clinical presentations to the extent that in some patients, canines and mandibular incisors were unaffected. Similarly, the premolars could be unaffected by mercury and by the disease itself (Hutchinson, 1878, 1887; Moon, 1884). This variation can be explained by the age at which secondary stages of syphilis and its treatment with mercury occurred and by the age of crown formation of specific teeth. Hard tissue of the tips of the crowns of permanent maxillary central incisors begins forming at approximately 3 to 4 months of age, with crown completion between 4 and 5 years of age (Nelson and Ash, 2010). Crown formation of the first permanent molar begins approximately at birth, with crown completion at 2 1/2 to 3 years of age (Nelson and Ash, 2010). Therefore, any insult, either syphilitic fever or treatment with mercury during initial crown formation, would lead to adverse effects on the development of the incisal edge or the occlusal surface. If mercurial treatment ceases before the age of 2 years, the cervical (proximal) portions of the crowns of incisors and first molars would not be affected. For the same reason, the second and third molars, and premolars would not be affected at all.

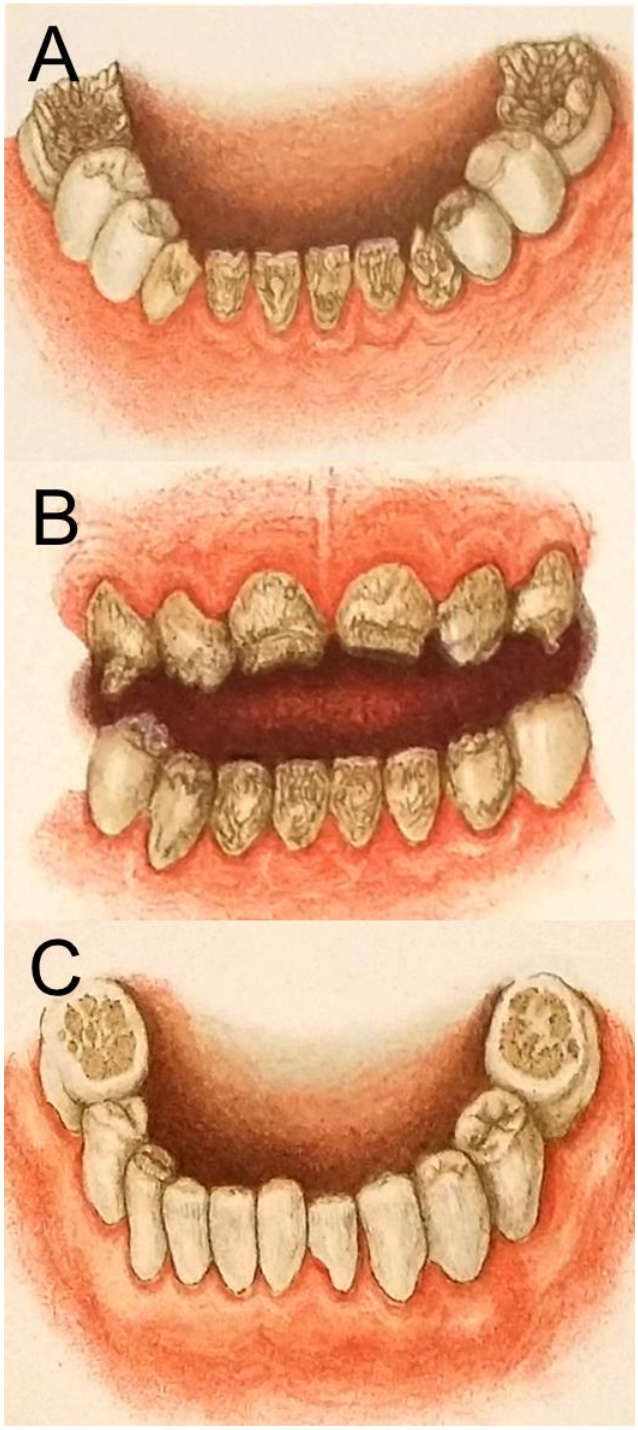

Figure 4. Enamel deficient teeth as a result of treatment containing mercury. Hutchinson, (1878; p. 53), Plate VI, Items III (A) I (B) V (C).

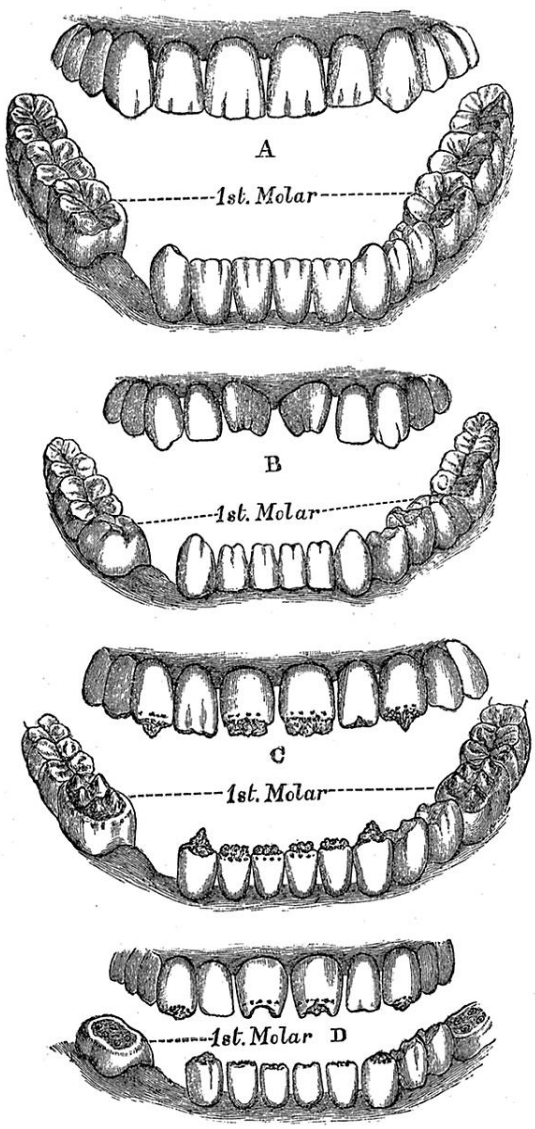

Figure 5. Moons illustration of pronounced changes ranging from (A) normal, (B) syphilitic, (C) mercurial, and (D) syphilitic-mercurial teeth to highlight the distinct changes (Moon, (1884; p. 646), Item 240.

Syphilitic-mercurial teeth. Teeth described as syphilitic-mercurial have varying degrees of super-imposition of the effects of each cause (Hutchinson, 1878, 1909; Moon, 1884). However, Hutchinson (1887, 1909) has clarified that the syphilitic notch cannot be mimicked by treatment with mercury. He described affected anterior teeth, particularly the maxillary central incisors, as notched, hypoplastic and discolored with extensive enamel loss and dentine apparent. This combination of pathological signs means that both syphilis and mercury were responsible (Fig. 6).

The first molars may be similarly malformed; approaching the dome shape (Hutchinson, 1909) and showing extensive enamel defects such as pitting, furrowing, linear hypoplasia, and honeycombing (Hutchinson, 1878, 1909). Along the occlusal surface, and in some cases over the whole crown, there is enamel loss, which depresses the cusps and exposes dentine. Areas where the dentine is exposed have a discolored appearance (Hutchinson, 1878).

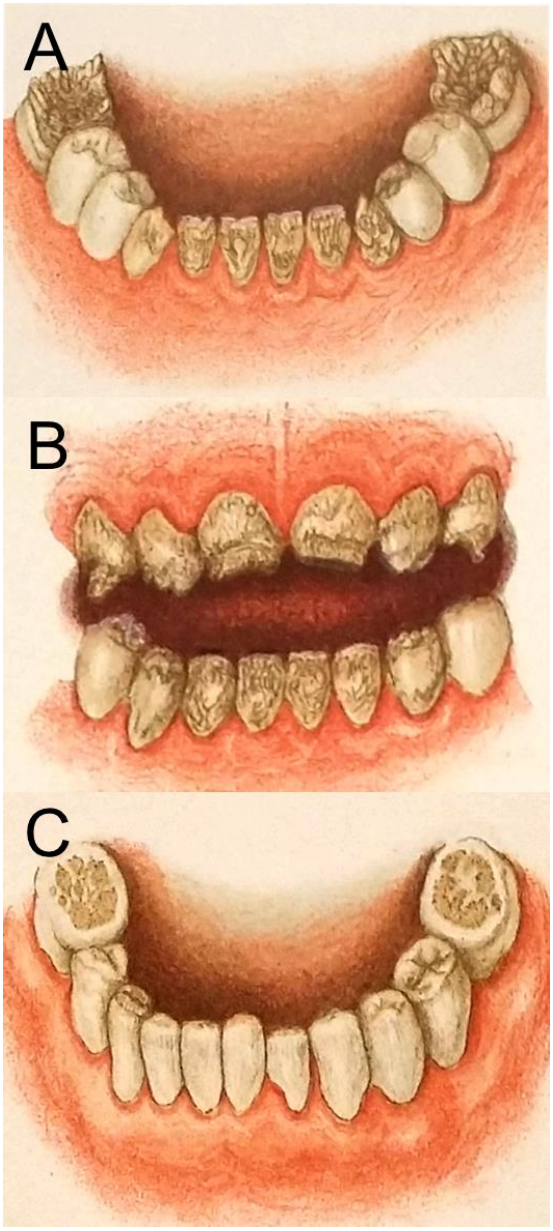

Figure 6. Dentition demonstrating the effects of both congenital syphilis and mercurial treatment. Hutchinson, (1878; p. 53), Plate VI, Items IV (A) VI (B) III (C).

DIFFERENTIAL DIAGNOSES

Differential diagnoses of the dental phenomena described above should include vitamin D deficiency, fluorosis, amelogenesis imperfecta, brucellosis and tuberculosis.

Vitamin D deficiency, or rickets, affects the mineralization of bone. Dental abnormalities can include enamel hypoplasia (Pinhasi et al., 2006; Ogden et al., 2007). Cuspal enamel hypoplasia in the first permanent molars of patients with rickets, as described by Ogden et al. (2007), does resemble Hutchinson and Moon's descriptions of mercurial molars seen in patients with congenital syphilis, however descriptions by Ogden et al. (2007) of hypoplastic pits, furrows and planes lower down on crowns of molars in rickets do not resemble the descriptions of molars by Hutchinson, Moon or Fournier. In the postcranial skeleton, rickets produces bending deformities of the long bones (Mays et al., 2006, 2009), metaphyseal flaring, porosity of cortical bone, and rib deformity (Ortner and Mays, 1998; Ortner, 2003). None of these were observed in the individual B70 studied here.

Fluorosis is a disturbance of the development of tooth enamel, caused by the ingestion of large quantities of fluoride during the time of dental development (Aoba and Fejerskov, 2002; Alvarez et al., 2009). Dental fluorosis is characterized by the appearance of horizontal opaque white patches in the enamel that can also appear mottled, pitted, porous, discolored and soft (Thylstrup and Fejerskov, 1978; Alvarez et al., 2009; Zou and Ashley, 2014). Skeletal signs of fluorosis include osteopenia, lines of arrested growth, and sclerosis (Teotia et al., 1971; Pettifor et al., 1989). Therefore, a differential diagnosis of fluorosis requires the presence of the above dental abnormalities and skeletal signs.

Amelogenesis imperfecta (AI) is a rare hereditary condition caused by a genetic mutation, either by autosomal dominant, autosomal recessive, or X-linked trait (Sekar et al., 2010). This genetic mutation disturbs the process of amelogenesis, affecting most or all teeth in both primary and permanent dentition (Crawford et al., 2007; Gadhia et al., 2012). Phenotypically AI manifests commonly in enamel discoloration, as well as delayed tooth eruption, congenitally missing teeth, tooth sensitivity, open bite, taurodontism, root and crown resorption and enamel hypoplasia. These manifestations result from the disturbance of ameloblast secretions, hypocalcification that is a result of disturbed matrix mineralization and hypomaturation of enamel (Crawford et al., 2007; Mehta et al., 2013; Chhaparwal et

al., 2014; Demirci et al., 2014; Bhandari et al., 2015). Depending on population size, the prevalence of this condition ranges from 1:700 to 1:14000 (Mehta et al., 2013).

Brucellosis, a bacterial disease caused by the *Brucella bacteria*, occurs in humans when an individual comes into contact with an animal or animal infected product. There is little information regarding the disease's effect on enamel; however, treatments including doxycycline and tetracycline have been noted to cause extensive yellow-brown enamel staining of all teeth (Ayaslioglu et al., 2005). Skeletal changes are common in the knee, hip, and ankle joints in children (Galanakis et al., 1996; Geyik et al., 2002; Alshaalan et al., 2014). None of the cases discussed in this article had yellow-brown enamel staining of all teeth. At least three individuals studied here died long before doxycycline and tetracycline treatments were available. A fever in congenital brucellosis may affect amelogenesis. However, the literature available indicates that children below the age of 8 years affected by brucellosis do not show enamel defects different from brucellosis-free controls (Cascio et al., 2004).

In clinical cases of tuberculosis, linear and occlusal surface enamel hypoplasia, such as those discussed in the above cases, have not been found (Mignogna et al., 2000; Ito et al., 2005). Common manifestations of skeletal tuberculosis in children are spondylitis, osteomyelitis, and involvement of the joints (Ortner, 2003; Cruz and Starke, 2010). Areas affected included the knee (Maltezou et al., 2000; Guillou-Debuisson et al., 2010), lytic circumscribed lesions of the cranium (Ortner and Putschar, 1981; Dawson and Brown, 2012), the spine (Teo and Peh, 2004; Lewis, 2011), hip (Guillou-Debuisson et al., 2010; Agarwal et al., 2014), elbow (Hosalkar et al., 2009), and ribs (Lewis, 2011; Dawson and Brown, 2012). No dental abnormalities have been noted in the juvenile tuberculosis cases referenced above. In other cases, linear enamel hypoplasia (Matos et al., 2011), carious lesions, and decreased enamel thickness have been briefly mentioned (Formicola et al., 1987). It has been noted that treatments with mercury were trialed in 1908 in adult cases of tuberculosis (Wright, 1908), however, its use does not appear to be widespread. The effects of mercury on enamel in this disease were also not documented. Paleopathological cases of congenital tuberculosis have not been documented in the literature. This is most likely due to the low survival rates of infants born with the condition (Amick et al., 1950; Figueroa-Damián and Arredondo-García, 2001). Since neither tuberculosis nor congenital tuberculosis is known to produce severe hypoplastic defects on teeth, it is

unlikely that these conditions produced the dental changes in the four cases discussed above.

The key characteristics of the teeth in cases of congenital syphilis and/or treatment with mercury as described by Hutchinson (1878, 1887) are: notched incisors, crescentic incisors with thin enamel on the incisal edges, severely hypoplastic incisors and permanent molars with their surfaces appearing rough, pitted, dirty, and craggy with multiple tubercles and exposed dentin. Changes similar to those seen on incisors can also occur on canines.

Comparing paleopathological specimens to Hutchinson, Moon, and Fournier's descriptions

Various individuals from paleopathological material fall within the spectrum of syphilitic, mercurial or syphilitic-mercurial teeth. Four paleopathological cases were re-examined to demonstrate this.

***St Mary's Church Cemetery, Adelaide, South Australia*.** B70 is an individual who was 8 to 10 years old (±24 months). An almost complete skeleton is preserved, which includes most elements of the skull, axial skeleton, and limbs. Some bones are damaged due to taphonomic factors. The skeleton belongs to one of a sample of 70 individuals excavated from a "pauper" section of the cemetery dating from 1846 to the early 20th century (Anson, 2004; Ioannou et al., 2015). In this section many individuals were buried in unmarked graves. They were mostly laborers and farmers who migrated to South Australia from the United Kingdom. Previous studies of B70 established that this individual might have suffered from two diseases: congenital syphilis and tuberculosis (Anson, 2004; Ioannou et al., 2015). This individual has mixed dentition. The right maxillary permanent central incisor is missing post mortem. The maxillary dentition is represented by the left permanent central incisor, partially erupted lateral right and left incisors, deciduous canines, first and second premolars, permanent first molars, and second permanent molar germs. The left maxillary central incisor's mesial and distal edges are narrow and rounded. The incisal edge is slightly crescentic in shape with minute mamelons and multiple notching. The incisal third of the labial surface has thinner, discolored (darker) enamel with pitting hypoplasia. Three transverse hypoplastic lines are on the middle third of the labial surface. The incisal third of the crown on the lingual surface has thinner enamel. A distinctive

hypoplastic grove extends to the mesial and distal surfaces. The lateral right incisor is hypoplastic and narrow. The labial views of the right and left maxillary lateral incisors, near the incisal third have round indentations in the enamel. The lateral left incisor on the lingual surface is notched mesially and has a central pit about 1 mm in diameter. Crowns of the maxillary deciduous canines are hypoplastic. Tips of the crowns are discolored (darker), and there is a distinct demarcation line between diseased and healthy looking enamel (Fig. 7).

Severe enamel defects occur on the entire surface of both permanent first maxillary molars. There are multiple tubercles of enamel present and the surfaces appear rough, pitted, dirty, and craggy (Fig. 8). The occlusal third of the crown is diminished in size and clearly separated from the rest of the crown with hypoplastic lines. The occlusal surface is covered by spike like tubercles. The cervical third of the enamel appears normal (Fig. 9).

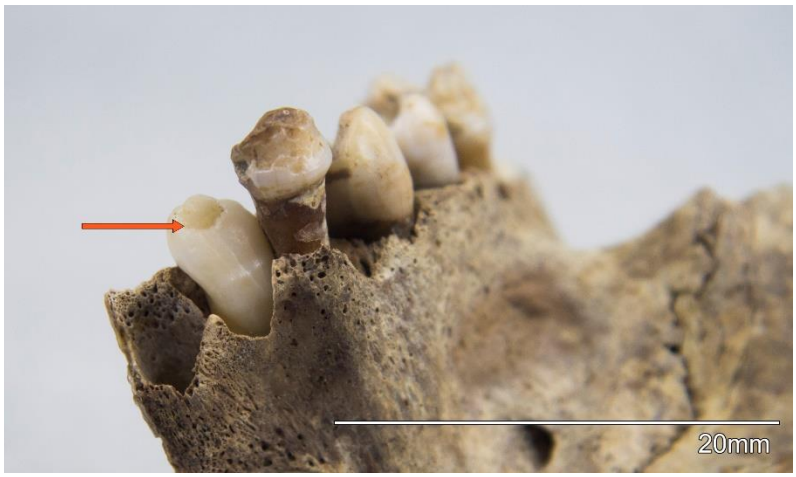

Fig. 7. Right deciduous maxillary canine of B70 demonstrates line of demarcation between healthy and diseased enamel. The middle third of the deciduous canine shows a mild to moderate pitting and discoloration. Note impression on lateral right incisor (the arrow).

Fig. 8. Left side of the maxilla of B70: L/R: Second permanent molar's morphology is normal and still in crypt. The first permanent molar's coronal structure has the typical craggy, roughened, and pitted appearance due to atypical enamel and dentine. The occlusal surface is carious. Note both premolars appear normal.

Fig. 9. B70: Left maxilla of B70. The first permanent molar's enamel surface from the buccal perspective has a clear line of demarcation from affected to unaffected. The cervical third is intact while the remaining middle and occlusal third shows the roughened and discolored enamel and dentine.

The permanent incisors, deciduous molars, right canine, first permanent molars and second permanent molar germs represent mandibular dentition. Permanent incisors are hypoplastic with linear and pitted hypoplasia on the crowns and small mamelons. Linear enamel hypoplasia crosses all four incisors at the same level (Fig. 10). The middle third of the crown of the mandibular deciduous canine has thin hypoplastic enamel (Fig. 10). The cervical third of the deciduous canine crown has normal enamel. First deciduous molars appear discolored.

Second deciduous mandibular molars have extensive carious lesions. The occlusal surfaces of the mandibular first permanent molars are severely hypoplastic with multiple tubercles. There are distinct lines on the cervical third of the mandibular molars that separate normal enamel from hypoplastic enamel (Fig. 11). The first permanent mandibular molars display the same degree of enamel damage as the maxillary first permanent molars. The occlusal surfaces appear rough, pitted, dirty, and craggy with multiple tubercles (Fig. 12).

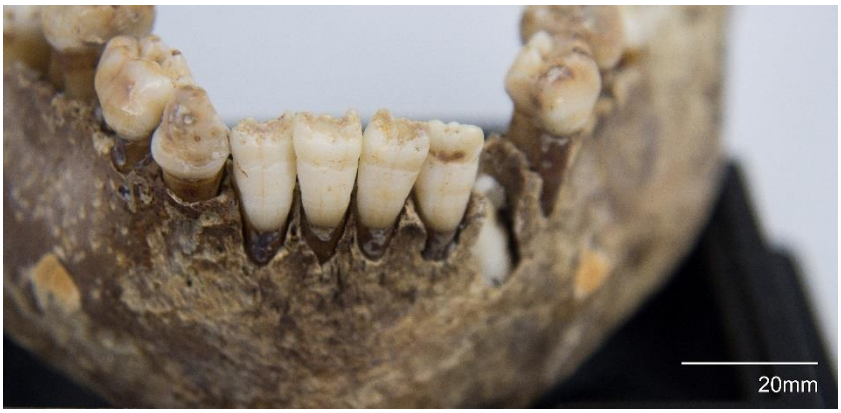

Fig. 10. Anterior view of the mandible of B70. The lower incisors all have characteristic thin and pitted incisal edges. A hypoplastic line is present at the same height along all incisors. Enamel deficiency is notable superiorly to the line, toward the tip of the incisal edge.

Fig. 11. B70: Mandibular teeth. (R/L) Cervical 1/3 of the first permanent left maxillary molar appears healthy while the 2/3 towards the occlusal surface is diseased. Second deciduous molar is carious and discolored while morphology of first deciduous molar appears normal.

Fig. 12. Right side of mandibular arch of B70. L/R: Deciduous molar has extensive occlusal decay and severe caries. The first permanent molar's occlusal surface is visibly rough, pitted and deficient of enamel; several tubercles and ridges are present. The second permanent molar is still in its bony crypt and is unaffected.

Skeletal lesions were also observed; these include a gummatous lesion on the cranial vault and destruction of the vertebrae resulting in kyphosis. Changes on teeth that are seen in fluorosis were not present in this case. The cuspal changes sometimes observed in rickets were also not observed (Ogden et al., 2007). In brucellosis, no changes appear in tooth enamel so this disease is not considered in this case. Amelogenesis imperfecta is also unlikely as it affects amelogenesis in most or all teeth, unlike congenital syphilis, which targets specific teeth. Also, amelogenesis imperfecta is not a systemic infection and cannot be associated with any of the present skeletal signs. Tuberculosis is not known to affect teeth beyond linear hypoplasia. Therefore, dental changes described in B70 are attributable to syphilis. The dental abnormalities observed in this individual resemble teeth described by Hutchinson and Moon as syphilitic treated with mercury.

"Neuer Schottenfriedhof" in Vienna, Austria. The Neuer Schottenfriedhof cemetery was in use between 1765 and 1784. FH-206, a 6-year old (±24 months), had congenital syphilis suggested as the cause of death (Gaul and Grossschmidt, 2014). Only dental remains, mandible and calcanei represent this individual. Pathological changes are present on both deciduous and permanent dentition. Both maxillary central incisors display two transverse furrows in the enamel that surrounds each tooth from the labial to lingual aspects (seen in Fig. 7 in Gaul and Grossschmidt, 2014, p. 36). Pitting is present in the middle third of each tooth. The mesial and distal incisal edges are rounded and the teeth are barrel shaped. The incisal edges have thinned enamel and display three mamelons. Similarly to the central incisors, the lateral left and right maxillary incisors display a single transverse furrow along the incisal third and they appear rounded (seen in Fig. 7 in Gaul and Grossschmidt, 2014, p. 36). Extensive carious lesions are present on the middle third of the incisal edges of the maxillary deciduous incisors. Depressions appear on the incisal thirds of both lateral incisors. The left canine is fang-like in shape. The tip of the crown is thin and narrow. The central and lateral incisors and the canine are discolored (yellow-brownish). Pitting occurs on the lingual surface of the left and right deciduous molars. No enamel hypoplasia is evident on the premolars. The morphology of both first permanent maxillary molars appears the same. Occlusal surfaces are severely hypoplastic with atrophic cusps and multiple enamel tubercles (seen in Figs. 3 and 4 in Gaul and

Grossschmidt, 2014, p. 35). The enamel towards the cervical third of the crown is normal, while the middle and occlusal third are hypoplastic.

The mesial and distal margins of the mandibular central and lateral incisors appear eroded or "waisted" (seen in Figs. 10–12 in Gaul and Grossschmidt, 2014, p. 37) and the mandibular canine demonstrates hypoplastic pits on the labial and lingual aspects. There is no evidence of enamel hypoplasia on premolars. Both deciduous mandibular lateral incisors demonstrate round defects in the enamel in the middle third of the labial surfaces while hypoplastic pits are present on the deciduous canines (Gaul and Grossschmidt, 2014). Attrition is observed on the occlusal surfaces of the first deciduous molars with pitting found towards the cervical third of both the first and second deciduous molar. The occlusal surface of the left deciduous second molar is completely hypoplastic, exposing dentine. The left and right mandibular first permanent molars are not fully erupted, still situated in the crypts. However, both demonstrate similar morphology as the maxillary first permanent molars, this includes severe hypoplasia, atrophic cusps, multiple tubercles, and distinct demarcation lines towards the cervical thirds of the teeth separating diseased from healthy looking enamel.

Due to the lack of postcrania availability, a differential diagnosis is based on the dentition only. The dental changes in this individual do not resemble enamel changes seen in fluorosis, rickets, or amelogenesis imperfecta. There is no mottled, opaque, or severely discolored enamel and not all teeth are affected, which can be the case in the diseases discussed above. Tuberculosis as a source of dental abnormalities is also unlikely as linear enamel hypoplasia is the only enamel deformity related to it. In brucellosis there are no enamel changes recorded. The dental abnormalities in this individual resemble Hutchinson's mercurial-syphilitic teeth.

Odontological collection at the Royal College of Surgeons of England. RCSOM/D 33.633 is a specimen that was deposited into the Collection in 1943. It consists of two isolated teeth. There is no skeleton available. According to the Collection entry, the maxillary right first permanent molar and mandibular left first permanent molar, belong to a 9-year-old male, who suffered from congenital syphilis. There is no date of death recorded. This case has been previously described in detail by Hillson et al. (1998). In 2014 independent observations of the original teeth were conducted by SI. The first permanent molars display hypoplastic defects. The teeth appear rough and

demonstrate deficiencies in the enamel and show multiple tubercles or nodule-like structures on the occlusal surface. The cusps are marked by multiple grooves and small tubercle defects exposing dentine at least on one occlusal molar surface (Fig. 13A,B). The sizes of the permanent maxillary right molar and mandibular right molar are not reduced. The changes in the molars resemble mercurial teeth as described by Hutchinson and are illustrated in the image (Fig. 4C).

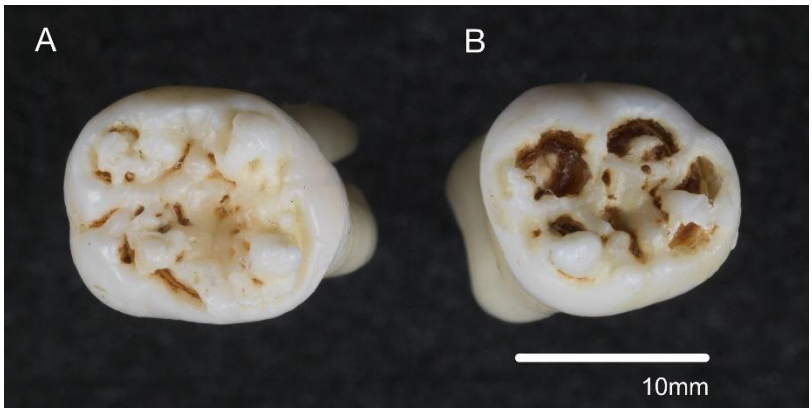

Fig. 13. The occlusal view of specimen RCSOM/D 33.633: (A) the maxillary right first permanent molar; the left side is the mesial side and the superior side is the buccal aspect. (B) the mandibular left first permanent molar; the buccal side is the superior surface and the mesial aspect is on the left. Both specimens illustrate multiple sharp tubercles, roughness and pitting exposing dentine. Note the deep denudation of enamel on the mandibular molar.

Iznik District of Bursa, Western Anatolia, Turkey. ITK'90 56/6 was a 15-year-old subadult, dated back to the 13th century (1222–1254) and described by Erdal (2006) as suffering from congenital syphilis. Most postcranial bones were present, with the exclusion of the atlas; the axis and three of the thoracic vertebrae were lost postmortem. Besides dental signs attributed to congenital syphilis, the skeleton displayed a radial scar on the frontal bone, sabre tibia, syphilitic dactylitis and gummatous and non-gummatous osteomyelitis on most bones. The maxillary permanent right incisor was lost ante mortem. The permanent maxillary left first premolar, maxillary left first molar and mandibular left central incisor were lost post mortem (Erdal, 2006). The incisal edge of the maxillary left central incisor is rounded off at the distal and mesial ends. The middle of the incisal third on the labial surface is

a notch of broken enamel (Erdal, 2006). Enamel is discolored (dirty yellow or greyish). The maxillary right lateral incisor resembles the shape of the left central incisor, and its round incisal edges and discoloration. The occlusal surface of the permanent maxillary right first molar is rough, pinched and pigmented (Erdal, 2006). The base of the cusps is marked with "plane form hypoplasia" and the occlusal surface is reduced in size; however, it does not resemble Moon's domed shaped molar (seen in Fig. 6 in Erdal, 2006, p. 21). Maxillary canines and the left mandibular canine display pit shaped enamel defects on the incisal third of the crown.

The skeletal changes in this individual are not compatible with any of the diseases listed above for the differential diagnosis but syphilis. The metaphyseal flaring, porosity of cortical bone, and rib deformity caused by rickets are not present. Fluorosis, brucellosis, and tuberculosis also produce metaphyseal flaring and changes in the joints. These, however, are not observed in this individual. Abnormalities produced by amelogenesis imperfecta such as discolored and opaque enamel, and the spread of abnormalities to the majority of teeth are not present. The combination of skeletal changes and dental abnormalities closely resembles those that are caused by congenital syphilis. The dental changes resemble "typical" syphilitic signs.

DISCUSSION

Clinical research has established that congenital syphilis produces specific dental changes during enamel development. Although these dental changes are specific, both clinical and archaeological cases have demonstrated that variation in enamel defects can occur in permanent and deciduous teeth (Fiumara and Lessell, 1970, 1983; Mansilla and Pijoan, 1995; Curtin, 2005; Nystrom, 2011; Liwén and Owczarek, 2012). The changes seen in the dentition of the individuals discussed above suggest that treatments with mercury may have disrupted enamel development, also producing specific enamel deformities.

Prior to the introduction of Salvarsan (arsenic) in 1910 and penicillin in the 1940s, mercury use was widespread in the treatment of syphilis and congenital syphilis. While an effective form of treatment, mercury produced dental enamel abnormalities that were thought to cause confusion among physicians in the diagnosis of the disease (Mansilla and Pijoan, 1995; Fiumara and Lessell, 1970, 1983; Nystrom, 2011). Having written his descriptions in the 19th century, Hutchinson (1878, 1887, 1888) focused on separating what should be considered pathognomonic of congenital

syphilis, from dental abnormalities produced by treatments with mercury. He could clearly distinguish changes he described on the maxillary central incisors as being signs of the disease not the effects of treatment with mercury. Hutchinson, however, disregarded Moon's molar as a characteristic sign of the disease. Perhaps Moon's (1877) descriptions of changes to the first permanent molar should be considered as a pathognomonic sign of congenital syphilis because they are different from changes on the molars caused by mercury.

Hutchinson (1861, 1878, 1887) selected and described only three sets of teeth with changes that may be present in patients with congenital syphilis, those attributed only to syphilis, those only attributed to treatments with mercury and, to both syphilis and mercuric treatment; however, these examples should not be used as a method of categorization when examining paleopathological specimens. There is likely to be a variation in morphological changes. This variation may be due to the individual's immune response, environment or to the amount of mercury administered. Thus in making a diagnosis, the spectrum of changes should be used. A clearer understanding of Hutchinson's descriptions of syphilitic, mercurial and syphilitic-mercurial teeth, may aid in the identification of the secondary effects of mercury and the diagnosis of congenital syphilis. This is significant in the differential diagnosis of paleopathological remains and especially where debates concerning diagnoses are continuing. While some cases of congenital syphilis may not demonstrate the "typical" or pathognomonic signs of the disease, the side effects of treatment with mercury should be tested for and considered as part of the set of characteristics seen in patients with congenital syphilis prior to the 20th century. This testing may include chemical tests for mercury content in teeth and bones (Rasmessen et al., 2008; Kepa et al., 2012).

CONCLUSIONS

In individuals with congenital syphilis; 1) variation in dental changes beyond the classical models of Hutchinson's incisors and Moon/Fournier molars can occur in response to the disease itself, 2) treatment of congenital syphilis with mercury produces dental changes in addition to those caused by the disease, thus, these changes can occur simultaneously in the same individual, 3) certain teeth, other than permanent central maxillary incisors and first permanent molars may be affected by the disease and by mercury including canines and lower incisors, and 4) signs of treatment with mercury might be considered indicative of syphilis in those individuals who do not

display classical signs of this disease, as besides syphilis, mercury has been very rarely used to treat any other disease with desirable effects. The four characteristics can be used to differentiate the dentition of patients with congenital syphilis from that of persons affected by other pathological conditions. Since there are no known applications of large doses of mercury to treat infant diseases other than syphilis, tooth defects caused by mercury can provide a fairly reliable diagnosis of congenital syphilis.

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Chapter 3

ARTICLE 2:

Diagnosis of mercurial teeth in a possible case of congenital syphilis and tuberculosis in a 19th century child skeleton.

Stella Ioannou, Maciej Henneberg, Renata J. Henneberg and Timothy Anson

(Published)

Chapter 3: Research Article 2: Diagnosis of Mercurial Teeth in a Possible Case of Congenital Syphilis and Tuberculosis in a 19th century Child Skeleton.

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Principal Author

Name of Principal Author (Candidate)	Stella Ioannou
Contribution to the Paper	- Data collection (examined specimen B70). - Data analysis a (of specimen B70). - Wrote entire paper. - Determined what type of photographs were required and took photographs of specimen.
Overall percentage (%)	65%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 18/8/17

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

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Contribution to the Paper	- Edited paper. - Provided feedback as he was the first person to describe specimen B70.
Signature	Date 18/08/17

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Purpose of Published Article

Since the first article re-established the significant differences between dental abnormalities produced by congenital syphilis and its treatments containing mercury, they can now be applied to paleopathological specimen that demonstrates dental signs that are not characteristic of the disease. Dental signs produced by mercury are valuable from a diagnostic perspective as enamel does not remodel. Therefore, the purpose of this paper is to re-examine a child (B70) from St Marys Cemetery, Adelaide, South Australia who presents with severe dental abnormalities. Burial records from St. Marys Cemetery indicate that during the 19th and early 20th centuries, treponemal diseases and tuberculosis were present in Adelaide, and that multiple diseases were present in a given individual. Congenital syphilis and congenital tuberculosis are known to cause fetal deaths, and as such, for the individual to survive into later childhood, treatments would have been in use. If dental signs resemble those attributed to mercury, this emphasises the medicinal use of mercury in Adelaide during that period.

Research Aims:

- To determine whether the dental abnormalities in a subadult from South Australia (B70) are associated with congenital syphilis or other infectious diseases.

Without the presence of "*caries sicca*", "sabre shins" and nodes/expansion of the long bones with superficial cavitation) differential diagnosis of venereal syphilis and tuberculosis (TB) may be difficult as various infections produce similar responses. However, congenital syphilis has distinctive features facilitating a diagnosis. A case study of remains of a juvenile European settler (probably male, 8-10 years old) (B70) buried in the 19th century and excavated in 2000 from the cemetery of the Anglican Church of St. Marys in South Australia is presented. B70 demonstrated the two diseases might have been present in the same individual, congenital syphilis and TB. Widespread destruction of vertebral bodies and kyphosis-related rib deformations indicate advanced TB. Severe dental hypoplasia is limited to permanent incisors and first molars; there is pitting on the palate, periosteal reaction on the skull vault and thinned clavicles. Dental signs are not limited to "screwdriver" central incisors and mulberry molars. Apical portions of the crowns of permanent upper, lower, central and lateral incisors have multiple hypoplastic-disorganized defects; deciduous canines have severely hypoplastic crowns while possibly hypoplastic occlusal surfaces of lower deciduous second molars are largely destroyed by extensive caries. These dental abnormalities resemble teeth affected by mercurial treatment in congenital syphilitic patients as described by Hutchinson.

1. Introduction

In the past, the presence of numerous diseases and the lack of an effective form of treatment meant individuals could have suffered from more than one disease. This is especially the case in relation to chronic afflictions that could be combined with congenital diseases or acute infections. Syphilis and tuberculosis (TB) were two of these diseases. Significant in the past, both diseases continue to be an important public health problem. Syphilis, caused by the spirochete Treponema pallidum is typically transmitted through sexual contact. It can also be transmitted via the placenta from an infected mother to the fetus while she is in the most infectious stages of the disease (early primary or secondary stage). It is known as congenital syphilis [1]. Syphilis affects more than 12 million adults [2–4] and a million pregnancies each year [4–6]. Tuberculosis, a chronic infectious disease caused by Mycobacterium tuberculosis, is usually transmitted through the inhalation of airborne droplets filled with bacteria produced by infected individuals usually when coughing [7, 8]. Approximately 9 million new cases were registered and 1.5 million people died from tuberculosis in 2013 [9].

In most palaeopathological studies, skeletal signs of diseases are diagnosed to one nosological unit. This finds some justification in the fact that only a small portion of diseases leave recognizable signs on hard tissues of the body (bones and teeth). It is, however, possible to find signs of more than one affliction on a single skeleton [10]. When this is the case, study of skeletal involvement should not be the only method applied when making a differential diagnosis.

The differential diagnosis of syphilis and tuberculosis in palaeopathological specimens remains difficult as both diseases rarely affect or leave any signs on hard tissues of the body. In syphilis, only 1/3 of individuals suffering from the tertiary stage of the disease will develop any bone lesions [10] while only about 3%to 5%of individuals with active TB will have skeletal changes [11–13]. The diagnostic characteristic of syphilis include “caries sicca,” sclerosis, and pitting of the outer table of the cranial vault resulting from accumulation of stellate scarring [11, 14] creating a “worm eaten” appearance [14], tibial bowing, known as sabre shin [11, 15, 16], and the expansion of the long bones with nodes with superficial cavitation [14]. In tuberculosis diagnostic elements include osteolytic lesions on the thoracic and lumbar vertebral bodies [10, 13, 17]. Rib involvement including new bone formation,

particularly periosteal reactions on the visceral surface [18–21] is now considered in the diagnosis of tuberculosis [22].

Lesions of congenital syphilis can also be difficult to identify in skeletal samples as many pregnancies can result in stillbirths, abortion, or death [15, 23] and those skeletons are not often preserved. However, in those patients that do survive, the disease causes a disturbance in dental development producing abnormalities that are distinguishable features of the disease. The most recognisable are Hutchinson's incisors, while others include Moon's molars and Fournier's "mulberry" molars [15, 16, 24–30]. It is this characteristic that can support a differential diagnosis of the disease.

However, in cases where these diagnostic changes are not present, differential diagnosis of a specimen can be difficult. Our knowledge of the type of treatments used to combat syphilis and tuberculosis throughout history is well known. They used natural remedies, chemical compounds, and recently penicillin; however, our knowledge of the effects of these treatments on hard tissues has not been explored in depth.

Mercury has been used as early as the 27th century BC in China [31]. It was recognised as a form of treatment for venereal diseases [31–33] prior to the introduction of salvarsan [34–37] and penicillin in the 20th century [38]. Mercury was provided to mothers during pregnancy [39] children, and infants in the form of ointments, calomel teething powders [24, 40, 41], and injections [41, 42]. Mercurial poisoning was noted by Sir Hutchinson [24, 25, 40] to grossly influence tooth development producing abnormalities of enamel formation (Figure 1). These may interfere with the expression of "classic" dental signs of congenital syphilis. When salvarsan was introduced, replacing mercury early in the 20th century, American military physicians recommended the use of mercury for the treatment of tuberculosis in adult patients [43, 44], but it is unclear how widespread this method of TB treatment became. There is no mention of its effects on dentition.

This paper presents a case study of the pathological lesions observed on a European subadult dated from the mid-19th to early 20th centuries who died during the early European colonization of South Australia, Australia [45]. The influences of mercury are considered in this case. In order to understand variation in skeletal lesions it is useful to consider the treatments used and their possible effects on the hard tissues of the body. This method may assist in a differential diagnosis.

2. Materials and Methods

The juvenile in this study (B70) was among a sample of 70 individuals excavated in 2000 from the cemetery of the Anglican Church of St. Marys, located at 1167 South Road, in St. Marys, Adelaide, South Australia. Many of those buried at the cemetery were in unmarked graves in a section of the grounds dating from 1846 to 1927, preventing individual identification [46]. These unmarked graves were considered colloquially as "paupers" graves due to their low socioeconomic status. Written records of burials can be found at the Church's Office. Signs of various infections were found on paleopathological analysis among the skeletal sample excavated including acquired syphilis, tuberculosis, pulmonary, and systemic infections. Some of these were also listed as causes of death in parish records [46]. Two thirds of the skeleton survives (Figure 2). Bone tissue is fragile and poorly preserved with some bones missing and others in fragments. The individual was aged by dental development, eruption, and formation using the Ubelaker chart [47] and primary ossification centres [47, 48]. Sex of a subadult is difficult to estimate [49–51] and the methods proposed do not produce highly reliable results. Using the morphology of the symphyseal region of the mandible [52] and the shape of the mandible [53] in combination with the robusticity of long bones [54], the shape of the sciatic notch would have been used to aid in determining sex; however, the majority of the pelvis is missing. To determine the effects of mercury on hard tissues and possible pathologies, a search of the literature was conducted and compared to B70.

3. Results

B70 is probably a subadult male. According to dental eruption and formation, the child is between eight and ten years of age. An osteoblastic lesion approximately 15mm in diameter is present on the cranial vault (possible periosteal reaction) on the posterior portion of the left parietal bone close to the lambdoid suture (Figure 3). Pitting is present on the maxillary alveolar process (Figure 4) and on both sides of the palate; however, it is stemming from the root of the right first upper molar (Figure 5).

3.1. Dentition. B70 demonstrates mixed dentition. The maxillary upper right central incisor is the only tooth missing postmortem. The dentition consists of a left central incisor, partially erupted lateral right and left incisors, deciduous canines, first and

second premolars, permanent first molars, and second permanent molar germs. The maxillary left central incisor demonstrates narrow and rounded medial and distal edges and is slightly crescentic in shape. It is hypoplastic. Its incisive edge is slightly narrowed with minute mamelons and multiple notching. The incisal 1/3 of the labial surface has thinner, discoloured (darker) enamel with pitting hypoplasia. This part of the crown forms a few months after birth [55]. The remainder of the labial surface has three transverse hypoplastic lines (Figure 4). On the lingual surface, the incisal 1/3 of the crown has thinner enamel. It is separated from the remainder of the crown by a distinct hypoplastic grove that extends to the mesial and distal surfaces. The lateral right incisor is narrow and hypoplastic. The right and left maxillary lateral incisors on the labial view, approximately a third of the distance from the apical point of the crown, are a round indentation in the enamel. The lateral left incisor has a central pit about 1mm in diameter and is notched mesially. Crowns of the upper deciduous canines have wide hypoplastic discoloured (darker) areas beginning below the tip of the crown and extending down to about 1/3 of the crown indicating that the changes occurred after birth (Figures 4 and 5). All maxillary premolars appear normal. Both first permanent upper molars have grossly abnormal crowns. Their occlusal surfaces have widespread hypoplastic defects (Figures 6(a) and 6(b). Extensive carious lesions are present on the mesial half of the occlusal surface of the right upper first permanent molar and small carious lesions on the occlusal surface of the left first permanent molar. Distinctive lines of thinner enamel are present on both permanent molars, separating the upper part of the crown (occlusal surface) from the rest of the crown. Areas constricted by the lines are smaller than the extent of the lower parts of the crowns. This indicates that the changes occurred shortly after birth [55]. The crown morphology of the second permanent molar germs is normal.

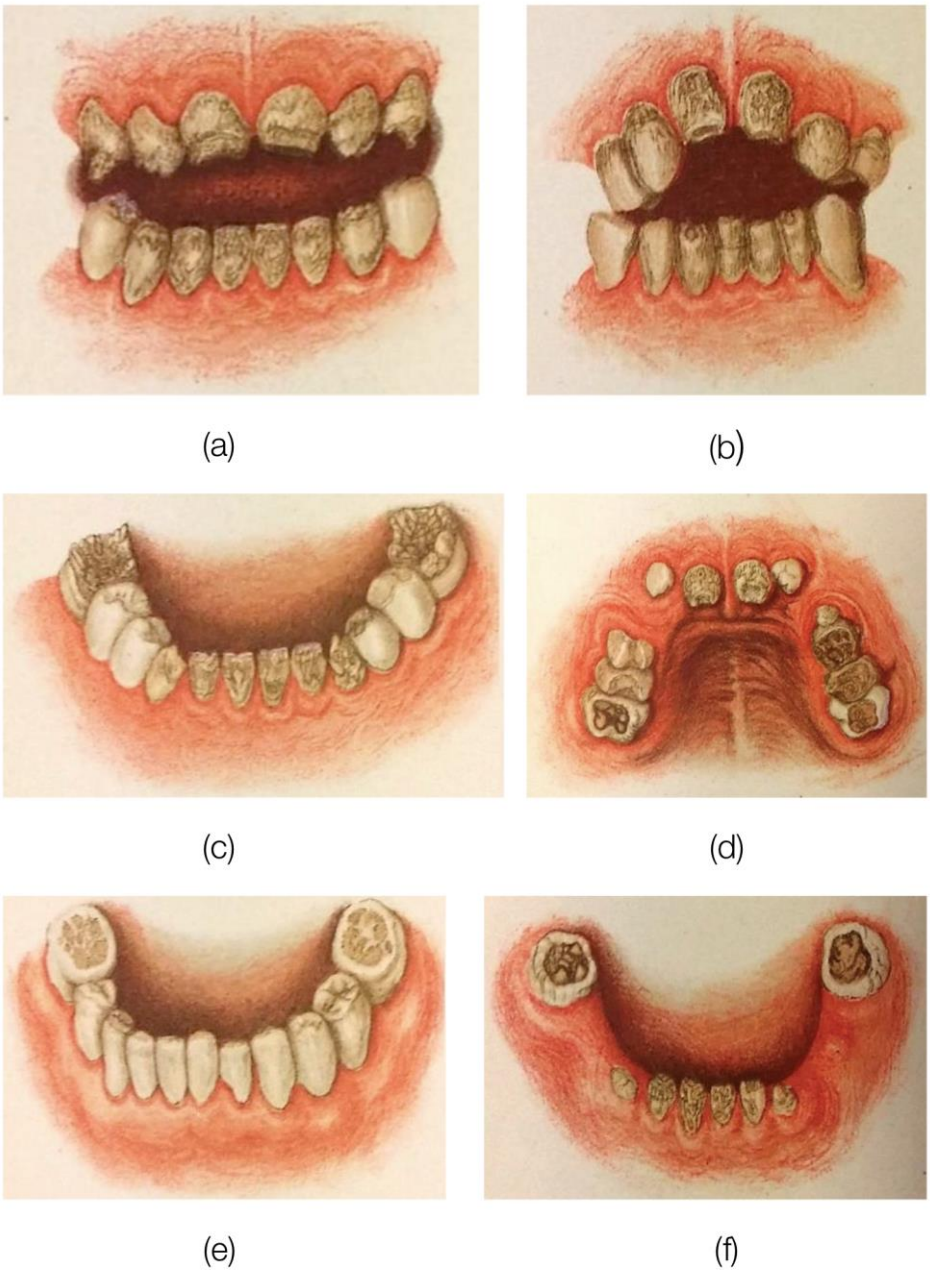


FIGURE 1: Diagrams of mercurial teeth seen in mercurial treated congenital syphilitic patients by Hutchinson. Hutchinson, J. 1878. Illustrations of clinical surgery consisting of plates, photographs, woodcuts, diagrams etc: illustration surgical diseases, symptoms and accidents, also operative and other methods of treatment, with descriptive letterpress, London, J. & A. Churchill.

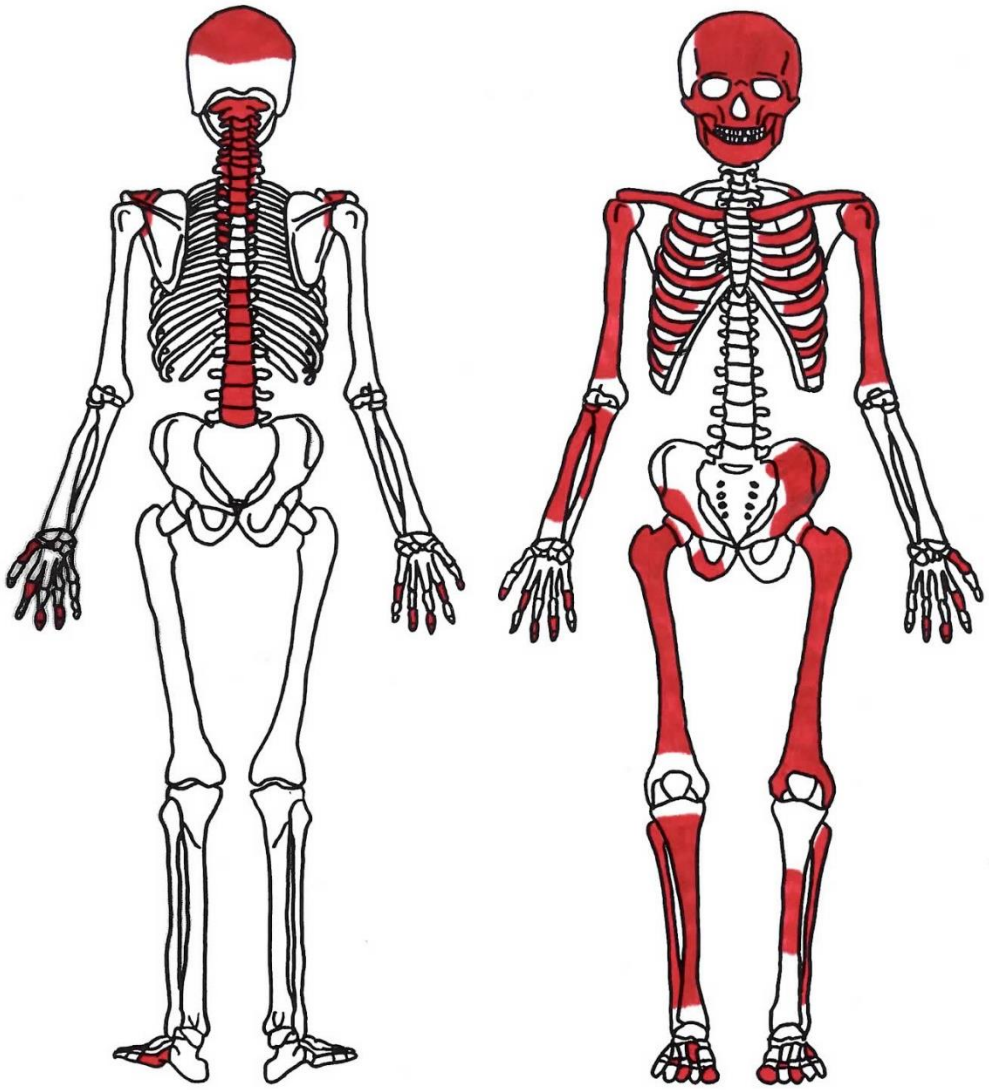


FIGURE 2: Shaded areas represent bones present.

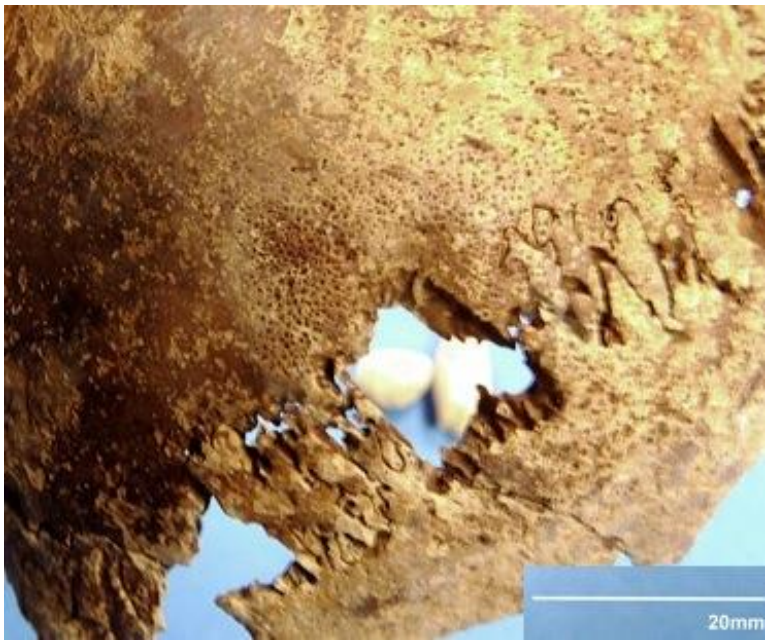


FIGURE 3: Periosteal reaction approximately 15mm in diameter on posterior portion of the left parietal bone close to the lambdoid suture. On close inspection there is no erosion of the cortical bone (Lamina externa).

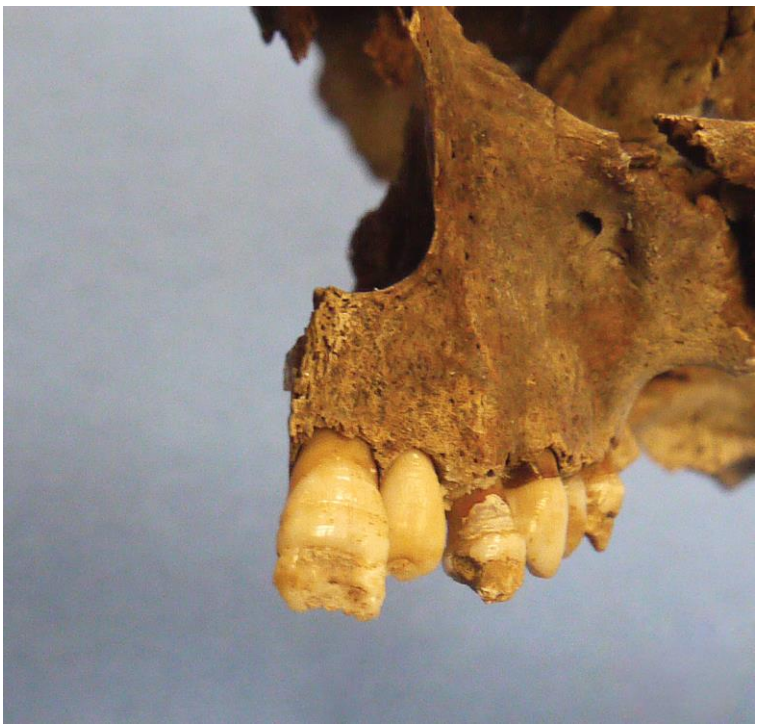


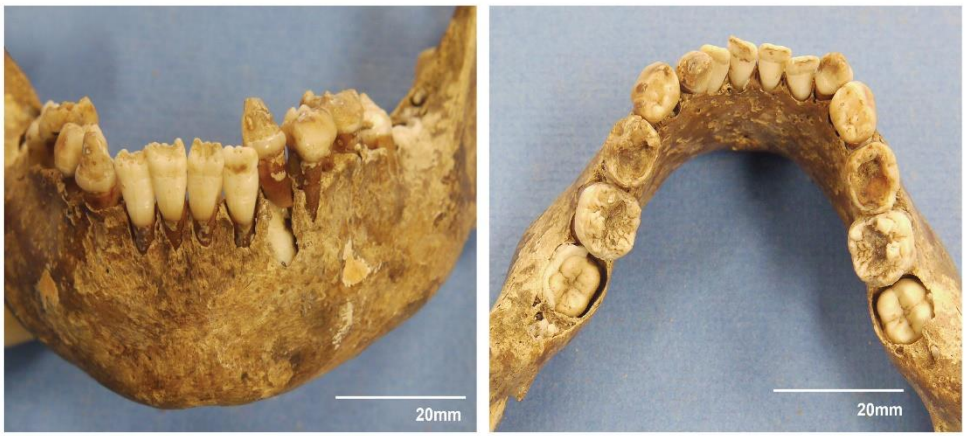
FIGURE 4: Pitting on maxillary alveolar process due to inflammatory response.

FIGURE 5: Pitting on palate stemming from permanent first molar due to inflammatory response.

Mandibular dentition includes all permanent incisors, deciduous molars, canines, first permanent molars and second permanent germs. The permanent incisors are hypoplastic with small mamelons and linear and pitted hypoplasia on the crowns (Figure 7a)). Distal 2/3 of the crowns of lower deciduous canines are very narrow with thinner hypoplastic enamel, and appear conical in shape (Figure 7a)). The remaining proximal 1/3 has rather normal enamel. The proximal 1/3 of deciduous canine crowns has normal enamel. First deciduous molars show discolouration but no caries. The second deciduous molars and canines have extensive carious cavities. The first permanent molars occlusal surfaces are grossly hypoplastic (Figure 7b)). Similarly to the maxillary dentition, hypoplastic changes indicate that they have occurred within the first few months after birth. The right lower permanent molar has an extensive carious lesion extending through most of the centre of the occlusal surface. A small carious pit in the centre of the mesial half of the occlusal surface is present in left (Figure 7b)). The crown morphology of both lower second molar germs is normal. Resorption of the alveolar bone is observed (Figure 7a)).

(a) (b)

FIGURE 6: (a) Right permanent upper first molar showing signs of dysplastic occlusal enamel. (b) Left permanent upper first molar with hypoplastic defects characteristic of dysplastic occlusal enamel.



(a) (b)

FIGURE 7: (a) Angled lower border of mandible, similar in shape to male juvenile mandible A.668 studied by Loth and Henneberg [52, Figure 2]. (b) Lower first permanent molars grossly hypoplastic.

3.2 Clavicle and Ribs. Morphology of the clavicle and several ribs appears abnormal. Thinning of the sternal end of the clavicle is evident (Figure 8). There is a small proliferative change on the upper portion of the 3rd rib. Localised inflammatory reaction is present on the right side, superior surface on the 4th or 5th rib (Figure 9). Added grooving is evident on the superior surface of several ribs.

3.3 Vertebral Column. There are extensive pathological changes on the vertebral column. The vertebral bodies of C5-Th3 show damage to their anterior parts. Signs of remodelling on C6 and C7 could indicate signs of healing (Figure 10). Cervical vertebrae C1-C4 show no pathological signs. Vertebral bodies of Th3-Th4 are largely destroyed, Th4 more so than Th3. Bodies of all other thoracic vertebrae, except Th10 and Th11, are absent, but it cannot be ascertained whether this was due to taphonomic processes or to actual pathological destruction. Zygapophyseal joints between what are likely to be Th5-Th6 are completely fused on both sides and there are no vertebral bodies (Figure 11(a)). The left zygapophyseal joints of Th6 -Th7 are also fused, while the right side is missing. Th9 is possibly in fragments. Vertebral body of Th10 is partially destroyed. Th11 and Th12 are represented by small fragments.

Two bodies and two arches of the lumbar vertebrae are preserved. One body has two deep pits on its anterior surface, which appear lytic (Figure 11(b)). The other body and the arches show no pathological signs. The body and right lateral mass of the first sacral segment are preserved without obvious pathological signs. The left lateral mass of the sacrum is completely fused with the left ilium at the sacroiliac joint. There are no clear signs of any inflammatory processes. Right sacroiliac joint appears normal. The first sacral segment has a normal body. Bodies of other sacral segments are preserved in fragments and no pathological signs were observed. No pathological signs were noted on the long bones.

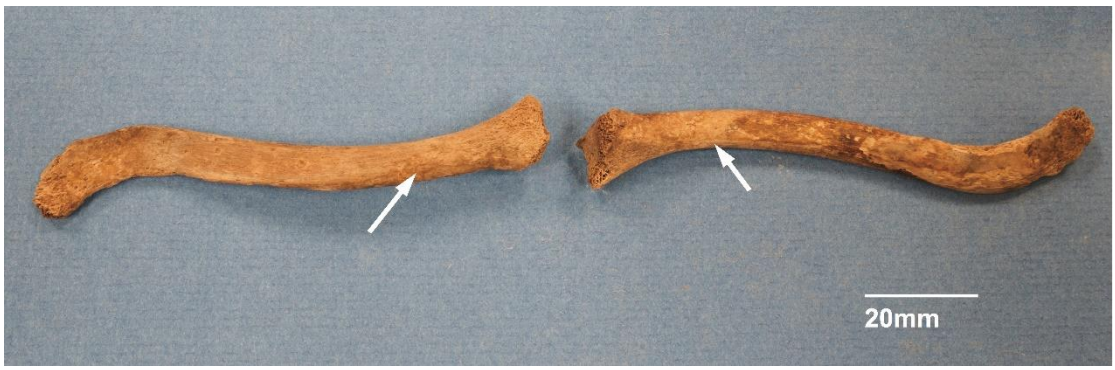


Figure 8: Thinning at sternal ends of clavicles.

Figure 9: Inflammatory reaction of inferior surface on 4th or 5th rib.

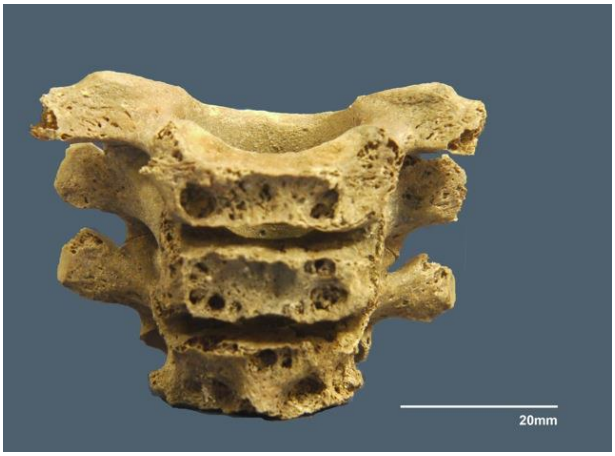
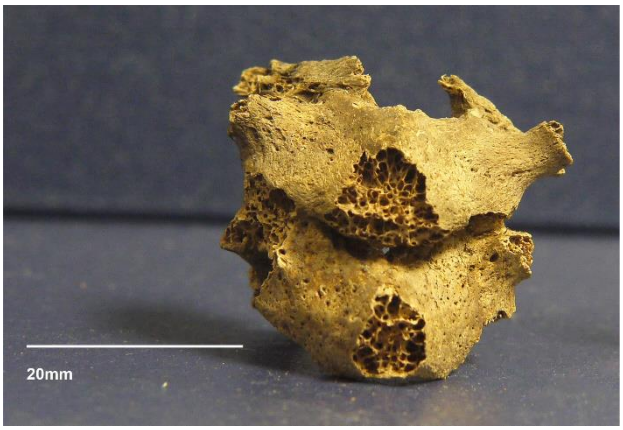
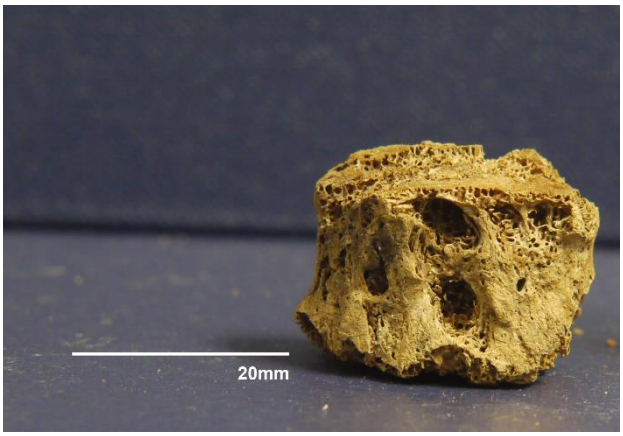


Figure 10: Destruction of anterior bodies of lower cervical vertebrae.



(a)



(b)

Figure 11: (a) Fusion of zygapophyseal joints between Th5 andTh6 completely fused with no vertebral bodies. (b) Lumbar vertebral body with deep pits.

4. Discussion

4.1 Differential diagnosis. In this case, it is possible that B70, a mid-19th to early 20th century specimen, suffered from multiple conditions. Differential diagnosis of B70 includes infectious and non-infectious diseases including congenital syphilis, tuberculosis, brucellosis, rickets and fluorosis.

Lesions in congenital syphilis can vary from periosteal reactions and osteomyelitis in the early stages [56–58] and cranial gummatous lesions and frontal bossing of the bone, destruction of the nasal bridge, a high arch palate, sternoclavicular thickening, and tibial bowing (sabre shin) in the late stage of the disease [15, 16, 59–61]. With the exception of a possible localised periosteal reaction on the cranial vault of B70, there is minimal skeletal evidence to support the differential diagnosis of congenital syphilis.

The dental changes in B70, although not “typical” (Hutchinson’s incisors, Moon’s molars, or Fournier’s mulberry molars), may still be a result of congenital syphilis through the mercurial treatment of the disease. Hutchinson recognised that mercury produced enamel defects in particular pairs of teeth. In severe cases it would affect dentine, too. With the tooth enamel deficient, the tooth would appear rugged, pitted, and dirty [40]. The first permanent upper and lower molars are the “test teeth” for mercurial influence, similar to the upper central incisors considered to be the “test teeth” in congenital syphilis. The crown enamel is deficient, with dentin growing through and revealing numerous discoloured tubercles [40]. A distinct demarcated line separating healthy enamel from diseased enamel was also evident on the sides of the molars. In severe cases, the tooth could appear dwarfed. Upper and lower incisors and canines were usually affected, with enamel deficiencies occurring below a line that would cross them at the same level; however, premolars usually escape all damage [40]. Hutchinson also noted that it was common for both syphilitic and mercurial teeth to be present at the same time which may have caused confusion among physicians [40]. He did not specify, however, exact ages or developmental stages of dentition at which the changes occurred.

B70’s dentition closely resembles the descriptions and images (Figure 1(c)) of congenital syphilis patients treated with mercury as provided by Hutchinson. The first upper and lower permanent molars demonstrate enamel deficiency across the occlusal surface exposing multiple tubercles, appearing rugged, pitted, and dirty. There is a clear distinction between diseased and healthy enamel on all four molars and all three canines. All upper and lower incisors exhibit enamel deficiencies apical to the linear enamel hypoplasia. All upper premolars appear normal. Taking into account individual variation in formation of deciduous and permanent tooth crowns, the most likely age at which the changes in B70’s dentition occurred is shortly after birth. The cervical ends of enamel on all teeth appear normal, suggesting that ameloblasts were disturbed during the early years of life [62]. Tips of deciduous canine crowns seem to be normally formed, but the crown area below them is hypoplastic in contrast to first deciduous lower molars whose morphology is normal. Permanent tooth changes affected apical or occlusal portions of specific crowns that form in the first few months of life. It is possible that the type of enamel damage to the first permanent molars in B70 could be classified as cuspal enamel hypoplasia [62]; however, to confirm this, scanning electron microscopy would need to be performed.

Clinical presentations of congenital syphilis present similar dental features to those seen in B70.These include multiple notching or serrated edges which were seen in five patients [63] pitted enamel hypoplasia of the upper central and lateral incisors and primary and secondary dental caries on numerous teeth [64]. Narrowing and a reduction of the dentinoenamel junction of the permanent incisors and first molars, with a reduction in the size of the crowns and constriction of mamelons, was also noted by Sarnat and Shaw [27].

In comparison to palaeopathological specimens, similarities to B70 include the round indentation in the enamel on the maxillary right and left lateral incisors [65–67] and pitted enamel hypoplasia in the lower right incisors. Others include linear enamel hypoplasia in all four incisors with a deficiency in enamel above (apically) a hypoplastic line [67, 68], the distinct demarcation between healthy and diseased enamel, and severe enamel deficiencies exposing multiple tubercles in molars [67].

The lack of skeletal lesions on limb bones of B70 could be supported by clinical cases of late congenital syphilis, which found no periosteal lesions or perichondritis [69, 70]. This may be related to the stage of infection in maternal syphilis and transmission [69]. The later stages of the disease in the mother produce lesser risk of infection [15] and possibly less severity.

Tuberculosis is typically diagnosed by osteolytic skeletal lesions in the vertebral bodies and in large joints of palaeopathological specimens [11]. The most common manifestations of skeletal tuberculosis in children are spondylitis, osteomyelitis, and involvement of the joints [11, 71]. In children, common areas affected by the disease included the knee [72, 73], lytic circumscribed lesions of the cranium [7, 74, 75], spine [71, 76], hip [73, 77], elbow [78], and ribs [76]. There is no documentation with regard to dental abnormalities found in juvenile tuberculosis [7, 79]. Dental changes briefly mentioned include linear enamel hypoplasia [80, 81], carious lesions, and decreased enamel thickness [80].

Comparing B70 to skeletal signs of tuberculosis, osteolytic lesions evident on the thoracic and lumbar vertebrae resemble few juvenile specimens [81, 82]. A circumscribed periosteal lesion on the superior surface of rib four or five in B70 is similar to that found in the case of TB in the Hamann-Todd Osteological Collection [83]. However, no lytic lesions were apparent on the cranial vault of B70, neither was there involvement of the joints as in the cases mentioned above. Linear enamel hypoplasia and dental abnormalities as seen in B70 have not been noted in clinical

cases of primary tuberculosis [84–86]. There are no documented palaeopathological cases of congenital tuberculosis. This may be due to the rarity of the disease and the low survival rates of infants born with the condition [87–89]. Therefore, congenital TB is not known to produce extensive hypoplastic defects on incisal edges nor on occlusal surfaces of teeth. It is likely that B70 suffered from TB acquired during childhood.

While we know that mercury has been used in the treatment of tuberculosis, its descriptions and suggested use begin from 1908 and they do not seem to be widespread. B70 was buried in a cemetery dating from 1846 to 1927, so it is unlikely that mercury's use in treatment of tuberculosis would be the cause of described dental changes.

Brucellosis affects different areas of the skeleton in adults and in children. In adults the spine or sacroiliac joint is more commonly affected, whereas in children, the knee, hip, and ankle joints are more common [90–94]. While the left sacroiliac joint is fused in B70, who is a child, there do not appear to be any signs of inflammation and there are no other pathologies that resemble those seen in brucellosis; therefore, it is difficult to make a confident differential diagnosis. However, the sacral segments that are present do not show any pathology. There are also no lesions present on the knee joint or the rest of the appendicular skeleton, and thus brucellosis is unlikely.

Rickets is a vitamin D deficiency, affecting the metabolism of calcium and phosphorus and the mineralization of bone. Skeletal changes include bending deformities [95, 96], metaphyseal flaring, and porosity of cortical bone [11, 95, 97]. These changes can affect the cranial vault, long bones, pelvis, ribs, and vertebrae. In conjunction with the skeletal pathologies of rickets, abnormalities in dentition are common, particularly linear enamel hypoplasia, pitting, dental opacities, and caries [98–100]. Considering that there are no bending deformities, flaring, porosity of the cortical bone, and dental opacities and while hypoplasia is not limited to linear defects, rickets in B70 is unlikely.

Fluorosis is a disturbance of dental development resulting from ingestion of large quantities of fluoride [11, 101]. These dental abnormalities include opaque white patches in the enamel. This can result in pitting, striations, and widespread brown staining [101–104]. Skeletal pathologies include abnormal bone formations on the appendicular or axial skeleton, mostly linked with the insertions of tendons and ligaments [11]. In clinically diagnosed cases of fluorosis in children, skeletal

manifestations included osteopenia, growth lines, and sclerosis [105–107]. Considering that there is no widespread dental staining nor skeletal lesions relating to fluorosis, it is unlikely that B70 suffered from fluorosis.

5. Conclusion

B70 was excavated from St. Marys cemetery, from a section of the grounds dating from 1846 to 1927, when European settlers colonized South Australia. B70 was buried at the expense of the Government in a section of the cemetery referred to as the "paupers" graveyard [108]. Burial records of St. Marys indicate that treponemal diseases and tuberculosis were present among the skeletal sample B70 originated from and other skeletons (B10, B6, and B53c), demonstrated possible cases of treponemal disease [46]. Considering that B70 was excavated from the pauper's section of the graveyard and multiple diseases were present in the sample (syphilis and tuberculosis), it is probable that B70 suffered from multiple diseases in congenital syphilis and tuberculosis. The significance of this skeleton is that it displays dental signs that are not typically seen in congenital syphilitic cases. It is possible that this specimen displays the effects of mercury that was used to treat the disease. It is possible that chemical elements or compounds have not been considered in paleopathology to have an effect on hard tissues. Hopefully, this paper will reintroduce an interest in the work of Hutchinson who noted that mercury, used to treat syphilis, plays a role in the disruption of enamel formation. Mercury's effects are separate from tooth development (size and shape), caused by the disease and yet they are indicative of the disease through its treatment. Therefore, Hutchinson's incisors, Moon's molars, and Fournier's molars are not the only dental abnormalities that should be considered in the diagnosis of syphilis when examining specimens from antiquity up to the introduction and usage of modern treatments.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Chapter 4

ARTICLE 3:

Five Cases of Dental Anomalies Attributable to Congenital Syphilis from Early 20th Century American Anatomical Collections

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(Published)

Chapter 4: Research Article 3: Five Cases of Dental Anomalies Attributable to Congenital Syphilis from Early 20th Century American Anatomical Collections.

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Name of Principal Author (Candidate)	Stella Ioannou
Contribution to the Paper	- Thought of idea for paper and its significance to literature. - Data collection of specimens from the Smithsonian Institute in Washington, DC. - Data Analysis of specimens. - Took photographs of specimens for paper. - Wrote and edited paper.
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Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 18/8/17

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	David Hunt
Contribution to the Paper	- Conducted (pXRF) spectrometry to test for mercury levels. - Edited paper, added references to strengthen paper, and provided feedback.
Signature	Date 8/17/2017

Name of Co-Author	Maciej Henneberg
Contribution to the Paper	- Contributed to defining the purpose of the paper. - Analysed photographs - Edited paper
Signature	Date 18/8/17

Purpose of Published Article

As described in the introduction, the use of mercury to treat congenital syphilis is well known, particularly its use through Europe. The first paper demonstrated that dental changes produced by treatments containing mercury are significantly different from those caused by the disease itself. However, its use throughout America prior to the introduction of penicillin is not well known or described in paleopathology. Therefore, the purpose of this paper is twofold: (1) to conduct a search of the historical medical literature to explore whether mercury was used for medicinal purposes as throughout Europe to treat congenital syphilis in the United States (2) and if so, search for dental variations associated to congenital syphilis and its treatments in American skeletal collections.

Research Aims:

- To discover the extent to which mercury was used for medicinal purposes in the United States.
- To determine whether dental signs associated with congenital syphilis and treatments containing mercury are present in the Smithsonian Institute skeletal collections.
- To determine whether dental variations associated with congenital syphilis are found in individuals with a cause of death not related to syphilis.

Keywords: congenital syphilis, disrupted amelogenesis, severe hypoplasia, tooth morphology

ABSTRACT Specific dental abnormalities are considered pathognomonic of congenital syphilis (CS); however, European physicians recognized their variation during the late 19th to mid 20th centuries. Observations of syphilis-related dental abnormalities in American individuals from similar time periods are made to determine types of variation among the American population.

From a survey of the Smithsonian Institution's National Museum of Natural History anatomical human skeletal collection, five individuals demonstrated dental characteristics consistent with CS (P00011R, P219398, P000707, P000679, and P000161). Hutchinson's three categories of dental anomalies were used to describe variations among syphilitic individuals.

Previously identified pathological dental characteristics related to CS were present in the analyzed individuals. P00011R, 24-year-old Black female, has a maxillary right Moon's molar. P219398, approximately 20-year-old Black female, has Hutchinson's incisors and Fournier's molars. P000707, 26-year-old Black male, displays severe hypoplasia on all incisors, canines and maxillary first molars. P000679, 33-year-old Black female has "screw-driver" shaped maxillary central incisors, altered occlusal morphology of first maxillary molars and hypoplasia. P000161, 45-year-old Black female, demonstrates severe hypoplasia on incisors and canines (molars lost).

"Classic" dental characteristics of CS are not ubiquitous to all identified cases. This study exemplifies that dental anomalies associated with CS do not all have to be present for diagnosis. Although other causes for some of these anomalies are possible, observations in these five cases are most consistent with CS.

Prior to the introduction of penicillin in the 1940s, syphilis was a public health problem in the United States (Lancet, 1930; Lancet, 1937a). The prevalence of syphilis in the United States at that time is difficult to determine, as data collection for syphilis by state health departments did not begin until the early 20th Century, and the Venereal Disease Division of the U.S. Public Health Service was not created until 1918 (Nakashima et al., 1996).

To control venereal disease, various states implemented programs (free treatment, and clinics that offered free, pay, and part pay clinics) (Lancet, 1937a), and legislation (marital examination law and prenatal law) (Lancet, 1917; Prebble, 1938; Lancet, 1940; DePorte, 1941). In cases of medical intervention, mercury was used to treat congenital syphilis in the 19th and early 20th centuries throughout the United States (Conrad and McCann, 1922; Cole et al., 1929; Scheer and Fraser, 1930; Cole et al., 1933; Chargin and Saunders, 1939). Treatments of syphilis also included chemotherapies of arsenic and bismuth compounds (Lee, 1878; Cole et al., 1929; Eller and Maloney, 1929). The chemotherapies most favored in the treatment of congenital syphilis included mercury, arsphenamine and potassium iodide (United States. Public Health Service. Division of Venereal Diseases, 1930).

The effectiveness of mercury as a treatment for syphilis has been questioned (Miller, 1858: Weatherill, 1833); although, the treatment remained popular with some physicians. In some cases, syphilitic lesions completely healed and patients became seronegative (Wakerlin, 1934). In syphilitic women treated with mercury during their pregnancy, 91.5% were efficient in completing their pregnancies successfully by live birth, while 47.6% non-treated women experienced fetal death (United States. Public Health Service. Division of Venereal Diseases, 1930). Mercury and its compounds were seen to have antibacterial properties that actually reduced, or cured infections with *Treponema pallidum* (Smith, 1844; Hare, 1858; Warner, 1881; Wakerlin, 1934). Despite their possible curative effects on syphilis, mercurial treatments yield serious side effects including scarlatiniform rashes, stomatitis, pyrexia, bleeding of the rectum, and death in some cases (Chopping, 1899; French, 1909). Therefore, the use of mercury was abandoned later in the 20th century when other effective forms of treatment (i.e., penicillin) became available and mercuric treatments were dropped from clinical practice.

In paleopathology, the diagnosis of congenital syphilis (CS) is based on skeletal and dental signs. However, when skeletal signs are not present specific dental abnormalities caused by a disturbance in odontogenesis are associated with the disease (Hillson et al., 1998). Signs include Hutchinson's crescentic notched or screwdriver incisors (Hutchinson, 1859; 1887), Moon's dome-shaped molar (Moon, 1884), and Fournier's molars of "upset appearance" (Bouleversée d'aspect) (Fournier, 1886:84). These changes occur when odontogenesis is affected during the early stage of the disease. During the 19th century, Jonathan Hutchinson, was the first to note that syphilitic treatments containing mercury also affected dental development, disrupting amelogenesis. Hutchinson described that these mercury-induced dental malformations were significantly different from those caused by congenital syphilis alone, and in some cases, patients exposed to a treatment regimen involving mercury could manifest dental signs associated with the disease and treatment (Hutchinson, 1888; Moon, 1884; summarized in - Ioannou et al., 2015, 2016). It should be noted that 10-30% of patients clinically diagnosed with congenital syphilis do not manifest changes associated with disturbed odontogenesis (Švejda, 1952; Lipski and Przylipiak, 1959). It is clear that these inconsistencies caused confusion among physicians in the past (Hutchinson, 1878) and with diagnoses in both clinical and paleopathological settings.

During late 19th and early 20th centuries, various institutions produced collections of skeletons for future research purposes. These collections included skeletons of individuals who suffered from various diseases including treponemal diseases. Today such collections provide hard evidence of the disease and its treatments, independent of government records and the literature. For some individual skeletons, there is medical documentation stating the cause of death, while others have been given differential diagnosis based on the skeletal evidence by the curator. Such diagnoses were based on paleopathological knowledge of the curator at the time.

While previous studies have focused on "typical" dental characteristics associated with congenital syphilis, this paper will also assess the possibility of some of the dental anomalies being from the medical treatments. Therefore, the aims of this paper are: (1) to describe the variation and similarities in dental abnormalities associated with congenital syphilis in individuals either medically diagnosed with the dis-ease or who were posthumously diagnosed by skeletal pathological conditions or dental anomalies to have been afflicted with congenital syphilis, and (2) to evaluate

whether there are any indications of dental features that could be the result of treatments for congenital syphilis. Differential diagnoses of other diseases or genetic conditions that could have effects on dental characteristics are reviewed, including tuberculosis, leprosy, amelogenesis imperfecta, rickets, fluorosis, and some of the chemicals used to treat these diseases are also considered, such as mercury, arsenic, bismuth, lead and cadmium.

MATERIALS AND METHODS

As stated above, 10-30% of patients clinically diagnosed with congenital syphilis do not manifest dental anomalies (Švejda, 1952; Lipski and Przylipiak, 1959). To assess the range of expression of the dental anomalies attributed to congenital syphilis, those conditions as described by Jonathan Hutchinson (1859, 1863, 1878, 1887, 1888), Henry Moon (1877, 1884), Alfred Fournier (1886), and Hillson et al. (1998) are used as the criteria for the cases observed here to evaluate the likelihood of congenital syphilis in the anatomical collections and to see if comparable dental abnormalities are present. The criteria are reviewed and described by Ioannou et al. (2016).

A review of dentition in the early 20th century Robert J. Terry anatomical skeletal collection and cadaver room skeletons from the Howard University Medical School was made at the Smithsonian National Museum of Natural History (NMNH) in Washington DC. The survey focused on individuals listed as having pathological conditions related to the following: congenital syphilis, treponemal disease, lues disease, syphilis, tuberculosis, and rickets. These pathological identifications came from death certificate records, reports from the morgue records, or diagnoses made by observations of the cadavers or the skeletal elements in dissection or after skeletonization. Some of the observations made by curators were independent from the cause of death of these individuals.

Out of 38 individuals that were narrowed down from the initial survey, five individuals exhibited various dental malformations consistent with those in patients diagnosed with congenital syphilis (Excel file with data is available from SI upon request). The five individuals were P00011R, P219398, P000707, P000679 and P000161, of which only P00011R was clinically diagnosed with congenital syphilis while living. The dentition of these individuals was analyzed to document the types and range of malformations in tooth morphology. Since human variation and their

effects from disease are individualistic and often do not present the "typical" pathological manifestations of a particular disease.

To evaluate the possibility of mercury treatment of any of these subjects, portable x-ray fluorescence (pXRF) spectrometry was conducted to determine whether mercury could be detected in the enamel and bone in each of the individuals.

Dental Malformation Criteria for Evaluation of Treponemal Disease

Hutchinson (1859, 1863, 1878, 1887, 1888) recognized that dental malformations observed in children with congenital syphilis varied so considerably that he deemed it necessary to create various categories to distinguish kinds of anomalies in dental formation. His three categories of dental malformations were - syphilitic teeth, mercurial teeth, and syphilitic-mercurial teeth.

In the syphilitic category, the maxillary central incisors are the "test teeth". The central incisors can appear "peg like" or screwdriver in shape, are dwarfed and display a crescentic notch on the incisal edge (Hutchinson's incisors). Some of these features can also be observed in the maxillary lateral incisors and mandibular incisors (Hutchinson, 1887; Hillson et al., 1998). Other characteristics within the syphilitic category include malformations observed in the first permanent molars (Hutchinson, 1887) labeled as Moon's molar and Fournier's molars. Moon's molar is "smaller than usual and dome-shaped" (Moon, 1877), while Fournier's molars either have several nodules and tubercles or have a flat surface (Fournier, 1886). Both varieties of Fournier's molars have a clear demarcation between healthy and diseased enamel.

Mercurial teeth demonstrate severe enamel hypoplasia, caused by treatments containing mercury. The first permanent molars are the "test teeth". The enamel is deficient and appears rugged, pitted, and dirty with a honeycomb appearance (Hutchinson, 1878; Ioannou et al., 2016). Dentine is affected in severe cases with the appearance of multiple spines or tubercles. The entire occlusal surface or a central area can be affected. Incisors and canines are also affected with severe linear enamel hypoplasia that crosses these anterior teeth at the same level. The enamel between the linear enamel hypoplasia and the tip of the crown is deficient (Hutchinson, 1878), and pitting hypoplasia is also common. Premolars in most cases appear normal. However, the characteristic notch observed in syphilitic incisors is not mimicked in mercurial conditions only (Hutchinson, 1878). Syphilitic-mercurial teeth demonstrate a combination of both syphilitic and mercurial dental malformations (Hutchinson, 1878;

Moon, 1884; Ioannou et al., 2016). The upper central incisors can have a peg-like or screw-driver shape (outline), the incisal edges appear characteristically notched, and any part of the enamel surface can be hypoplastic, pitted and discolored. The first permanent molars can show an absence of enamel on the occlusal surface of the crown but have healthy enamel on its sides (Hutchinson, 1878).

RESULTS

Terry Collection P00011R (Fig. 1) is an African American female, born in 1918 and died in 1942, at 24 years old. The primary cause of death was attributed to lobar pneumonia, but was clinically diagnosed with congenital syphilis in 1930 and was subsequently institutionalized until her death, 11 years and 2 months later. This is the only individual that was diagnosed with congenital syphilis during the life of the individual.

All maxillary incisors and left maxillary canine were lost many years before death (Fig. 1A). The first right upper molar has a clearly narrowed occlusal surface with pitting hypoplasia resembling a dome shape (Moon's molar) (Fig. 1B & 1C). The left first upper molar has a narrowed occlusal surface, and is largely destroyed by dental caries. All the premolars and right canine have normal morphology. The second and third permanent molars have normal molar morphology. The left third molar has a single carious lesion on the disto-buccal aspect. Upper alveolar process shows periodontal changes on both sides.

The mandibular teeth present include the left and right lateral incisors, left canine, left and right first premolars, left second premolar and left and right second and third permanent molars. The lateral incisors appear peg like in shape (Fig. 1D & 1E). Both first permanent molars were lost many years before death, and the alveoli are completely healed (Fig. 1F). The occlusal surface of the left second premolar and second and third permanent molars are destroyed by caries. Bone resorption suggests periodontal disease (Fig. 1D & 1F). Cranial morphology is normal, no 'saddle nose' is present, and the nasal cavity and palate are normal. The molars in P00011R are syphilitic.

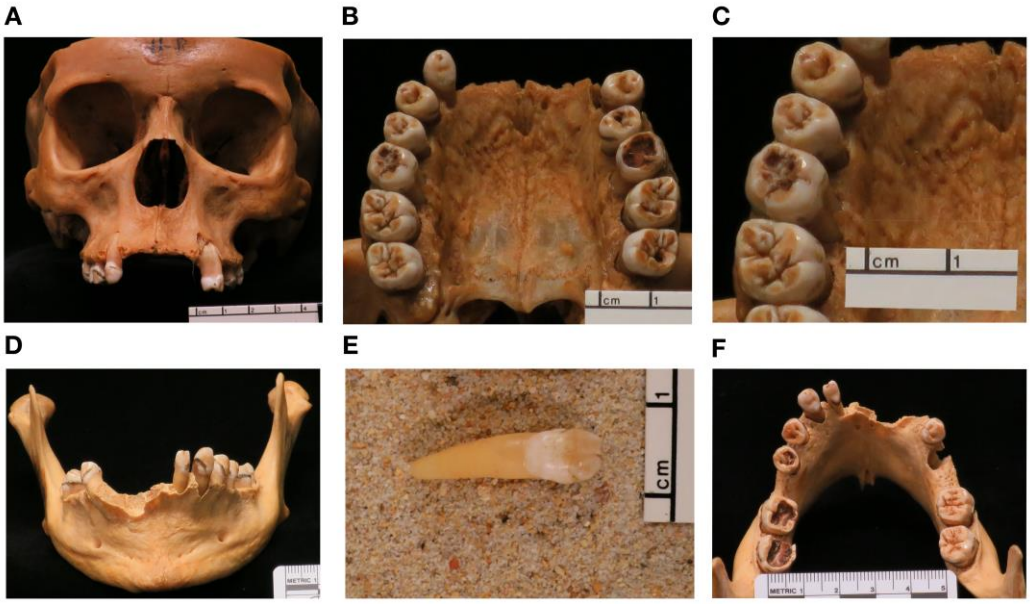

Figure 1. Individual P00011R, 24yrs old female. (A) Anterior view of maxilla: Central and lateral incisors, and left canine missing. No saddle nose. (B) Occlusal view: Most teeth have normal morphology. Carious destruction of the left first molar does not allow precise observation, but it seems that the crown has a narrow occlusal surface. (C) First right permanent molar has a narrow and reduced occlusal surface resembling Moon's molar. Pitting is also present. (D) Anterior view of the mandible. Periodontal disease is evident. (E) Loose anterior tooth of mandible; lateral right incisor. (F) Occlusal view of mandible: No first molars, most likely lost to caries.

Howard Collection P219398 (Fig. 2) is an African American female who died in 1903 in Washington, DC with no recorded cause of death and was autopsied at Howard University School of Medicine. There is not a reported age at death, but dental and skeletal development indicators suggest this individual died between 20 and 25 years of age. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All maxillary teeth are present, except the left second and third permanent molars. The maxillary central incisors are marked by rounded mesial and distal incisal edges. The labial aspects of the incisal one-third of both crowns have centrally located hypoplastic defects. On the right central incisor, this hypoplasia resulted in a smooth crescentic pit, while on the left central incisor there is irregular hypoplastic pitting in the same location (Fig. 2A). Multiple short lines of hypoplastic

enamel are also apparent on the lingual surface of both teeth. The mesial and distal edges of the right and left lateral incisors are also rounded off, giving both teeth a peg-like shared crown. Multiple pits are present on the lingual surface of both lateral incisors. The tips and lingual aspects of the canines display hypoplastic pitting. The occlusal surfaces of the first permanent molars have diminished areas compared to the dimensions of the rest of the crown (Fig. 2B & 2C). There are also scattered hypoplastic pits and various areas of the occlusal surfaces have irregular grooves (Fig. 2C). The molars resemble both types of Fournier's molars. The second right permanent molar has normal molar morphology. The left second molar was lost during life, as the alveolar bone has healed.

The mandibular dentition is nearly complete. The left canine was lost post-mortem, while the alveolus of the lower left third molar is healed. The central incisors are affected by severe enamel hypoplasia and exposed dentine on the incisal one-fourth of the crown (Fig. 2D). The morphology and enamel of all other teeth, except the first permanent molars, appears normal. The occlusal surfaces of the crowns of the first permanent molars are reduced in size and severely hypoplastic (Fig. 2E & 2F). The cusps appear to be reduced in size and multiple tubercles are visible (Fig. 2F). This appears similar to Fournier's nodule-type molar. The dentine is also exposed in places. The morphology of the second permanent molars appears normal, with the left demonstrating signs of crenulation. The entire crown of the third right permanent molar is missing with only the root present while the left was lost during life as indicated by healed alveolar bone. The morphology of the alveolar bone suggests some periosteal inflammation was present at the time of death. The dental abnormalities in P219398 are most consistent with syphilitic malformations.

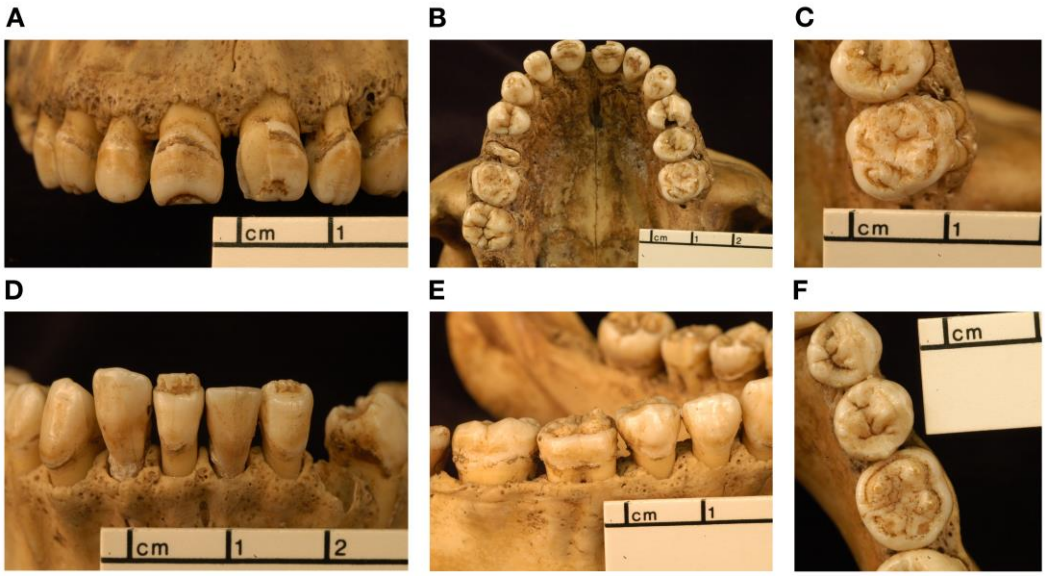

Figure 2. P219398, 20yrs old female. (A) Anterior view of maxilla: Labial aspect of permanent central inci-sors. Right incisor has thin enamel along incisal edge forming a crescentic pit. Irregular pitting is noted in the same location on the left incisor. Lateral incisors are peg-like in shape. (B) Occlusal view of maxilla: Occlusal surfaces of the first permanent molars are reduced and demonstrate scattered hypoplastic pits and irregular grooves. (C) Occlusal view of the left first permanent molar of maxilla demonstrates pitting and grooves in enamel. The occlusal surface is also reduced. (D) Anterior view of mandible: Central incisors demonstrate enamel hypoplasia and exposed dentine on the 1/4 of the crown. Note, the central and lateral incisors ap-pear to be incorrectly inserted into mandible post mortem. (E) Lateral view of right side of mandible: First permanent molar resembles that in the maxilla. (F) Occlusal view of right mandibular first permanent molar: it has reduced surface, multiple tubercles and pitting hypoplasia.

Terry Collection P000707 (Fig. 3) is an African American male, aged 26 years at the time of his death in 1929 in St. Louis, Missouri from pulmonary tuberculosis. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All permanent teeth, including the third molars, are present. The central incisors are marked by minor notches and isolated pits along the incisal edges. Enamel adjacent to the incisal edge appears healthy with minor pitting, however, the

middle third of the crown shows progressively more severe pitting hypoplasia that ends with extremely deep defects that likely penetrate the pulp cavity (Fig. 3A). The cervical portion of the crowns appears normal. The left lateral incisor is affected by a similar progressively pitted enamel defect on the incisal third of the crown (Fig. 3A). The incisal third of the right lateral incisor has been lost at a point where the pitting morphology appears like that observed in its left-side antimere. A similar enamel defect affects the left canine (Fig. 3B). The enamel of the right canine appears to have broken off postmortem. The lingual surfaces of these anterior maxillary teeth are affected by irregular hypoplastic defects, demonstrating a mottled like appearance. The premolars have normal morphology. The occlusal two thirds of the crown of the first permanent molars are hypoplastic, with pitting hypoplasia and reduced surfaces in comparison to the other permanent molars present (Fig. 3C). However, some normal groove patterns of the occlusal surfaces are preserved. Minor pitting is present on the second and third permanent molars. The second left and third right permanent molars demonstrate crenulation. The alveolar bone suggests some periosteal inflammation was present.

The mandibular dentition consists of all permanent teeth, except the left and right first molars. Two thirds of all incisors and canines are affected by severe hypoplastic defects (Fig. 3D). The left and right first molars were lost antemortem. The alveoli for the first molars are healed but not completely resorbed (Fig. 3E). The second permanent molars and the left third permanent molars have normal molar morphology but demonstrate crenulation (Fig. 3F). The third left molar appears larger than the second permanent molars. A supernumerary fourth molar is present on the left side (Ioannou & Henneberg, 2016). It is smaller in size in comparison to the other molars and has normal molar morphology (Fig. 3F). P000707 demonstrates dental signs that are suggestive of mercuric treatments.

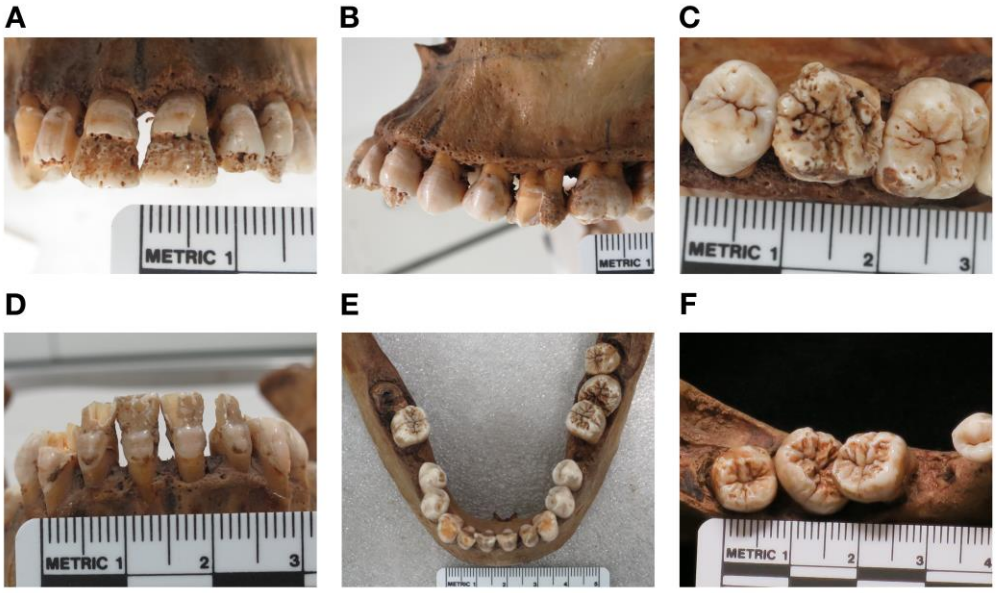

Figure 3. P000707, 26yrs old male. (A) Anterior view of maxilla: Incisal edges of the maxillary central incisors appear healthy with isolated pits. The middle third of the crown demonstrates progressively severe enamel hypoplasia. Similar enamel hypoplasia is evident on the lateral incisors and canines. (B) Lateral view of the left side of maxilla: The lateral incisor and canine display enamel defects similar to the central incisors. (C) Occlusal view of upper right first permanent molar, note unusual configuration of enamel on the occlusal surface. Two thirds of the occlusal surfaces of the first permanent molars are severely hypoplastic, although some normal groove patterns are preserved. (D) Anterior view of the mandible: Two thirds of all incisor and canines crowns are affected by severe hypoplastic defects. (e) Occlusal view of mandible, note both first molars are missing. (F) Close up of supernumerary fourth molar. Note crenulation on occlusal surfaces of other molars.

Terry Collection P000679 (Fig. 4) is an African American female, who died of tuberculosis at 33 years of age in St. Louis, Missouri in 1928. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. The maxillary dentition is complete, except for the left third molar. It is unclear whether the absence of this tooth was due to agenesis or antemortem tooth loss. The maxillary central incisors have narrowed incisal edges with rounded corners. Located at the midcrown on the labial surface are hypoplastic defects that consist of an

approximately oval-shaped area of thinner enamel, which is surrounded by pitting that extends distally to the one -third of the crown from the incisal edge (Fig. 4A). Shoveling is apparent on the lingual aspects, as is one linear hypoplastic line on the cervical third of the crowns (Fig. 4B). The lateral incisors appear peg like in shape with round mesial and distal edges. A couple of isolated pits are evident on the right lateral incisor. One hypoplastic line runs at the same level on both lateral incisors on the labial aspect. The left canine has isolated pits on the tip of the crown. Pits and grooves are present on the lingual aspect of the canines. Pitting is on the occlusal surface and lingual aspect of the first premolars. The right second premolar has a deep groove on the lingual surface. Maxillary first molars have occlusal surfaces that are reduced in size and have abnormal enamel formation (Fig. 4C). There is a demarcation between diseased and healthy enamel by pitting hypoplasia (Fig. 4D). The second molars and third right molar have nor-mal morphology.

The mandibular dentition is represented by a full set of anterior teeth from the left first premolar to the right first premolar. The right third molar and the left second molar are present. All other posterior teeth were lost antemortem as indicated by complete alveolar remodeling (Fig. 4E). The incisors are marked by multiple notches on their incisal edges. Shallow indistinct furrows are present about one-third the length of the crown (Fig. 4F). Isolated pits are present on the lateral incisors. Part of the enamel on the labial surface of the left central incisor has broken off post-mortem. The first premolars have isolated pits on their surfaces. All other remaining mandibular teeth have normal morphology. The dental defects in P000679 are comparable to Hutchinson’s dental observations for CS and suggestive of mercurial teeth morphology.

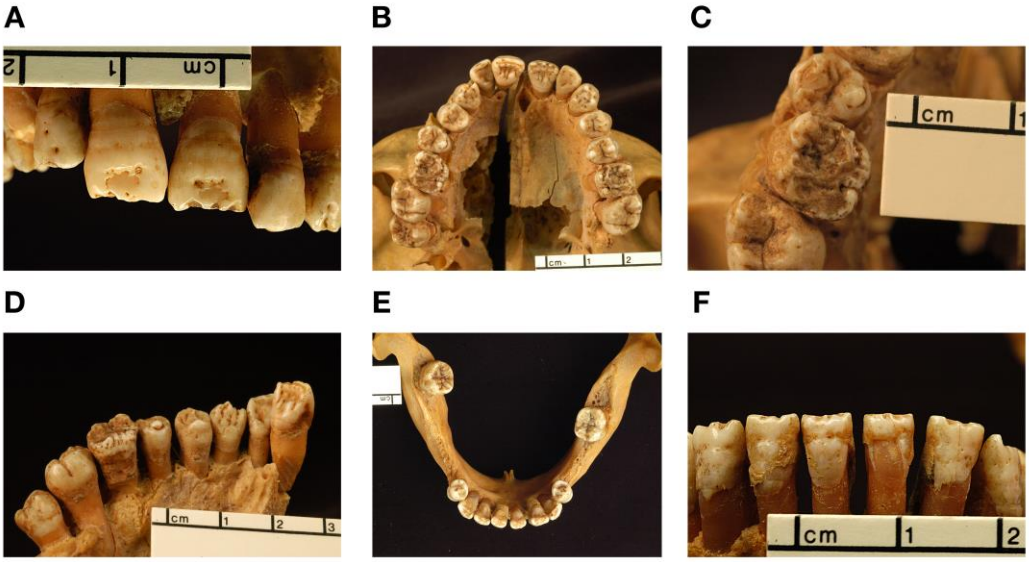

Figure 4. P000679, 33yrs old female. (A) Hypoplastic defects on labial surface of central incisors. Those that are in the incisal third of the crown are large and oval in shape and are centrally located with small-scattered pits. Some other teeth also display pitting. (B) Occlusal view of maxilla: occlusal surfaces of first permanent molars have abnormal formation of the enamel. (C) Close up of upper right first molar. (D) Palatine view of the right maxillary dentition: Note demarcation between diseased and healthy enamel in the first permanent molar. (E) Occlusal view of mandible. (F) Anterior view of mandible: Incisors are marked by multiple notches on their incisal edges while shallow indistinct furrows are present about one-third the height of the crown.

Terry Collection P000161 (Fig. 5) is an African American female who was approximately 45 years of age at the time of death and added to the skeletal collection in 1925. No cause of death is recorded in the morgue records. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All maxillary teeth are present, except the right second premolar and the left first molar. The incisal margins of the central and lateral incisors are notched. The labial surfaces of crowns of anterior teeth have malformed enamel, featuring irregular pitting and a deep furrow located about one-third of the crown height proximal to the incisal edge (Fig. 5A). A second furrow appears on the left central incisor on the cervical third of the crown. The furrows of the anterior teeth appear approximately at the same level.

Some enamel was lost postmortem on the cervical third of the right central incisor and parts of the mesial aspect of the left central incisor. Numerous dark colored pits run horizontally along the middle third of the crown of the central incisors and the incisal third of the lateral incisors and tip of canines. (Fig. 5A). Similar pitting and linear hypoplastic defects occur on the lingual surfaces of these teeth (Fig. 5B). The morphology of the premolars and other molars still present appears normal. A fragment of the occlusal surface of the right first permanent molar is marked by irregular enamel and pitting. A large carious lesion is present in the disto-lingual area of the right first permanent molar, while an interproximal carious lesion is evident towards the mesio-lingual end of the crown. The left first molar has been lost most likely due to dental caries. The alveolar bone has not healed completely, so it is possible the loss occurred shortly before death. The morphology of both second molars and third molars appears normal. On the palate anteriorly on the right side there is a circular bony depression surrounded by elevated bone. There is a large perforation on the right side of the palate. There is also some pitting in the palate that is more apparent near the right first permanent molar.

The mandibular dentition consists of the left and right lateral incisors, canines, first and second premolars, second molars and the left third molar. The central incisors were lost post mortem, while both first molars and the right third molar were lost antemortem. The alveoli for both first molars are completely remodeled, but the alveolus for the left has been less remodeled than the right. The third right molar alveolus is healed. Similar to the maxillary dentition, severe linear and pitted enamel hypoplastic defects are present on the lateral incisors and canines (Fig. 5C). The multiple hypoplastic lines run along at the same level of the crown of these teeth on both labial and lingual surfaces (Fig. 5C & 5D). The tops of the crowns of the first premolars appear hypoplastic. Pitting and two small carious lesions are present on the occlusal surface of the left first premolar. The crowns of both second premolars appear normal. The abnormalities seen in the dentition of P000161 are consistent with Hutchinson's description of patients with CS and possibly some features suggestive of mercury effects.

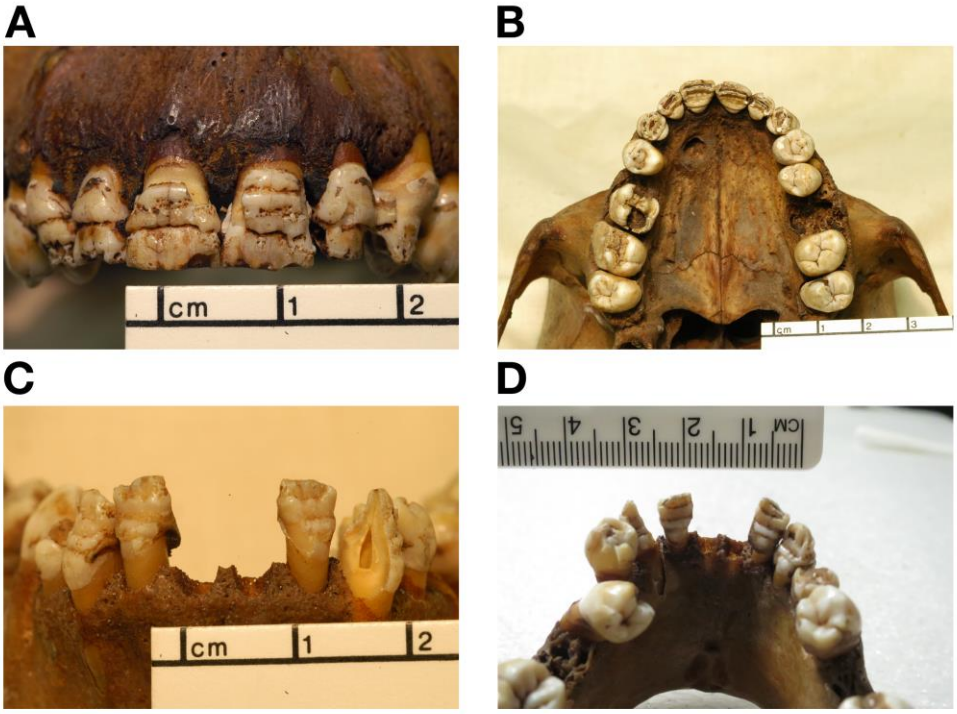

Figure 5. P000161, 45yrs old female. (A) Severe hypoplastic enamel of the maxillary incisors and canines. Incisal thirds of the central and lateral incisors' and canines' crowns are hypoplastic with deep furrows. Dark colored pits run horizontally across the crowns. (B) Occlusal view of maxilla: Linear and pitting hypoplasia noted on the lingual surface of anterior teeth. (C) Anterior view of mandible: Severe linear and pitted enamel hypoplasia on the lateral incisors and canines. (D) Lingual view of mandible: Pitted and linear enamel hypoplasia evident on lateral incisors and canines corresponds to that on labial surface.

Mercury testing using pXRF

An exploratory, qualitative analysis using a portable x-ray fluorescence analyser (pXRF) was performed to see if any of the individuals above might have mercury or other chemical elements possibly related to treatment for CS and the cause of the dental abnormalities. The analysis was conducted using a Bruker Tracer III-V handheld analyser on portions of hypoplastic enamel on the central and lateral incisors for all of the individuals, except individual P00011R, which lacked central incisors - instead, a lateral incisor and canine were tested. The analysis was conducted with settings optimized for mercury (0.001" Cu, 0.001" Ti, 0.012" Al filter at 40 keV/16 micro amps

for 300 seconds, without vacuum). Bone testing was done on the femur of the same individuals to test for contamination if high readings of any particular elements were found. No mercury was detected. The lack of mercury in these individuals most likely can be attributed to amounts of mercury that may be too minute for the instrument's detection capabilities (see Zuckerman, 2016:50 for discussion on mercury detection with pXRF).

Differential Diagnosis

Diseases that interfere with odontogenesis and amelogenesis are considered for a differential diagnosis. These include tuberculosis, leprosy, amelogenesis imperfecta, rickets and fluorosis, as well as elements that have been used as treatments or are known to affect tooth development such as mercury, arsenic, lead, bismuth, and cadmium.

Tuberculosis is a chronic disease that predominately affects the ribs, vertebrae, and the large joints of the body. In adult onset of tuberculosis, there would be no effect on the dentition. In cases of childhood tuberculosis, the most common dental abnormalities are associated with developmental stress - linear enamel hypoplasia (Dabernat and Crubézy, 2010; Bedić et al., 2015); carious lesions (Formicola et al., 1987; Hlavenková et al., 2015); and decreased enamel thickness (Formicola et al., 1987). Since dental signs observed in childhood tuberculosis do not resemble the dental abnormalities or the severity observed in the five cases, tuberculosis is not likely and would be ruled out as a differential diagnosis.

Leprosy is a chronic disease that affects the skin and peripheral nervous system with skeletal loss by resorption in the latter stages of the disease. It is a slow and progressive disease, signs of the disease can start to develop from six months to 30 years (World Health Organization. 2012). Dental abnormalities that have been reported in skeletal cases with evidence of leprosy include linear enamel hypoplasia (Boldsen, 2005) (which might be correlated to possible frailty in the individuals, rather than leprosy itself), and constriction of the roots of the upper permanent central incisors (leprogenic odontodysplaia) (Roffey and Tucker, 2012) that might be related to the resorption of the alveolus rather than development effects of dental formation (Roberts 2011). These observations are not common or diagnostic of the disease. If a child were to be infected with leprosy, since its macroscopic expression would be long-term, it is assumed that the disease would not severely affect dental development,

possibly only producing linear enamel hypoplasias from insults to development. It is unlikely that there would be the severity of dental pathology similar to those in the described cases here. Since leprosy is predominately an adult disease, if in children it would not have the severe effects as seen in CS, therefore, leprosy is ruled out as a differential diagnosis.

Amelogenesis imperfecta (AI) is a hereditary condition characterized by enamel defects. Phenotypic expression of the condition is caused by a disturbance in ameloblasts secretions producing hypoplasia, hypocalcification, hypomaturation and hypomaturation-hypoplasia with taurodontism (Gadhia et al., 2012; Prasad et al., 2016). Amelogenesis imperfecta also manifests in enamel discoloration, enamel pitting, and thin enamel (Kar et al., 2012; Gerdolle et al., 2015; Rogers et al., 2016). The prevalence of AI varies between populations from 43:10,000 in Turkey to 1.25:10,000 in Israel (Gadhia et al., 2012). Amelogenesis imperfecta is an unlikely differential diagnosis for the described cases since AI tends to affect amelogenesis in most all or all teeth – this is unlike congenital syphilis where only specific teeth are affected.

Rickets is a disorder caused by either a lack of vitamin D or phosphorus. These metabolic deficiencies affect tooth mineralization and bone development. Rickets may cause some non-severe linear or pitting-type enamel hypoplasia and in cases discoloration and enamel opacities (Zambrano et al., 2003; Davit- Beal et al., 2014). Like AI, rickets more uniformly affects the teeth. Therefore, with the severity of hypoplastic defects described and the specific tooth involvement, this is not consistent with rickets and their differential diagnosis can be ruled out. Consumption of large amounts of fluoride can lead to fluorosis, and specifically in developing dentition will cause disturbance of amelogenesis. Enamel will appear discolored (yellow to dark brown), demonstrate white opaque patches or lines, or pitted or mottled hypoplasia (Sherwood, 2010; Munñoz et al., 2013). Similar to AI and rickets, fluorosis does not affect selected teeth, and its hypoplastic effects are less severe than those described in the five cases presented here. Thus, the diagnosis of fluorosis is unlikely.

Mercury was used for medicinal purposes throughout the United States to treat syphilis and congenital syphilis (Cole et al., 1929; United States. Public Health Service. Division of Venereal Diseases. 1930). Mercury was administered in various forms but was most commonly injected intramuscularly or rubbed onto the skin. Treatments containing mercury ranged from one and a half to fourteen grams of

solution or ointment (Cole et al., 1929; Cole 1933). Since some of the malformations observed in P000707, P000679 and P000161 could be suggestive of the mercurial or syphilitic-mercuric category set by Hutchinson (1878) and Moon (1884), it is possible that mercury might have caused the dental malformations. There is no proof that any of these individuals may have had treatments and the one clinically diagnosed case (P00011R), was diagnosed at an age that would have excluded the severe effects of dental malformation if mercury were administered after her diagnosis.

Arsenic was also used to treat syphilis/congenital syphilis; however, its effects on enamel development in children with congenital syphilis are limited. Arsenical poisoning has been found to cause tooth sensitivity and tooth abrasion in children (Sunny, 2013), but nothing in the way of severity of the anomalies caused by mercury. Thus, the possibility of arsenic poisoning or treatment is an unlikely differential diagnosis.

Bismuth was introduced later than mercury and arsenic, and was used in conjunction with these to treat syphilis and congenital syphilis. Bismuth was noted to cause pigmentation of gums and the enamel, most frequently seen on the labial surfaces of the lower and upper central incisors and in prolonged acute cases, loosening of the teeth (McCarthy and Dexter 1935; Dean, 1943). The common factor observed in bismuth poisoning is that the cervical portion of the incisors was the most constant location for pigmentation (McCarthy and Dexter 1935; Dean, 1943). We see none of this pigmentation, and these individuals would have been too young to have received bismuth treatments, thus, excluding this as a differential diagnosis.

Lead was considered a possible cause in dental development, but previous studies have not found lead to cause enamel abnormalities. High levels of lead only result in a decrease in microhardness of enamel (Gerlach et al., 2002; Youravong et al., 2005) coupled with increases in abrasion and discoloration (Gil et al., 1996). Normal enamel morphology has been observed in cases where high levels of lead were present (Gerlach et al., 2002; Youravong et al., 2005).

Cadmium, although not used to treat syphilis or congenital syphilis, is known to accumulate in enamel; however, its effects on enamel development are limited in the literature. Wilson and Deeds (1939) noted that cadmium toxicity caused bleached white enamel discoloration. Since that is not observed in the discussed individuals, cadmium is unlikely diagnosis.

DISCUSSION AND CONCLUSIONS

Syphilis was a disease that caused serious problems in the United States during the late 19th and early 20th centuries, with various measures taken to control its spread (Lancet, 1930; Lancet, 1937a; Lancet, 1917; Prebble, 1938; Deporte, 1941). While various programs and legislations were initiated, treatments (including mercury) were of primary importance to reduce prevalence rates (Lancet, 1921; Lancet, 1937a; Lancet, 1939). Even though mercury was known to produce side effects, similarly to other chemotherapies (arsenic and bismuth), it was still considered the most effective, being used on its own or in combination with other pharmaceuticals (Lancet, 1937b). However, the healing nature of mercury has also been called into question due to non-systematic recording of treatments and outcomes in the 19th century, as well as misdiagnosis of the decades-long quiescence of the disease as "cured" (Zuckerman, 2016).

Individual P00011R was diagnosed in life with congenital syphilis. The only detectable manifestations of this diagnosed condition are visible in her teeth. While some of her teeth are missing, those that are present, especially the first permanent molars, are highly consistent with the anomalous condition found in cases of congenital syphilis. The dome-shaped and reduced occlusal surface of her first permanent molars is obviously a consequence of developmental disruption caused by congenital syphilis. They resemble those described by Moon (1884), but due to developmental variability, are not identical to the description.

While congenital syphilis was diagnosed and recorded only in this one individual, the other four individuals display dental changes that fit the broad range of changes described by Hutchinson (1859, 1863, 1878, 1887, 1888), and Moon (1877, 1884). Individual P219398 demonstrates tooth morphology that fits the syphilitic category described Hutchinson. The right central incisor displays a crescentic groove towards the incisal edge. Hutchinson (1863) describes that once this thin enamel has broken off, the characteristic notch is present.

The hypoplastic lesions in the dentition of individuals P000707 and P000161 are of significant severity. In P000707, enamel malformations in the maxillary central incisors begin approximately 2mm from the incisal edge and a normal groove pattern is visible on the very occlusal surface of the first permanent molars, indicating malformation in amelogenesis in the first months of the infant's life. The lateral incisors and canines demonstrate similar enamel defects but are located at different

crown heights that correspond to the differences in the timing of formation of these teeth. Crown development of first permanent molars begins perinatally, permanent central incisors begin to form at approximately 3-4 months of age, lateral incisors at approximately 10-12 months and canines at six months (Nelson & Ash, 2010). The crown of first molars is completed at about 2.5-3 years of age, both incisors at approximately 4-5 years of age, and at about 6-7 years of age for canines (Nelson & Ash, 2010). Judging from the position of hypoplastic defects (reflecting the mercurial category features by Hutchinson) these changes would occur at about 2.0-2.5 years of age.

The pathological changes in the dentition of individual P000161 follow similar interpretation for development and hypoplastic events similarly to individual P000707. However, hypoplastic defects are positioned somewhat earlier in the individual's life and ceased later than in individual P000707. The severe enamel abnormalities observed in individual P000161 are changes that are more similar to the examples of the mercurial category as described by Hutchinson. But as presented above, no record of this treatment can be attributed to this individual.

Individual P000679 has enamel defects of the maxillary central incisors that are much like the mercurial category described by Hutchinson. Whatever disturbances caused the anomalous formations of the teeth would have to have started not long after birth or from treatment to the mother - the abnormal enamel occurs much closer to the incisal margin than that seen in either individual P000707 or P000161. But again, there is no record of this treatment attributable to this individual.

In skeletal collections when medical information is not available, paleopathologists make differential diagnoses from the skeletal/dental evidence using the knowledge available at that time. During the turn of the last century and into the 20th century R. Terry, D.S. Lamb, A. Hrdlicka, T.D. Stewart and JL Angel made diagnoses of pathological conditions and anomalies on the anatomical and archaeological remains using their familiarity with the pathological understanding from their medical experience, and their knowledge of medical treatment for various diseases. For the individuals studied here, notations of the dental and skeletal observations related to or attributable to "treponemal disease" were made in the Smithsonian records from these scientists based on their observations and knowledge of the disease. In these records, differential diagnoses were often not listed, and thus in some cases, the labeling of a disease may have been from the observations, not from

the clinical record of cause of death. From what has been observed in this study, these individuals encompass a range of variation in the dental abnormalities that have occurred in syphilitic patients. The findings of this study provide examples of this range of manifestations, discussing the basis for the malformations, and provide additional insight into identifying CS in future studies.

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Chapter 5

ARTICLE 4:

A Rare Case of Congenital Syphilis and a Supernumerary Fourth Molar in an Early 20th Century African American Woman.

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(Published)

Chapter 5: Research Article 4: A Rare Case of Congenital Syphilis and a Supernumerary Fourth Molar in an Early 20th Century African American Woman.

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Contribution to the Paper	- Thought of idea for paper and its significance to literature. - Wrote paper. - Created images for paper.
Overall percentage (%)	70%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
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By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);

ii. permission is granted for the candidate in include the publication in the thesis; and

iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Maciej Henneberg
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Signature	Date 7.8.17

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Purpose of Published Article

It is well known that congenital syphilis affects odontogenesis and amelogenesis and it has now been re-established that past treatments of syphilis (mercury) can also affect these dental processes. The purpose of this paper is to demonstrate a case of an individual who was infected with congenital syphilis and possibly treated with mercury, both of which affect dental development, and presents with a supernumerary fourth molar with normal molar morphology. This highlights that the disease and its treatments impact on the development of supernumerary teeth is dependent on various factors such as the time at which disease and treatment begin, its duration, the quantity of treatment administered, and the time in which the supernumerary teeth develop.

Research Aims:

- To determine whether mercuric treatments can affect the development of supernumerary teeth.

Keywords: disease; mercury; mandibular distomolar; morphology; supplemental teeth

ABSTRACT Congenital syphilis is a disease recognized for interfering with odontogenesis, producing specific dental characteristics including Hutchinson's incisor, Moon's molar, Fournier's molar and mulberry molar, while its past treatments including mercury are known to affect amelogenesis. Supernumerary teeth, mainly associated with syndromes, are not commonly found in cases of congenital syphilis. A rare case of congenital syphilis in an individual (P000707) treated with mercury and a mandibular left fourth molar with normal morphology is presented.

Materials and Methods: During a systematic examination of 28 skeletons with treponemal disease at the Smithsonian museum in Washington, DC, a supernumerary mandibular distomolar in one individual (P000707) was revealed.

Results: P000707 was an African American female, 26 years of age. Dentition showed severe enamel hypoplasia of the maxillary and mandibular incisors, left canine, and upper first molars, consistent with the effects of treatment of congenital syphilis by mercurial compounds. Crown of the left mandibular distomolar has typical molar morphology but is smaller in size than other permanent molars. Arrangement of grooves resembles the +4 pattern, but is complex due to crenulation. Oblique x-ray revealed that the fourth molar had one root with a pulp chamber extending towards the apex, suggesting taurodontism. No other distomolar teeth were present.

Conclusions: Congenital syphilis and treatment containing mercury may not influence the development of supernumerary teeth due to: (1) the age at which the development of the fourth molar takes place, (2) the stage of the infection at the time of development and (3) the age at which treatments containing mercury are administered to patients with congenital syphilis.

Congenital syphilis is a disease caused by the transmission of Treponema pallidum, from the mother to the fetus during pregnancy or at birth. In the neonate, various systems are affected. Pathological signs appear in two stages of the disease. During the early stage, skeletal manifestations include periosteal reactions, osteochondritis, and osteomyelitis (Hira et al., 1985; McLean, 1931) while during the late stage, signs can include frontal bossing, short maxilla, high palatal arch, saddle nose, Higoumenakis's sign, diaphysitis, metaphysitis and sabre shins (Fiumara and Lessell, 1970; Rasool and Giovender, 1989). However, the disease is most recognized for interfering with tooth formation (odontogenesis), producing certain characteristic teeth including Hutchinson's incisors, Moon's molar, Fournier's molar and the mulberry molar (Fournier, 1886; Hutchinson, 1863; Karnosh, 1926; Moon, 1884). Even though these characteristic dental signs in congenital syphilis are seen in the permanent teeth (upper central incisors and first molars), which erupt approximately at 6-8 years of age, the dental abnormalities in these teeth are produced during the early stages of the disease, that is, once the infection and fever set in around the time of birth affecting initial crown formation. However, these dental abnormalities do not occur in all cases of congenital syphilis. The incidence of Hutchinson's incisors ranges from 30 to 50% (Putkonen and Paatero, 1961), while changes in first permanent molars range between 3 and 37% (Berfield, 1971).

In the past, mercury was used to treat congenital syphilis due to its antibacterial effects (Hutchinson, 1874, 1878; Warner, 1881). Even though mercury was seen to benefit infected individuals, it was also seen to produce dental abnormalities that were different from those caused by the disease. Hutchinson recognized that mercury affected amelogenesis resulting in severe enamel hypoplasia (Hutchinson, 1878). Treatments containing mercury were given to infants soon after birth, the time which enamel formation in permanent teeth begins. First permanent molars and incisors begin their formation around birth and this is when they are exposed to disease. Mercury used to treat syphilitic infants continued for months after birth, severely affecting other tooth formation, depending on the length of time the treatment was administered (Hutchinson, 1878). The abnormalities produced by congenital syphilis can be combined with the effects of treatment containing mercury (severe hypoplastic effects) (Hutchinson, 1878; Moon, 1884). Treatment with mercury was commonly used in cases of congenital syphilis until the early 20th century. The whole suite of changes

caused by congenital syphilis and treatments containing mercury have been discussed in detail (Ioannou et al., 2016).

Supernumerary teeth have been associated with various syndromes and disorders including Down's and Gardner's, cleidocranial dysostosis, and cleft lip and palate (Kumar and Gopal, 2013; Menezes and Vieira, 2008; Millhon and Stafne, 1941; Panjwani et al., 2011; Sandler, 1951); however, they have not been described in detail in cases of congenital syphilis. Supernumerary teeth are observed when more than 20 deciduous or 32 permanent teeth are present in an individual. They can erupt, remain unerupted, or become impacted (Kara et al., 2012; Mali et al., 2012). Their appearance can be unilateral, bilateral, as a single tooth or in multiples (Brinkmann et al., 2012; Cavalcanti et al., 2011; Harris and Clark, 2008). The morphology of supernumerary teeth can vary in each individual from normal in shape and size, normal shape and reduced in size, conical in shape and abnormal in shape and reduced in size (Harris and Clark, 2008; Kumar and Gopal, 2013; Rahnama et al., 2014).

This paper presents a case of congenital syphilis in an African American woman dating from the early 20th century with a fourth mandibular molar. A focus will be made on the development of the fourth molar in the presence of a disease, which primarily affects dental development.

MATERIALS AND METHODS

During a systematic examination of 28 skeletons held at the Smithsonian museum in Washington, DC, whose documentation stated that they had "treponemal or treponemal congenital" disease, a case of a supernumerary mandibular distomolar in one individual (P000707) was revealed. This individual was an African American female, who was born in 1903 and died of pulmonary tuberculosis in 1929, at 26 years of age. Occlusal and oblique X-rays of the mandible were taken using a Frankenstein unit to see whether a fourth molar was present on the right side. Chemical analysis was performed to detect any levels of mercury. A Bruker Tracer III-V handheld analyser was used on hypoplastic portions of the central and lateral incisors. The initial analysis used an all elements setting. The settings for the following test were elevated to (0.001" Cu, 0.001" Ti, 0.012" Al filter at 40 keV/16 micro amps for 300 seconds, without vacuum) (Ioannou et al., In press).

RESULTS

All maxillary permanent teeth were present, the central and lateral incisors, canines, premolars and all three molars. The enamel of the central incisors from the incisal third to the middle third of the crown appears mottled and thin (Figure 1). The incisal third of the lateral incisors and left canine demonstrate the same mottled appearance and pitted enamel hypoplasia. Deep pits are apparent toward the middle third of the crown of the central incisors and incisal third of the lateral incisors and canines. In addition to signs caused by mercury on the incisors and canines, other teeth display isolated hypoplastic pits. Maxillary premolars are not affected. First permanent molars have abnormal occlusal surfaces, with cusps reduced in size and pitting hypoplasia, which is also consistent with the side effects of mercury (Figure 2). Diseased enamel is clearly demarcated from the healthy enamel on the cervical third of the crown. The morphology of the second and third permanent maxillary molars is normal with normal groove patterns, but there is some enamel pitting on the occlusal surface.

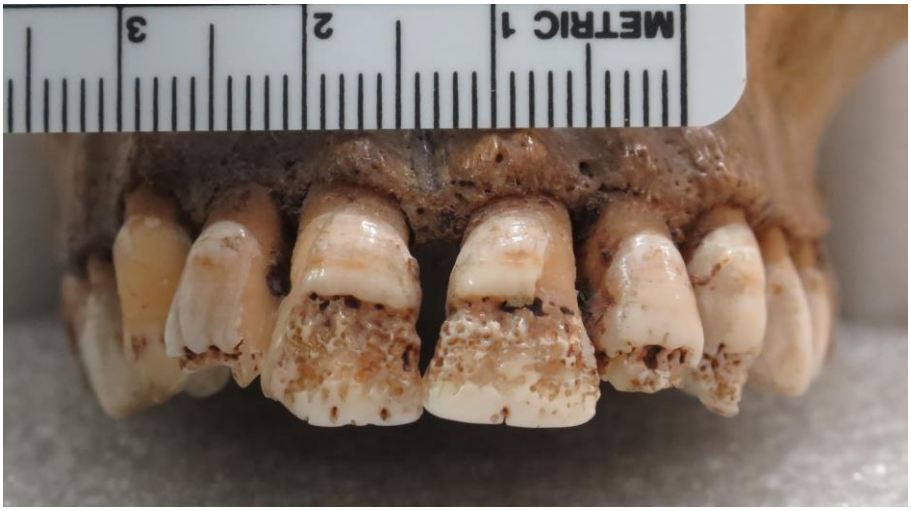

Figure 1. The maxillary central and lateral incisors and left canine display hypoplastic enamel seen in patients with congenital syphilis treated with mercury. Signs include thin enamel, pitted enamel hypoplasia (in some places very deep), and distinct demarcation separating diseased from healthy enamel.

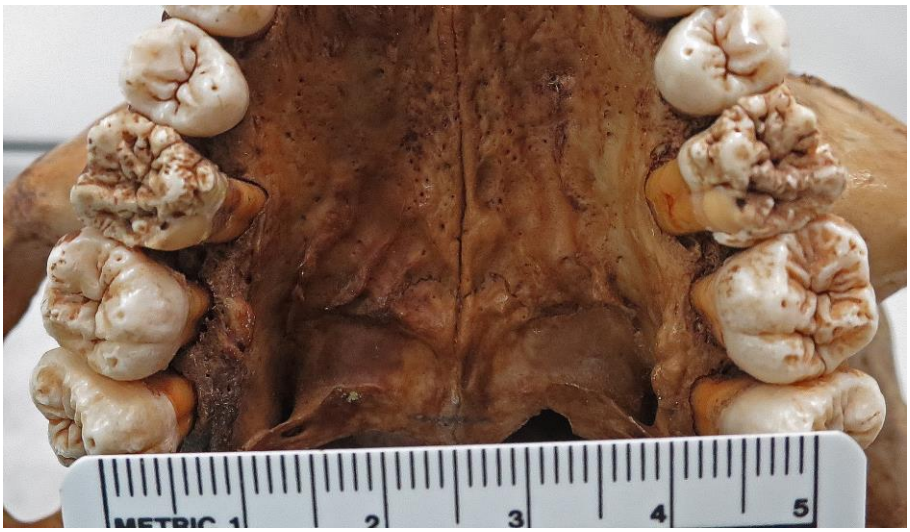

Figure 2. Occlusal view of the maxilla. First permanent molars have abnormal surfaces with small cusps and pitting hypoplasia.

Mandibular permanent teeth include the central and lateral incisors, left and right canines, first and second premolars, second and third molars and the distomolar. The first permanent molars were lost ante-mortem, possibly by extraction and their alveoli are completely healed. All mandibular incisors have mottled enamel (Figure 3). The left and right second molars and the third left molar do not display severe hypoplasia, save for minor pitting. Their occlusal sur-faces are crenulated. The third permanent molar on the right side is represented by its roots only. The crown has broken off probably after its destruction by dental caries. On the left side, in the mandible, there is a fully erupted fourth molar (distomolar). Its crown has normal molar morphology, but is smaller in size in comparison to the other permanent molars present. The arrangement of groves resembles the +4 pattern. However, the groove pattern is complex be-cause of crenulation. Entoconid, metaconid, hypoconid and protoconid are present, and it appears that there may be a narrow metaconulid, but crenulations make it difficult to determine (Figure 4). An oblique X-ray of the mandible shows that the distomolar only has one root with a large pulp chamber extending far down towards its apex, suggesting a taurodont condition (Figure 5). The third molar on the left is large and crowded between the distomolar and adjacent second molar. Its crown is rotated approximately 10 degrees and tilted mesially. Inspection of the X-ray does not reveal the presence of the antimeric distomolar (Figure 6). All molar crowns appear crenulated.

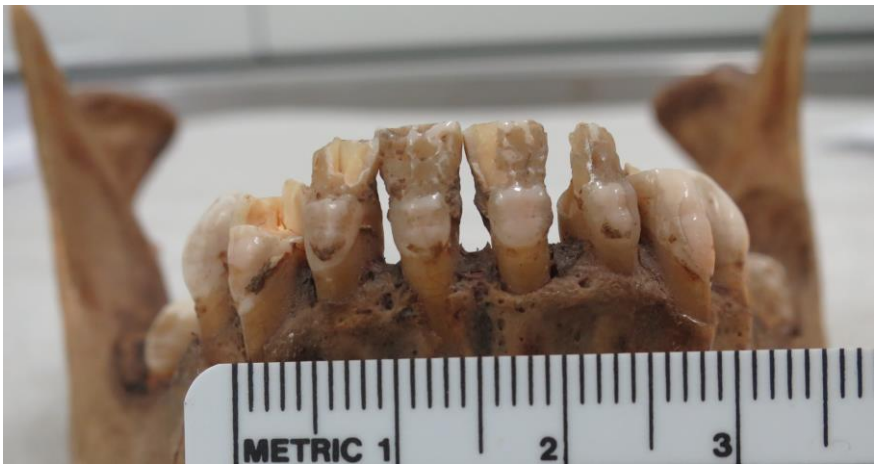

Figure 3. The anterior view of the mandibular incisors displaying enamel defects.

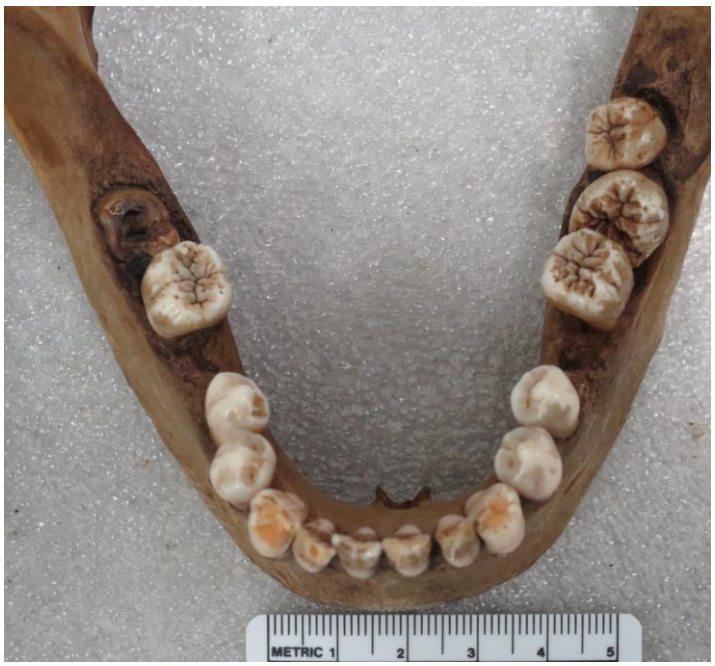

Figure 4. Occlusal surface of the mandible. The first permanent molars were lost ante-mortem. Both second molars, the left third molar and left fourth molar are present. The right third molar is represented by its root only. The fourth molar displays normal molar morphology.

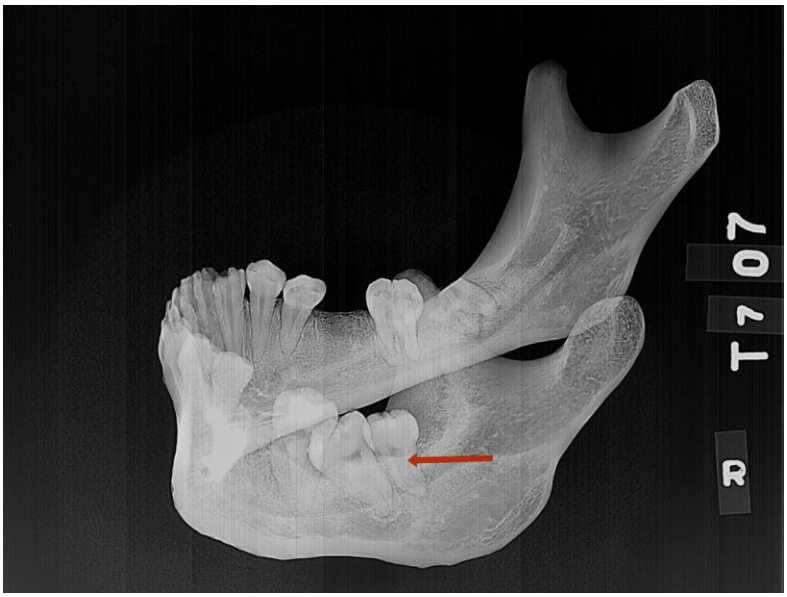

Figure 5. Oblique X-ray image of the mandible shows that the distomolar has only one root and that there is no antimeric distomolar. Note the large extent of the pulp cavity in the distomolar, suggesting it is a taurodont molar.

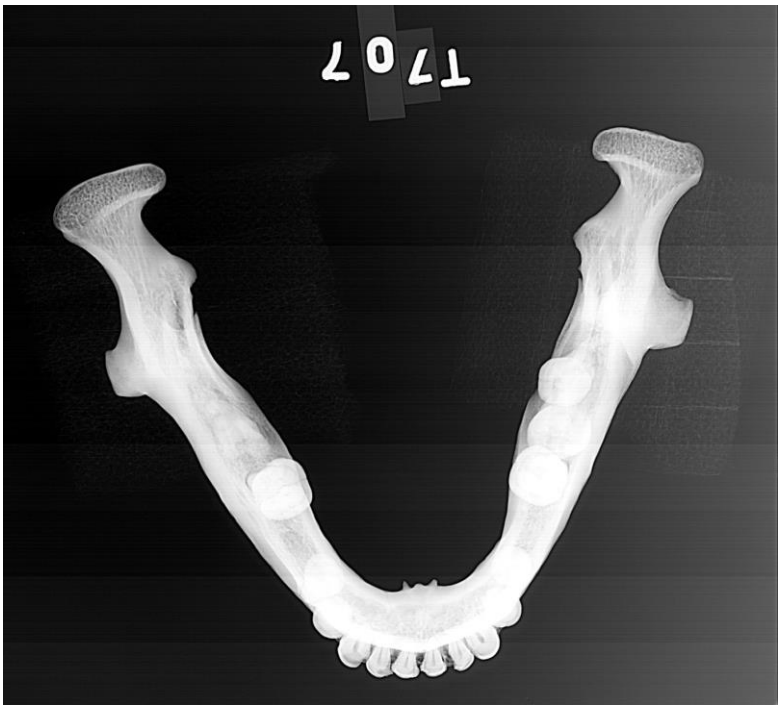

Figure 6. X-ray of the occlusal view of the mandible does not show any evidence of a right fourth molar.

In the post cranial skeleton, limited areas of nodular periosteal reaction were observed on the long bones including the right tibia, fibula, humeri, radius, ulnae, and femora, as well as the lateral surface of the left ilium. The left femur had lytic destruction along the lateral border of the head in the anterior aspect, “classic” striated periosteal reaction is not noticeable.

DISCUSSION

Here we present a case of congenital syphilis with a supernumerary distomolar in an African American woman. Although this condition is very rare during this time, it is probable, as one other case has been documented (Jacobi et al., 1992). However, in this case, the dental abnormalities in P000707 indicate that she was treated with mercury soon after birth. Changes in the morphology of the central maxillary incisors and left canine have enamel malformations that are compatible with dental abnormalities observed by Hutchinson in patients with congenital syphilis administered treatment containing mercury (Figure 7). Crown formation of the central permanent incisors begins at approximately three to four months postnatally and is complete at approximately 4 to 5 years of age (Nelson and Ash Jr, 2010). The specific changes in enamel caused by mercury are seen in one third of the crown, therefore, treatment would have started in the middle of the first year of life and ceased at approximately 2 years of age. Similarly, severe enamel malformations are observed on the lateral incisors and canines that start forming later than the central incisors.

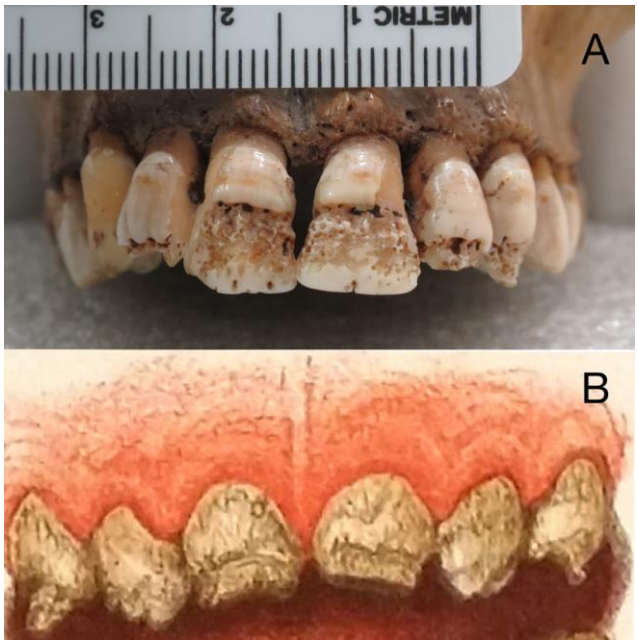

Figure 7. (A) Anterior teeth of P000707 (B) Patient treated with mercury as presented by Hutchinson in 1878 (16 year old boy). Both (A) and (B) display simi-larities in enamel abnormalities that occur as a result of treatments containing mercury. Mercury would have been administered at a somewhat older age in P000707 than in Hutchinson's patient. Hutchinson, (1878) p. 53, Plate VI, Items I (A).

The morphology of the maxillary first permanent molars demonstrates a normal groove pattern to-wards the mesial end of the crown, while the rest of crowns' occlusal surfaces are reduced in size and hypoplastic. As the incisal third of the central incisors and a portion of the occlusal surface of the first permanent molars appears to be normal, the rest of the crown is affected, which may be an indication that the onset of the infection was late in relation to tooth development.

Congenital syphilis is known to produce specific dental abnormalities characteristic of the disease. However, it has been noted that in some cases of con-genital syphilis, the classic dental changes that are usually observed such as Hutchinson incisors, Moon's molar and Fournier's molars do not occur (Švejda, 1952). Hutchinson also observed and de-scribed certain dental abnormalities that occurred as an effect of treatments containing mercury (Hutchinson, 1878). The dental abnormalities produced by the disease itself and treatments containing mercury were so distinct that Hutchinson deemed it worthy to document and illustrate both as

separate entities. It is worth noting that the crescentic notch that occurs in the maxillary central incisors of con-genital syphilis patients is not observable if they were treated with mercury (Hutchinson, 1878). The features observed in this P000707 are typical signs of teeth treated with mercury in patients with congenital syphilis (Hutchinson, 1878; Ioannou et al., 2016).

While the results of the chemical analysis detected no levels of mercury, this neither confirms nor disproves that mercury was administered to this individual. Various explanations could be considered. It is possible that the low levels of mercury in the enamel could not be detected by the equipment. Another possible explanation for the lack of mercury detected could be due to the quick turnover rate of mercury in the body. The half-life of mercury ranges from 58 days for elemental mercury, 1-2 months for mercuric mercury (e.g. HgCl2), to 70-80 days for methylmercury (National Research Council (US) 2000). Taking into account that this individual was treated with mercury for congenital syphilis in the early stages of life and died at 26 years of age, it is not abnormal to find extremely low levels of mercury. As indicated by Hutchinson, if 648 mg (10 grains) of mercury were introduced in a body of a young individual, after 20 years only a minute quantity of mercury would remain (2.13*10-25mg). Thus, it is more likely that a majority of the mercury would be cleared out, making it undetectable.

Other elements considered in the differential diagnosis include lead, zinc, copper and cadmium. High levels of lead can cause a decrease in microhardness of enamel (Gerlach et al, 2002) but cannot cause malformations of the enamel (Gerlach et al, 2002; Youravong et al, 2005). Fosse and Berg-Justesen (1977, 1978, 1978) and Tvinnereim et al. (1999) examined concentrations of zinc, copper, and cadmium in teeth and bone in humans and mice and recorded the difference in concentration of these elements between enamel, dentin, and bone, but did not record any changes or malformations in enamel development.

In relation to changes on the post cranial skeleton of P000707, since the individual died of tuberculosis, it is difficult to say which of those described pathological changes could be due to treponemal infection.

The crown morphology of the distomolar is nor-mal, unaffected by the disease, nor by treatments containing mercury. The smaller size of the distomolar is unlikely to be caused by congenital syphilis. Clinical studies have shown that distomolars can demonstrate normal molar morphology, have as many as three to seven cusps and be reduced in size, in comparison to the other permanent molars (Asrani et al., 2006; Ceperuelo et al., 2015; Kumar and Gopal, 2013; Ohata et al., 2013; Shahzad and Roth, 2012). The normal crown morphology in this case may be due to the time at which the development of the fourth molar began. It is the early stage of the disease that affects dental development. It occurs soon after birth and becomes the tertiary stage after several weeks. Tertiary syphilis does not affect tooth development. The development of the third permanent molar begins at approximately 7 to 10 years of age and the tooth is fully erupted between the ages of 17 and early 20s (Liversidge, 2015). It is possible that the fourth distomolar could have developed at the same age or even later. If the fourth molar had developed soon after the third molar, P000707 would have been in the tertiary stage of the disease; therefore, the disease could be asymptomatic and would not have affected amelogenesis or odontogenesis of the supernumerary fourth molar. However, it is possible that the fourth molar developed sooner. Studies have shown that fourth molars can appear between the ages of 11 and 16 years (Delgado et al., 2014; Menardía-Pejuan et al., 2000; Orhana et al., 2006; Vlaykov et al., 2015).

It also appears common that distomolars demonstrate a single root, unlike the multiple roots observed in the other permanent molars (Ceperuelo et al., 2015; Ohata et al., 2013; Rahnama et al., 2014). However, root formation can vary among individuals (complete with closed apex or incomplete) (Ceperuelo et al., 2015; Kokten et al., 2003; Ohata et al., 2013). Since the distomolar in this case is taurodontic, it is not possible to determine whether it had fused multiple roots or a single root because no separate root canals can be seen. At least formally, the root is a single unit. The cause of taurodontism is unclear. It has been associated with various syndromes (Andersson et al., 2013; Keeler, 1973; Rajić and Mestrović, 1998) and multiple theories have been suggested in the literature (Alvesalo and Varrela, 1991; Witkop Jr et al., 1988). In this case, it should be considered that the proportions of the root to crown size and pulp cavity to root canal volumes may have developed abnormally in the supernumerary, thus not normal, tooth without any special causes.

The development of extra teeth is not fully under-stood, although multiple theories have been suggested such as hyperactivity within the dental lamina, and dichotomy of the tooth germ and these may be linked to genetic factors (Kokten et al., 2003; Kumar and Gopal, 2013). For instance, Martínez-González et al. (2012) found them in 0.96%, Shahzad and Roth (2012) in 2.2% and Kara et al. (2012) in 0.33%. It has been found that supernumerary molars were also more prevalent in African Americans (6.4%), than in European Americans (0.9%) (Shahzad and Roth, 2012). It has been suggested that African Americans exhibit extra teeth more often than European Americans (Harris and Clark, 2008), which may be related to African Americans having larger dental arches and greater crown and root dimensions. This would in-crease a probability of the appearance of the distomolar in an African American suffering from congenital syphilis.

CONCLUSION

A systemic infection such as congenital syphilis and its treatment with mercury may not influence the development of supernumerary teeth due to: (1) the age at which the development of the fourth molar takes place, (2) the stage of the infection at the time of development and (3) the age at which treatments containing mercury are administered to patients with congenital syphilis.

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Chapter 6

ARTICLE 5:

Dental signs attributed to congenital syphilis and its treatments in the Hamann-Todd Skeletal Collection

Stella Ioannou and Maciej Henneberg

(Submitted)

Chapter 6: Research Article 5: Dental signs attributed to congenital syphilis and its treatments in the Hamann-Todd Skeletal Collection

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Name of Principal Author (Candidate)	Stella Ioannou
Contribution to the Paper	- Came up with concept of paper. - Collected data at Cleveland Museum of Natural History. - Wrote entire paper. - Took photographs for paper.
Overall percentage (%)	80%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 11/9/17

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Maciej Henneberg
Contribution to the Paper	- Examined photographs and provided feedback. - Edited paper and provided feedback.
Signature	Date 15.09.17

Purpose of Article

As discussed in the introduction and first manuscript, mercury was used to treat congenital syphilis prior to the introduction of penicillin, and had a distinct effect on dental development, producing dental abnormalities significantly different from those caused by the disease alone. The previous manuscript indicated that mercury was used to combat syphilis/congenital syphilis in the United States, and that levels of mercury administered were significantly higher than what is accepted by current safety standards today. As such, the toxicity of mercury would have interfered with various developmental process including dental development in American children. Therefore, the purpose of this manuscript is to apply dental observations seen in children affected by treatments containing mercury to individuals from the Hamann-Todd skeletal collection at the Cleveland Museum of Natural History, whose cause of death was syphilis or related to syphilis. The main reason for this, is that it is possible that dental signs associated with mercury may not have been observed or documented in the records, as they have not been considered in any form of study (paleopathology, archaeology etc).

Research Aims:

- To search for dental signs and variations associated with congenital syphilis and its treatments to determine the range of variations.

Abstract

INTRODUCTION

Syphilis in the United States during the 1800s and 1900s had a high prevalence rate causing great concern to health officials. Various measures were taken to control its spread. Mercuric treatments were used up until the introduction of penicillin.

STUDY AIM

The aim of this paper is to determine whether dental abnormalities related to congenital syphilis in individuals who died of syphilis or syphilis-related causes, in the Hamman Todd Osteological Collection, occur and whether mercurial treatment was effective.

MATERIALS AND METHODS

Hutchinson, Moon and Fournier's works were analyzed to determine dental abnormalities associated with congenital syphilis and its treatments and used as criteria. Hillson et al. (AJPA,107:25-40) standardized method of description of dental changes was used. In the Hamman Todd Osteological Collection in Cleveland, Ohio, 102 individuals had cause of death recorded in the catalogue as syphilis or lues, and 69 had causes of death relating to syphilis which included paresis (53), aortic insufficiency (15) and pericarditis (1). Thus altogether 171 individuals were studied. Dentition was examined to determine if dental abnormalities associated with congenital syphilis and its treatments were present in individuals not recorded as having congenital syphilis. Crania were examined for any osteological changes.

RESULTS

One individual (2266) demonstrated dental malformations possibly related to the congenital disease itself, while three demonstrated dental abnormalities associated with mercuric treatments in childhood (2118, 2263 and 3097). No remarkable bone pathologies were evident on any skull.

CONCLUSION

The use of pre-penicillin treatment of congenital syphilis may have been effective to maintain health into adulthood but not always in eradicating the infection. Effects of

mercury on enamel formation and bone changes, need to be considered when making a differential diagnosis of syphilis/congenital syphilis.

Keywords: congenital syphilis, hypoplasia, mercury, molars, United States

Introduction

Syphilis in the United States was a highly prevalent disease that caused public health concerns during the 1800s and early 1900s, with reportable cases increasing from 145.3 (per 100 000) in 1920 to 359.7 in 1940 (United States Census Bureau 1999). Various actions were taken by some states to contain the disease, including the introduction of public programs and legislations. Programs ranged from dark-field microscopy to free, pay, and part-pay clinics (Lancet 1937a). To control the congenital form of the disease, legislation included compulsory premarital and prenatal blood tests. Those applying for a marriage license were required to have a premarital examination for syphilis and submit a certificate from a physician stating whether they were free from the disease or whether it was communicable if present (Lancet 1938a; Prebble 1938; Lancet 1940a; DePorte 1941). The restrictions by law varied between states. The prenatal examination required a pregnant woman to be tested for syphilis either during pregnancy or at the time of delivery. The birth certificate of the infant had to show whether a blood test for syphilis was made, the date of the test, and the results (Lancet 1938a; Lancet 1940b; DePorte 1941). Again, the conditions of the laws varied between states. Other control measures were also taken to contain the disease. Federal grants increased yearly to provide treatment and education to infected individuals and the general public (Lancet 1939). The number of treatment centers for syphilis reporting to public health services through state health departments increased from 713 in 1936 to 1773 in 1939 (Lancet 1939). Various methods were also employed to inform the public of syphilis: the daily press, radio, popular magazines, journals, lectures, posters, sound films, and pamphlets (Prebble 1938).

Chemotherapies including mercury, arsenic and bismuth were used in the United States to treat syphilis, including in Cleveland, Ohio (Cole et al. 1929; Conrad and McCann 1922; Lancet 1922), while mercury, arsphenamine, and potassium iodide were used to treat congenital syphilis (United States. Public Health Service. Division of Venereal Diseases 1930). In the United States, the most common method of administering mercury was by injection intramuscularly or by inunction/rubs (ointments) (Wile and Elliott 1917; Conrad and McCann 1922; United States. Public Health Service. Division of Venereal Diseases 1930; Cannon and Karelitz 1931; Lancet 1937b).

The efficacy of mercury as a form of treatment for syphilis has been debated (Weatherill 1833; Goldwater 1972; O'Shea 1990; Swiderski 2008; Zuckerman 2016) even though mercury is known to be spirilocidal, reducing the number of spirochetes in cutaneous lesions (Keogh 1913; O'Shea 1990), and inducing a Jarisch-Herxheimer reaction (Holmes 1984). Some physicians found mercury to be effective in producing negative Wassermann reactions (Conrad and McCann 1922; Wakerlin 1934), and in resolving signs and symptoms of the congenital syphilis after treatment (Lancet, 1858; Lancet, 1881; Lancet, 1885; Fedtchenko, 1898; Hutchinson 1888). However, there are those who argue that there are various issues that need to be considered, and there is no sufficient evidence to support the effectiveness of mercury. Some of the issues raised include that there are no in vitro studies to support mercury's efficacy (O'Shea 1990); that prior to the discovery of *Treponema pallidum,* it was difficult to diagnose syphilis, so those who were treated with mercury were presumed to have syphilis; mercury was used to treat skin lesions of the primary and secondary stage of the disease which would often clear in a few weeks without any treatment, appearing 'cured' rather than considering the nature of disease, and mercury was known to cause severe side effects (Goldwater 1972; Swiderski 2008). Without in vitro studies, it is difficult to establish whether mercury was an effective form of treatment for syphilis. Even after the introduction of other treatments such as arsenic and bismuth, mercury was still used on its own and in combination with these treatments (Wakerlin 1934; Norris et al. 1939; United States. Public Health Service. Division of Venereal Diseases 1930), producing mixed results.

Venereal syphilis manifests in three stages, primary, secondary and tertiary. While skeletal involvement is rare during the primary stage (Ehrlich and Kricun 1976), and minor during the secondary stage (periosteal lesions, osteitis) (Ortner 2003; Powell and Cook 2005), these are not diagnostic of the disease. Diagnostic skeletal lesions occur during the tertiary stage of the disease. They are considered to be the caries sicca sequence of calvarial changes, and nodes and expansion with superficial cavitation in long bones (Hackett 1975). However, it should be noted that not all individuals infected with syphilis will develop bony changes, with frequencies of such changes occurring between 10% and 25% (Steinbock 1976) and 2%-13% (Rothschild 2005). In congenital syphilis, most cases present with some form of bone manifestations during the early and late stages of the disease, however, in

approximately 50% to 75% of cases, the bony changes will be minimal or will heal, thus not appearing in skeletal remains (Steinbock 1976). Skull involvement occurs in approximately 5% to 10% (Steinbock 1976), also not making it a dependable indicator of the disease.

In congenital syphilis, lesions will vary depending on the stage of the disease (early or late). Metaphysitis, periostitis, (Rosen and Solomon 1976; Sachdev et al. 1982; Rasool and Govender 1989), osteochondritis, osteomyelitis (Jaffe 1972), and diaphystitis (Rasool and Govender 1989) have been observed during the early stages of the disease. Signs observed during the late stage include frontal bossing, short maxilla, high arch palate, saddle nose (destruction of nasal bridge and cartilage), Higouménakis' sign (sternoclavicular thickening), flaring scapulae, Hutchinson's teeth, Moon's molars and Fournier's molars (Yang 1940; Fiumara and Lessell 1970; 1983).

Dental abnormalities observed in congenital syphilis are those produced by the disease itself, and those produced by treatments containing mercury. Those considered characteristic of the disease include Hutchinson's incisor (notched), and Moon's dome shaped molar (Hutchinson 1859; 1863; Moon 1877; Fiumara and Lessell 1970; Hillson et al. 1998). Other distinct dental signs associated with congenital syphilis in the permanent dentition include sharp grove-like hypoplastic defects around the cups of the permanent canines, and Fournier's molars which demonstrate a plane-form hypoplastic defect cutting into the base of the cusps (Hillson et al. 1998). These dental changes are the result of inflictions caused by the early stage of the disease. While Fournier's molars have been observed in some cases of congenital syphilis, they are not considered to be characteristic of the disease, as they are said to occur in other growth and development conditions (Harper et al. 2011). Dental abnormalities produced by mercury are distinct from those produced by the disease itself (Hutchinson 1878; Moon 1884; Ioannou et al. 2016). The first permanent molars are considered the "test teeth" in reference to mercury, unlike the upper central incisors, which are the "test teeth" for the disease itself (Hutchinson 1878; Hutchinson 1888), although other teeth may also be affected by mercury. Rather than affecting the entire shape of a tooth during odontogenesis, as the disease does, mercury disturbs only the formation of enamel (amelogenesis). In severe cases, mercury can affect dentine and cause molars to appear dwarfed (Hutchinson 1878). Molars affected by mercury display deficiencies in enamel on the occlusal surface and to varying degrees, appear

rugged, pitted and dirty (Hutchinson 1878). In some cases, dentine is observed with multiple discolored tubercles or spines (Hutchinson 1878). The whole occlusal surface can be affected or in patches. The incisors and canines are also affected by mercury. They display linear enamel hypoplasia that crosses all incisors and canines at the same level corresponding to crown formation times. Enamel between the linear enamel hypoplasia and the incisal edge or tip of the crown is deficient. In cases where mercury has been used to treat congenital syphilis, the crescentic notch is never replicated (Hutchinson 1878). However, dental abnormalities produced by both the disease and its treatment have been observed in the same individual and the crescentic notch is present (Hutchinson 1878).

The Hamman-Todd collection at the Cleveland Museum of Natural History in Cleveland, Ohio, was visited in 2016 to examine dentitions and skulls of all individuals with a cause of death recorded as syphilis or relating to syphilis. The purpose of this paper is to describe dental changes of individuals whose cause of death is explicitly given as syphilis or syphilis-related. Since there is evidence in the literature that mercury was used to treat syphilis in the United States, including Cleveland, Ohio, we are interested to see whether there is any dental evidence that mercury was used and whether or not it was effective.

Materials and Methods

The original works of Hutchinson, Moon and Fournier were analyzed to determine the dental abnormalities associated with congenital syphilis and treatments containing mercury (Hutchinson 1859; 1863; 1874; 1878; 1887; 1888; Moon 1877; 1884; Fournier 1886). The criteria used to identify dental stigmata associated with congenital syphilis include Hutchinson's clinical observations of teeth in patients with congenital syphilis, Moon and Fournier's description of the first permanent molars, and Hillson and colleagues (1998) summary of characteristic and distinct deformities in the permanent dentition. To identify dental abnormalities associated with treatments containing mercury, Hutchinson's descriptions and illustrations of patients with congenital syphilis treated with mercury were used for comparison.

The Hamman Todd collection in Cleveland, Ohio consists of unclaimed individuals, who died between 1912 and 1928. Out of the 3726 cadaver-derived human skeletons,

a total of 171 individuals who died from syphilis or syphilis related issues were examined. Out of 171 individuals, 102 were recorded in the catalogue as having a cause of death of syphilis or lues, while 69 were recorded as having a cause of death related to syphilis. The causes of death related to syphilis included paresis (53), aortic insufficiency (15) and pericarditis (1). It is possible that these recorded deaths were medically diagnosed as Dr. Wingate Todd (who began the collection), documented age at death, sex, stock, cause of death, pathologies, and if possible, a case history of each individual (Krogman, 1939). However, this is difficult to determine due to the lack of medical documentation, and as such signs of congenital syphilis and its treatments sought for.

Dentitions of the 171 individuals were examined to determine whether certain dental abnormalities associated with congenital syphilis and its treatments were present. Although the notes of causes of death did not distinguish between acquired and congenital syphilis, it can be expected that congenitally infected individuals would be among those dying later in life of syphilis, lues or related causes. Four individuals were recorded in the catalogue as having congenital syphilis but were no longer in the collection (were repatriated, returned to families), therefore were excluded from this study.

The dentitions were studied to determine: (1) whether any individuals suffered from congenital syphilis during childhood which had not been documented and (2) types of dental stigmata that may be present related to congenital syphilis or its treatments. Since it is only recently, that dental signs associated with treatments containing mercury have been applied to paleopathological cases (Ioannou et al. 2015; 2016), this was an element that wanted to be explored in this collection. The cranial skeleton of individuals displaying dental abnormalities was then examined for any bone pathologies. To identify the stages of the caries sicca sequence, Hackett's (1975) standardized method was used.

Results

The average ages at death for the individuals in the sample of 171 who died of syphilis are as follows: black adult males (46.5yrs), black adult females (39.2yrs), black females including one 13-year-old (37.8yrs), white adult males (52.6yrs), and white adult females (53.9yrs). These results fall within the average age at death range of the

entire population for their respective groups in the data collected between 1910 and 1925 by the United States Census Bureau (1999) (Table. 1).

Table 1. Newborn life expectancy between 1910-1925 in death registration states of Unites States of America and average age at death of individuals having died from syphilis or syphilis related causes in the Hamman Todd Osteological Collection.

United States Census Bureau newborn life expectancy between 1910 and 1925 in death registration states in the United States.			Age at death in Hamman Todd Osteological Collection		
	1925	1910	Average	SD	Min-Max
Black Males	33.8	44.9	46.5	12.9	22-84
Black Females	37.5	46.7	39.2	11.7	22-73
White Males	48.6	59.3	52.6	11.4	33-80
White Females	52.0	62.4	53.9	15.9	28-77

In the 171 individuals, no remarkable bone pathologies were evident on any skull in the sample

Dental Observations of four individuals from Hamman-Todd Collection

Four out of 171 individuals demonstrated dental malformations, 2266, 2118, 2263 and 3097.

Individual 2266

Individual 2266 is a 44-year-old African American male. Cause of death was aortic insufficiency. All teeth are present except the left second premolar and the right first permanent molar. The upper central incisors demonstrate uneven incisal edges (Fig. 1). Slight concavities are evident on the central portion of the incisal edge of the upper right central incisor, and the distal portion of the incisal edge of the left central incisor. The crown surfaces of central incisors have shallow vertical grooves in the enamel, both located on the distal portion. The upper lateral incisors are peg like in shape and display isolated pits. No hypoplasia is observed in the mandibular teeth. No bone pathologies were observed.

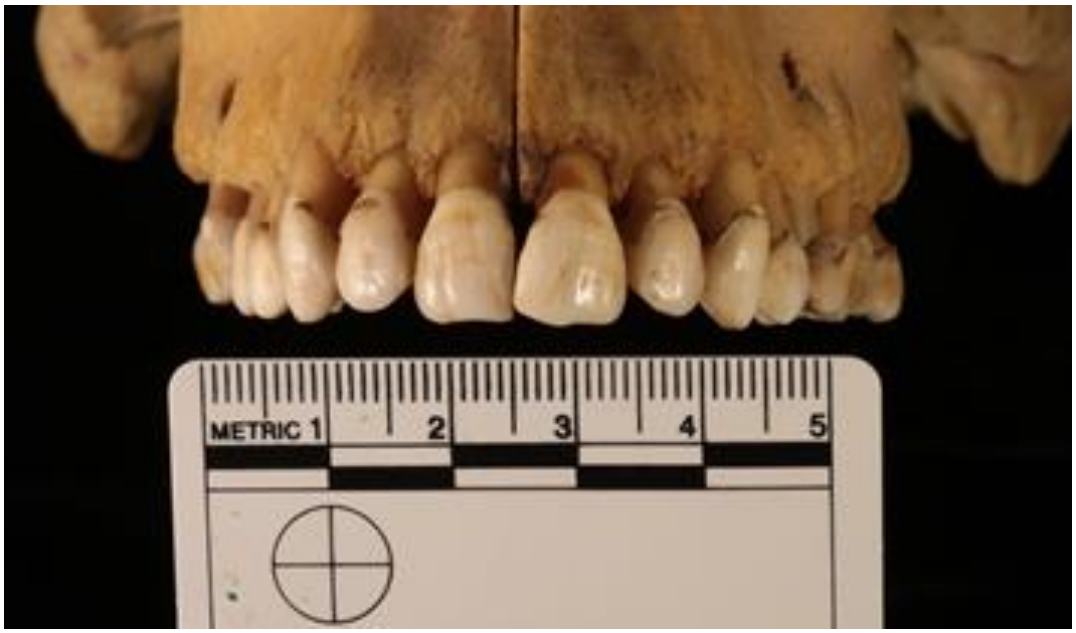

Figure 1. Slight concavities are evident on the central portion of the incisal edge of the upper right central incisor, and the distal portion of the incisal edge of the left central incisor.

Individual 2118

2118 is a 13- year-old African American female. Cause of death was pericarditis. Skull morphology was normal. Permanent teeth include the maxillary central incisors, right lateral incisor, both canines (not fully erupted), first and second premolars (right second premolar not fully erupted), and first permanent molars. Mandibular teeth include all incisors, both canines, right first premolar, right and left second premolars (still in crypt) and first permanent molars. The second permanent molars are still in the crypt. The crowns of the upper central incisors, up to the second third of the crown, are severely hypoplastic (pitting and linear hypoplasia) (Fig. 2). The same type of hypoplasia can be seen on the incisal third of the right lateral incisor from the middle third to the tip of the crowns of the canines. The occlusal surface of the right upper permanent molar is reduced, and hypoplastic (Fig. 3). Pitting is also observed on the occlusal surface. Severe linear and pitting hypoplasia is also observed on the mandibular anterior teeth (Fig. 4). The mandibular first permanent molars resemble the maxillary right first permanent molar (Fig. 5).

Crowns of the upper central incisors, right lateral incisor, and tips of canines are severely hypoplastic, possibly caused by mercury. The maxilla bone in the region above the incisors shows resorptive remodeling.

Figure. 2. Crowns of the upper central incisors, right lateral incisor, and tips of canines are severely hypoplastic, likely caused by mercury.

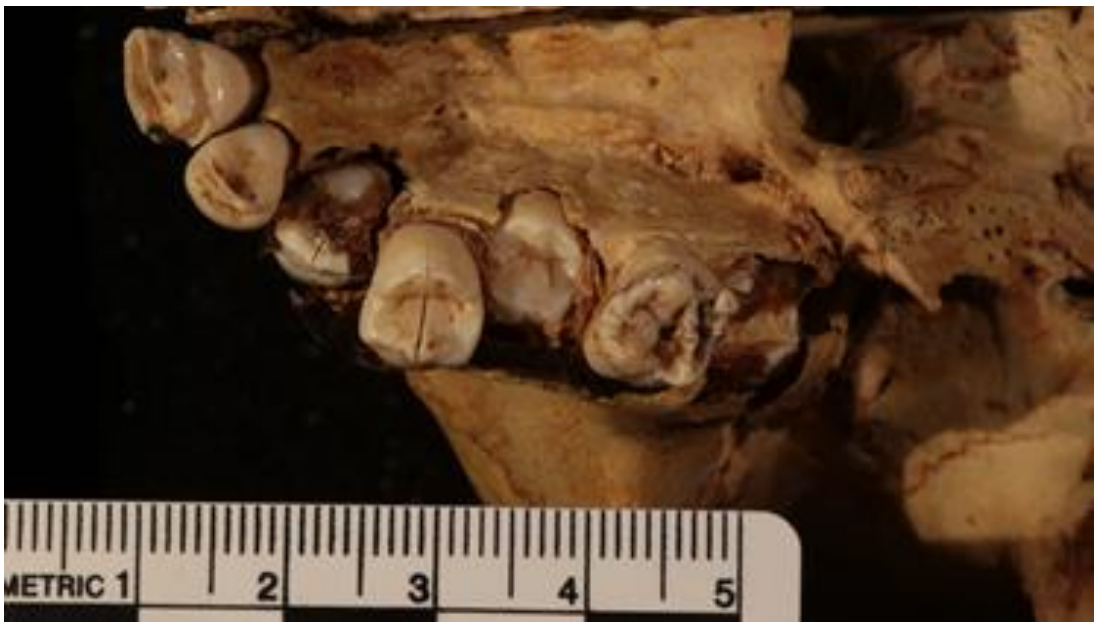

Figure. 3. Occlusal surface of the upper right permanent molar is reduced in size and hypoplastic.

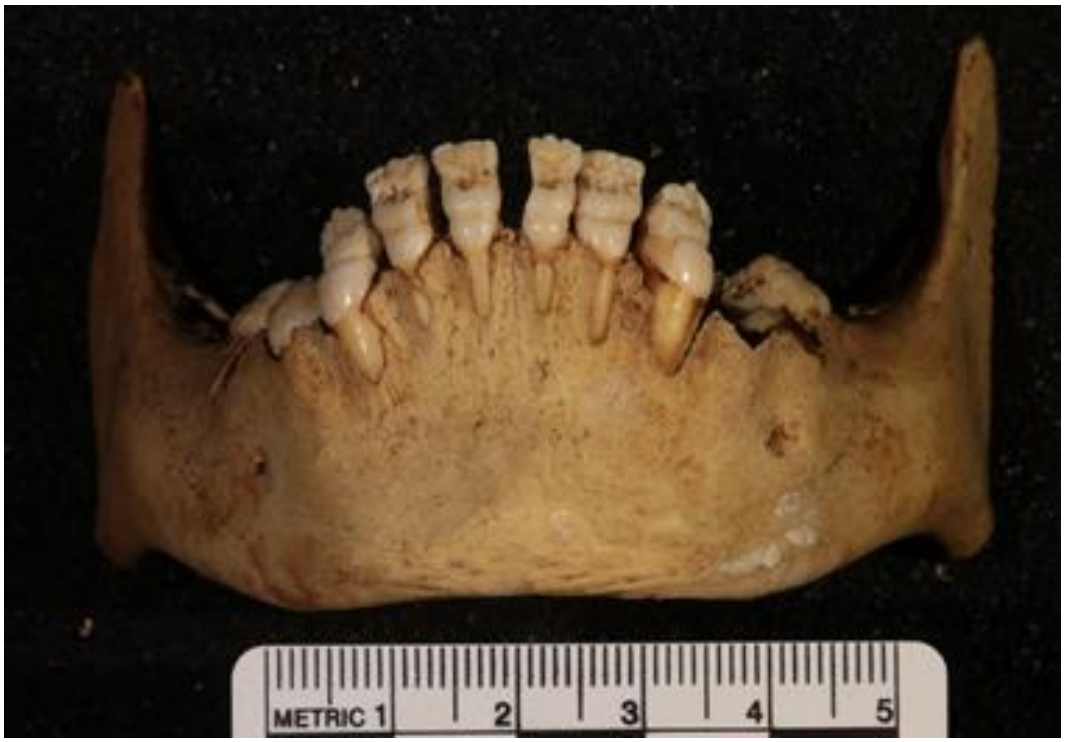

Figure. 4. All anterior teeth demonstrate pitting and linear hypoplasia. Both pitting and linear enamel hypoplasia cross all anterior teeth at the same levels.

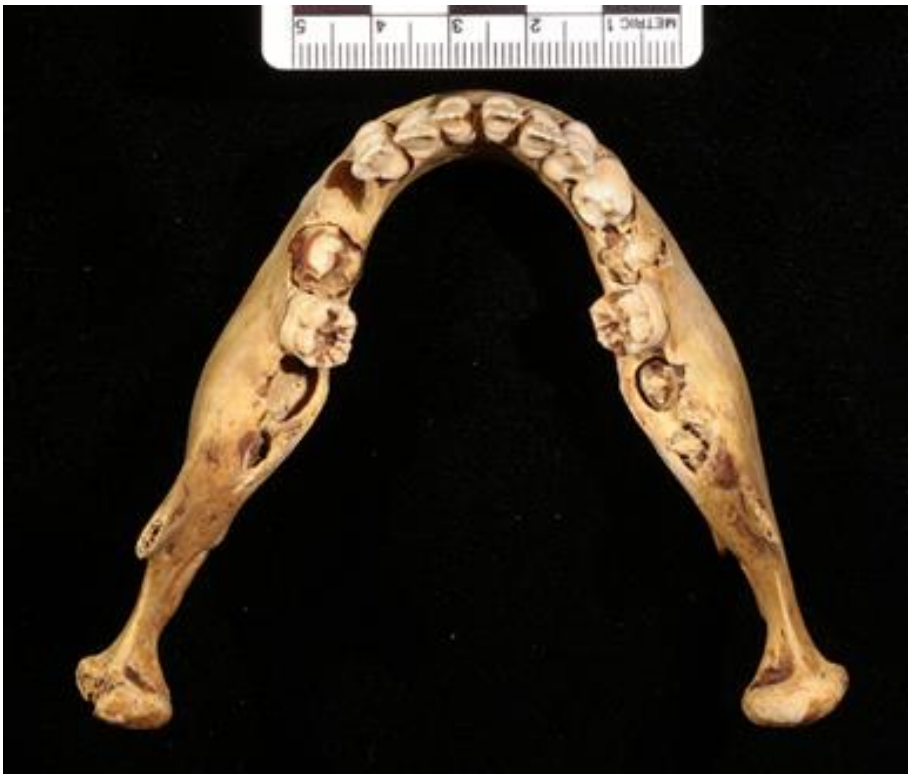

Figure. 5. The mandibular molars resemble those in the maxilla.

Individual 2263

Individual 2263 is a 46-year-old African American male. Lues was the cause of death. Skull morphology was normal. All maxillary and mandibular teeth are present. Linear and pitting hypoplasia is evident on the incisal and middle third of the maxillary central right incisor and the incisal third of the lateral incisors and canines (Fig. 6). Black spots are visible on the middle third of the crown of the right central incisor. The crown of the left maxillary central incisor has broken away from the middle third of the crown to the incisal third. Black spots are just visible on the left central incisor at the same level as the right incisor. On the mandibular anterior teeth, linear and pitting enamel hypoplasia is evident on all anterior teeth at the same level (Fig. 7). The enamel crown of the left canine has broken off.

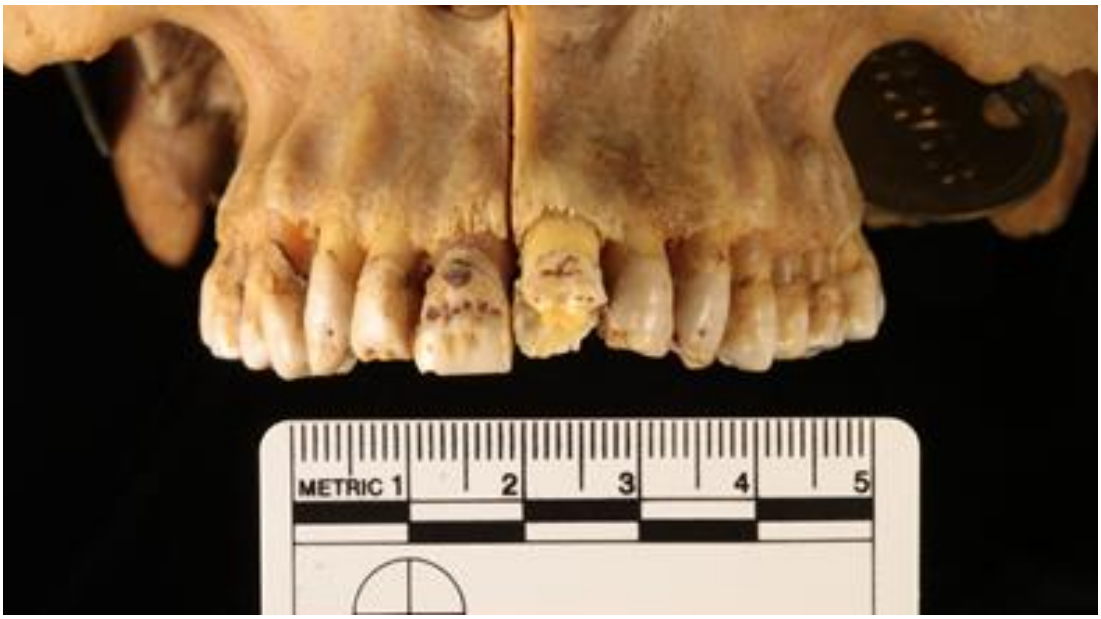

Figure. 6. The upper central incisors demonstrate linear and pitting hypoplasia on the incisal and middle third of the crowns. The same hypoplasia is evident on the incisal third of the lateral incisors and canines.

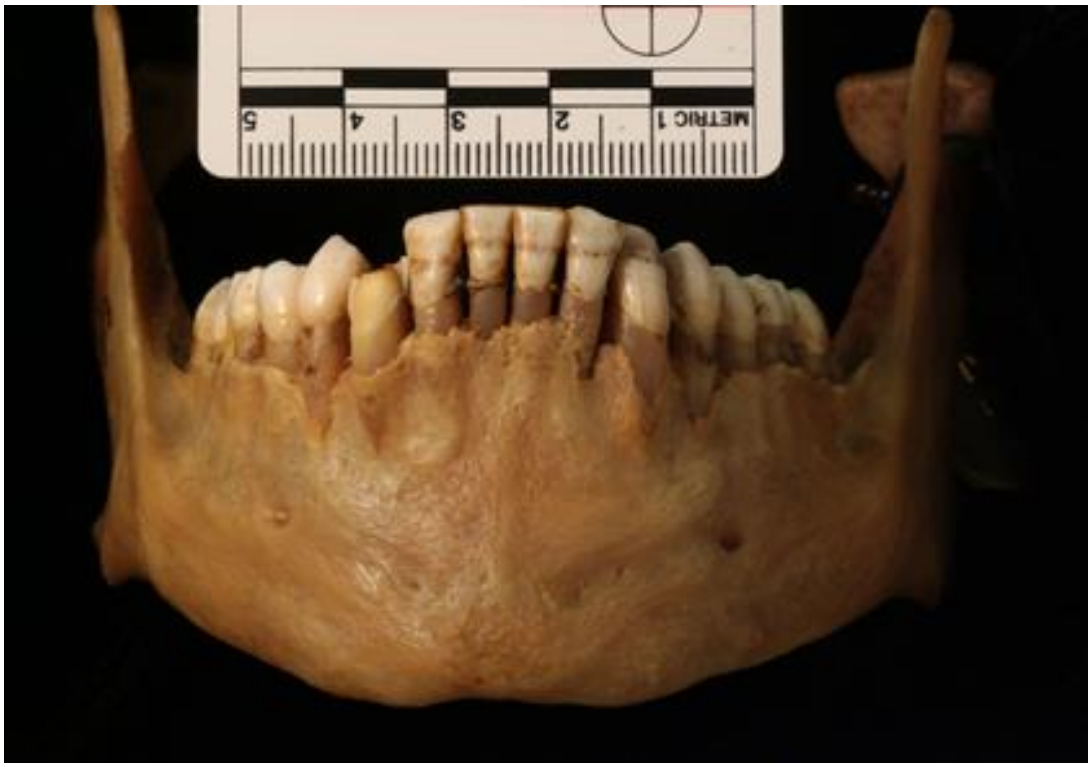

Figure. 7. Linear and pitting enamel hypoplasia are evident at the same level across all anterior teeth.

Individual 3097

Individual 3097 is a 36-year-old African American male. Syphilis was the cause of death. All teeth are present except for the maxillary right canine and left permanent first molar and mandibular central incisors. Minor pitting enamel hypoplasia is on the second third of maxillary central incisors. A single deep linear enamel hypoplasia runs along the cervical third of the lateral incisors and left canine (Fig. 8). This hypoplasia also occurs on the lingual surface. Along the cervical third of the central incisors are black lines that penetrate into the enamel. On the mandibular lateral incisors and canines is linear enamel hypoplasia. No bone pathologies are present.

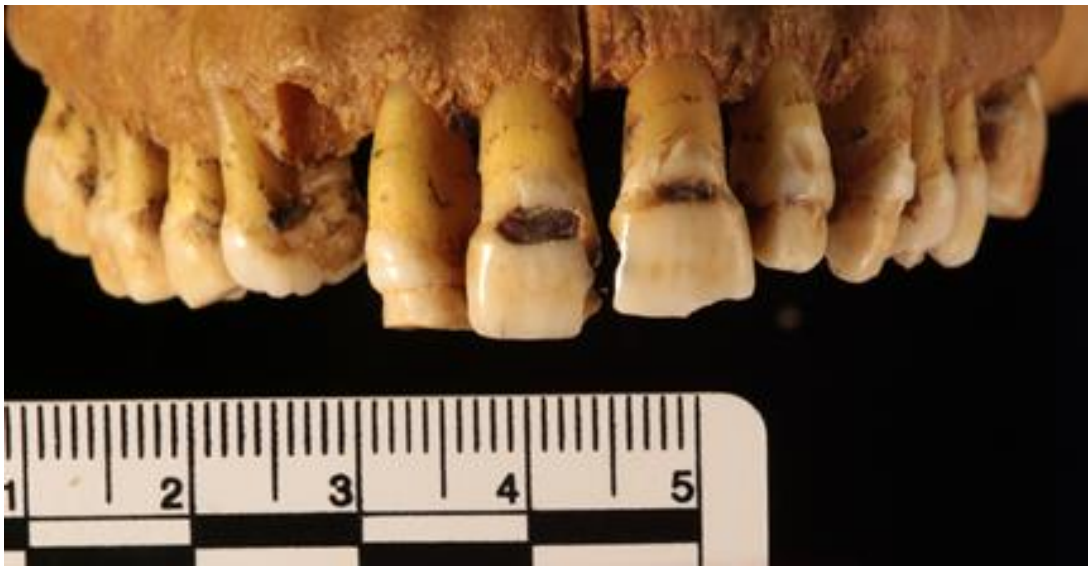

Figure. 8. Linear enamel hypoplasia runs along the cervical third of the lateral incisors and left canine. Black markings penetrate into the cervical areas of the upper central incisors, possibly cavities.

Differential Diagnosis

Other pathologies and chemicals can affect odontogenesis and amelogenesis and are therefore considered in making a differential diagnosis. Pathological conditions considered include tuberculosis, rickets, fluorosis, and amelogenesis imperfecta. Chemicals include mercury, arsenic, potassium iodide and bismuth.

Clinical cases of tuberculosis in children (Mignogna et al. 2000; Ito et al. 2005; Ebenezer et al. 2006), have not shown any type of enamel hypoplasia nor the dental abnormalities resembling those described in the cases above. In skeletal cases of possible tuberculosis, dental abnormalities including linear enamel hypoplasia (Matos et al. 2011; Bedić et al. 2015), bands of decreased enamel thickness and carious lesions have been observed (Formicola et al. 1987). The dental abnormalities in tuberculosis do not resemble those discussed in the above cases therefore, is ruled out as a possible diagnosis.

Rickets is a disorder due to a lack of vitamin D which affects bone mineralization and enamel formation. Dental abnormalities associated with this disorder include caries and enamel hypoplasia in the forms of pits and linear grooves (Zambrano et al. 2003;

Davit-Béal et al. 2014). The types of enamel hypoplasia seen in rickets are not comparable to the cases from Cleveland.

Fluorosis refers to changes in enamel during tooth development, caused by ingesting large amounts of fluoride for a long period of time. In individuals with dental fluorosis enamel can appear with opaque white demarcated areas on parts or all of the tooth depending on severity, and/or be pitted or porous and may be stained yellow or brown color (Thylstrup and Fejerskov 1978; Masumo et al. 2013). The dental signs observed in fluorosis are not observed in the individuals discussed here. Fluorosis also tends to affect most or all teeth which is not seen in any cases here.

Amelogenesis imperfecta (AI) is a hereditary condition caused by a genetic mutation that interrupts the process of amelogenesis, affecting most or all teeth in both deciduous and permanent dentition (Crawford et al. 2007; Gadhia et al. 2012). AI can cause enamel discoloration, delayed tooth eruption, tooth sensitivity, congenitally missing teeth and enamel hypoplasia (Hu et al. 2012; Wang et al. 2015). Dental abnormalities caused by AI are not evident in the cases described in this study, plus syphilis and treatments containing mercury affect specific teeth unlike AI. Therefore, AI is dismissed as a diagnosis.

Mercury was used to treat syphilis/congenital syphilis throughout Europe, the United States Asia and Australasia (United States. Public Health Service. Division of Venereal Diseases 1930). The compound was used in various forms such as pills, ointments and was injected intramuscularly (Hutchinson 1887; Cole et al. 1929; Cole et al. 1933). Treatments containing mercury ranged from one and a half to fifteen grains of solution or ointment (which in milligrams equivalates to a range between 97.19 mg to 971.984 mg) (Hutchinson 1878; 1887; Lee, 1878; Warner 1881; Cole et al. 1929; Cole 1933). Established in 2004, the tolerable intake of methylmercury to protect the fetus from any adverse effects is 1.6 μg (= 0.0016 mg) per kilogram of bodyweight per week (World Health Organization, 2007). This tolerable intake is doubled for adults (3.2 μg or 0.0032 mg). The levels of mercury used to treat congenital syphilis in the United States during the early 20th century, surpassed what was considered to be safe. Therefore, disturbances in amelogenesis are to be expected, resulting in enamel defects. While abnormalities in enamel can be present in various forms (Seow 2013), the type of hypoplasia evident in 2118, 2263 and 3097, ranges

from pitting and linear hypoplasia to missing enamel. Defects in the secretory stage of amelogenesis are said to result in enamel that is thin or hypoplastic with either pits or grooves (Gadhia et al. 2012: Prasad et al. 2016).

Arsenic and potassium iodide have been considered as possible causes of the dental malformations observed in the four individuals in this sample since they were used as treatments for syphilis/congenital syphilis. However, they are not known to or recorded to produce dental malformations such as those observed here. Arsenic has been noted to cause tooth abrasion and sensitivity (Sunny et al. 2013) and linear hypoplasia (Konishi et al., 1977), but not major enamel defects.

Bismuth has been noted to cause pigmentation of the enamel, loosening of the teeth in case of prolonged use and a blue line on the gums (Ling 1929; McCarthy and Dexter 1935; Dean 1943). The most constant location for pigmentation was the cervical portion of the incisors (McCarthy and Dexter 1935; Dean 1943).

Discussion

Attitudes towards syphilis have changed over the centuries. The 19th century saw physicians primarily concerned with the clinical manifestations of syphilis, and finding what they considered effective ways of treating the disease. As various treatments were not completely successful in some cases, attitudes towards syphilis in the early 20th century in the United States changed. It was now considered a social problem and a public health concern, with a focus on controlling the spread of the disease (Breakey 1896; Post 1889). Researchers were now concerned with producing an effective test for the disease. In 1901, Jules Jean Baptiste Vincent Bordet (1870-1961) and Octave Gengou (1875-1957) produced a complementing fixation reaction (Ligon 1998; Bialynicki-Birula 2008). As a result of this discovery, a test for syphilis, known as the Wassermann reaction test, was developed by August von Wassermann, Albert Neisser and Carl Bruck in 1906 (Lancet 1925; Sachs 1925; Bialynicki-Birula 2008). This enabled a way to detect the presence of the bacterium *Treponema pallidum* discovered in 1905 by Fritz Richard Schaudinn and Paul Erich Hoffmann (Lancet 1925).

Due to the fear of the spread of syphilis, legal action was taken making syphilis a "reportable" disease (Lancet 1911). Social concerns grew, as did stigma towards certain groups including males, African Americans, prisoners and prostitutes (Shoemaker 1887; Breakey 1886; Post 1889; Lancet 1900; Lancet 1929; Lancet

1938b; Journal of the National Medical Association 1944). Government efforts could not control the disease with individuals either avoiding testing or being non-compliant in their treatment program.

An important thing to note is that, determining accumulated levels of mercury does not prove, nor disprove the use of mercury as a form of treatment in cases of congenital syphilis, since mercury has a quick excretion rate out of the human body (Bürgi 1906; Cole et al. 1929). If someone was treated with mercury for two years from the age of two, and lived to adulthood, little to no mercury would be found. However, if an individual were treated with mercury closer towards the time of death, mercury levels would be detectable as various studies have shown (Tucker 2007; Rasmussen et al. 2008; Rasmussen et al. 2013; Zuckerman 2016). Since the excretion of mercury is the issue, it highlights the very importance of dental changes associated with treatments containing mercury and its use when considering the differential diagnosis of congenital syphilis, especially in older individuals The interruption to amelogenesis caused by mercury produces significantly different changes to the dentition than those caused by the disease and as such should be considered when making a differential diagnosis of congenital syphilis even if levels of mercury are not detected.

If mercury was an effective form of treatment (Warner 1881; Cole et al. 1929), mercury would prevent any changes in the bone from occurring, thus making a differential diagnosis of syphilis difficult. It is, however, certain that in the case of the four individuals discussed here, if mercury was used as a form of treatment, it was not effective in eradicating the pathogen, because these individuals died in adulthood from syphilis. All the treatment has done was reduce the severity of the disease so as to allow these individuals to reach adulthood which has been noted by Goldwater (1972). Alternately, these individuals may have been completely cured of congenital syphilis, but acquired the venereal form later in their lives.

In the 171 individuals given a cause of death of syphilis or syphilis-related, four demonstrated dental signs (2266, 2118, 2263, 3097).

The dental abnormalities observed in 2266, are not typical of congenital syphilis, however, the shape of incisal edges may be simply due to tooth wear.

The most significant dental malformations are present in 2218. They appear to be a characteristic sign associated with treatments containing mercury, which is plausible

since mercury was used throughout the United States to treat syphilis in the early 20th century. It is possible that 2218 would have been administered treatment not long after birth and the treatment ceased at approximately 2.0-2.5years of age. Crown calcification of the maxillary central incisors begins approximately 3-4 months after birth and crown completion occurs approximately at four to five years. Due to the extensive damage to the enamel on the first and second thirds of the crown of the central maxillary incisors, it is plausible that a large dose of mercury would have been administered. The permanent molars resemble those observed in syphilitic patients in the United Kingdom by Hutchinson (1878), from Australia (B70) (Ioannou et al. 2015) and Austria (Gaul and Grossschmidt 2014). Despite the large doses of mercury, the individual was not completely cured and died of syphilis later.

The enamel malformations in 2263, suggest that he may have been treated with mercury, however, the severity is not of the same extent as those observed in 2118. In this case, mercury would have been administered around 4 to 5 months after birth and treatment ceased around 3.5 years of age. It is difficult to determine whether treatment was regular or intermittent. The fact that treatment would have lasted for some years is not unusual as treatment could last up to two years (Hutchinson 1888; O'Leary et al. 1937). The concentration of mercury may have also varied, which was also common (Wernigk 1908). Despite the administration of mercury, the individual was not completely cured and died of syphilis later.

It is possible that 3097 could have been treated with mercury, which could have lasted a couple of years as lateral incisors, and canines are affected. The cervical portions of central incisors are discolored possibly due to mercury. The discoloration could also be a carious defect caused by thinned enamel, which may have been the result of mercuric treatment. Alveolar resorption may have been caused by mercuric treatment administered during adulthood, due to reinfection, or disease resurgence.

Mercury was widely used to treat and contain the disease. As our analysis of age at death shows, individuals who were given mercury were surviving to the average age of other members of the population with no morphological changes to the skull in cases of congenital syphilis. The earliest age at death among studied skeletal remains is 13 years, which indicates that this person survived congenital syphilis for at least 10 years after possible treatment.

The fact that the vast majority of individuals recorded as dying of syphilis show no bone changes makes it difficult to confirm recorded diagnosis of syphilis by a paleopathological observation. In studies of skeletal remains from the New or Old World, absence of syphilis-related bone pathologies does not confirm the absence of the disease. Antibiotics were not available during the early 20th century, resulting in the use of metallic antibacterials. Throughout the United States, including Cleveland, Ohio, mercury was used to treat syphilis and congenital syphilis (Cole et al. 1929; Driver and Barney 1935). The paucity of bone pathologies in the collection studied and the high age at death of affected individuals, indicate that metallic antibacterial treatments were largely effective, if not in complete elimination of bacterial infection, at least in limiting seriously its pathological effects. Comparison of very infrequent changes found in the Hamman Todd Collection with findings of Steinbock (1976) and Rothschild (2005) of frequencies reaching up to 25% or 13% of bony changes in syphilitic individuals confirms the observation of successful pre-antibiotic treatments. In cases studied here, either mercury was effective or syphilis was asymptomatic more often than in individuals studied by others. Depending on the exact components used and the timing of treatment, mercury may not have been as toxic as currently thought since individuals with congenital syphilis treated at a young age, as indicated by dental changes, lived to adulthood. A majority of other syphilitic adult individuals in this sample either had no teeth, had loose teeth or dentures. It could be possible that some individuals may have been treated with mercury at some stage during adulthood, which increases the likelihood of tooth loss. However, tooth loss could be the result of other causes.

A major limitation of this study is the fact that only individuals with cause of death recorded as syphilis or syphilis-related were studied. Were the pre-antibiotic treatments of syphilis really effective, the individuals who died of conditions not related to syphilis, but showed signs of congenital syphilis or its mercuric treatment, would be the best proof of the treatment's effectiveness.

Conclusion

Determining syphilis in skeletal samples can be difficult due to a number of issues. The effects of treatments containing mercury, on enamel formation and bone changes, need to be considered and applied when making a differential diagnosis of syphilis/congenital syphilis as this may be a good indication of the disease without the

presence of bone changes. The most reliable way to know whether someone with congenital syphilis was treated with mercury, is by changes in enamel formation. If the individuals in this sample were treated with mercury, whether in childhood or as adults, mercury may have been effective in limiting or eradicating the infection due to the lack of notable bone pathologies.

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Chapter 7

ARTICLE 6:

Presence of dental signs of congenital syphilis in Pre-modern specimens

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(Accepted for Publication)

Chapter 7. Research Article 6: Presence of dental signs of congenital syphilis in Pre-modern specimens

Statement of Authorship

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Name of Principal Author (Candidate)	Stella Ioannou
Contribution to the Paper	- Came up with concept for paper. - Wrote paper. - Obtained images and permissions for use. - Created images for publication.
Overall percentage (%)	65%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 6/10/17

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Renata Henneberg
Contribution to the Paper	- Examined individuals 320 and 306 originally and took original photographs. - Edited paper and provided feedback.
Signature	Date 10.10.2017

Name of Co-Author	Maciej Henneberg
Contribution to the Paper	- Examined individuals 320 and 306 originally and took original photographs. - Provided feedback on concept of paper and edited manuscript.
Signature	Date 10.10.17

Purpose of Article

As discussed in the introduction and previous manuscripts, dental abnormalities associated with congenital syphilis and its treatments (mercury) vary considerably between each other and among individuals. Therefore, the purpose of this manuscript is to apply these dental variations to the oldest possible cases of congenital syphilis in the literature.

Research Aims:

- To determine if dental signs in the oldest possible cases of congenital syphilis are attributable to congenital syphilis and its treatments (mercury) rather than to any other disease.

This article was submitted to Archives of Oral Biology, and was accepted with revisions. The manuscript was revised and resubmitted to the journal. The reviewer's comments are on the next page, followed by the revised manuscript.

Reviewers Comments

Reviewer #1: The aim of this study is to re-assess the dentition of the oldest cases attributed in earlier publications to congenital syphilis in order to determine whether their dental development processes have been affected by either congenital syphilis itself, its treatments (mercury) or a combination of both (syphilitic-mercurial).
So the authors the collected the possible pre-Columbian cases of Syphilis from the literature and they found five cases. Four of them are syphilitic, but only one adolescent from Byzantine site Nicaea, Turkey, shows dental signs characterised as syphilitic-mercurial.
We focus on this interesting fifth case: ITK'90 56/6: Nicaea.
Reason for this diagnosis are the changes in the occlusal surface of the upper first molar, caused - so the authors – by mercurial treatment. Description is very short: Central areas of the occlusal surface are devoid of enamel resulting in some visible dentine … The argumentation is based on the similarities in enamel deficiencies in the central areas of the occlusal surfaces of the first permanent molars, of this individual with a 8-year-old, 20th century case of congenital syphilis from London … thought to have been treated with mercury during childhood. However, the autors admit, that the cases could either be the result of the disease itself or mercuric treatments, but they conclude, that these changes caused by congenital syphilis and its treatments should as a diagnostic procedure taken into account in the paleopathological assessment. Both, the effects of the disease as of this disease-specific marcurial therapy should be used for the diagnosis of congenital syphilis since they do not occur in any other disease. So, these mercurial dental signs suggest the affection with syphilis.

But some questions arise:
– The damages of a mercurial therapy are charatcerized by Ioannou (2016) as large expanses of deficient enamel … rugged and pitted, ultimately producing an appearance of a dirty grey honeycombed tooth - and is accordingly illustrades by illustrations of Hutchinson.
Mercury –so the authors argue–produced widespread severe enamel hypoplasia [as]… the result of disrupted amelogenesis that produced deep irregular pitting and irregular enamel with patches of exposed dentine–as any long-lasting intoxication will do. The localisation of the irregularities depens on the moment, when the toxic

substance was administrated during the amelogenesis. Besides, the incisor of the Nicaea case shows only the notch, which is characteristic for syphilis, accoringly Erdal a Hutchinson's Incisor - for Ioannu (2016) 'typical' syphilitic. Also, the pathological chaged first upper molar is for Erdal only a mulberry molar – pathognomic for syphilis.

– Surely, the dental abnormalities caused by mercury were so substantially different from those produced by congenital syphilis itself -but are they specific of mercury treatment? – so specific, that the effects of treatment, the 'mercurial'changes, can be used as a diagnostic method in paleopathological diagnoses (Ioannou 2016). And, is this true for the 13th century in in Nicaea, where venereal syphilis is a sporadic disease, (Erdal 28)? Are there written sources existing in which mercury is specifically used as a therapy for syphilis? In the Dynameron of Nicholas Myrepsos (late 13th century), a court physician at Nicaea, mercury ointments are used for itch and other skin troubles (Rowe V., 1971).

– The basis for the reasoning of existence of 'syphilitic mercurial dental signs' from the 15th century is very narrow (n = 1) and moreover there is a wide variation of dental changes related to congenital syphilis. Why not take the chance, and discuss the hitherto not published syphilitic-mercurial teeth of two juvenile from Oplontis. Thus, the criteria of pre-Columbian mercurial-syphilitic teeth could eventually be better are worked out.

So, it is an interesting article, but some additional precicions and additional informations should be made.

Reviewer #2: A very worthwhile addition to the syphilis controversy. Use of congenital signals in teeth, versus the very difficult diagnosis from bones, is a very sharp method. I am sure the authors elsewhere discuss in more depth the difficulties that nevertheless arise with the congenital signs -- namely paucity of subadults of just the right age, attrition etc.

Della Cook once spoke of the utility of dental markers of congenital syphilis to track controversial pre- Columbian New World syphilis -- or for that matter, Old World syphilis -- however I am not sure she ever published on that method.

Even if there is this very limited uncontrovertible evidence for pre- Columbian syphilis (on either side of the Atlantic Ocean!), it seems so rare that at some point (perhaps not here in this treatment) the authors need to address why the disease was extremely rare (although present) in both Old and New World until the time of the Columbian exchange, when it becomes so common.
Figures are good.

Editor:
When submitting a revised manuscript please address each of the concerns of the reviewers in your covering letter indicating where and how the manuscript has been modified. Please track or highlight the changes made in the manuscript.

Highlights

- Congenital syphilis produces specific dental hypoplastic abnormalities.
- Crowns of permanent incisors and first molars are mainly affected.
- Mediterranean and Central European cases are well diagnosed by dental changes.
- 15th century cases indicate syphilis was not imported by Columbus from America.

Abstract

Objective

Tooth morphology can vary due to genetic factors, infectious diseases and other environmental stresses. Congenital syphilis is known to interrupt tooth formation i.e. odontogenesis and amelogenesis, producing specific dental characteristics. Variation of those characteristics can occur, resulting in dental signs "not typical" of the disease, however, they are described in the 19th century literature. Past treatments of congenital syphilis with mercury also interrupted dental processes resulting in significantly different dental signs. The aim of this study is to examine the dentition of the oldest (pre 15th century) cases attributed to congenital syphilis to determine whether their dental processes have been affected by either congenital syphilis itself, its treatments (mercury) or a combination of both (syphilitic-mercurial).

Design

Comparisons of dental signs of congenital syphilis and its mercuric treatments as described by Hutchinson, Moon and Fournier in the 1800s and in standardized methods as established by modern studies, are made with the dentition of specimens found in archaeological sites in Mexico, Italy, Turkey and Austria dating back to the Terminal Formative Period, Classical Antiquity, Byzantine times and Middle Ages.

Results

The dentitions of a child from Oaxaca, Mexico, St. Pölten, Austria, and two juveniles from Classical Antiquity site Metaponto, Italy, show signs attributed to syphilis only. One adolescent from Byzantine site Nicaea, Turkey, shows dental signs characterised as syphilitic-mercurial.

Conclusions

Dental abnormalities observed in Mediterranean individuals match a range of signs attributable to congenital syphilis and its treatments, more so than the New World case. Therefore, it is likely that these individuals suffered from congenital syphilis.

Keywords: first molar, Hutchinson, hypoplasia, incisor, mercury

1. Introduction

Human odontogenesis, although regulated by genetic factors, also depends on the interaction with pathogens, and the quality of nutritional and physical environments. The tooth crown is shaped by amelogenesis, which has two stages, the secretory stage and maturation stage. Disruptions of enamel matrix formation tend to produce hypoplastic defects such as pits, grooves and thin or even missing enamel (Seow, 2015). Their appearance on the crown surface depends on the stage of tooth development affected and the duration of an insult. The location of the defect on enamel is a good indication of the approximate time the insult occurred (Seow, 2015).

Congenital syphilis is known to interrupt tooth and enamel formation, producing specific dental characteristics. Hutchinson (1859, 1863, 1887, 1888), Moon (1877, 1884), and Fournier (1886), have described specific dental signs (notched incisors, dome shaped molars and noduled molars) that they observed in individuals with congenital syphilis during the 19th century. However, variations of those characteristics can occur, resulting in dental signs that are "not typical" of the disease (Hutchinson, 1878, 1888). Numerous descriptions of dental signs have been made (Bradlaw, 1953; Putkonen, 1962) to establish a standardised method determining dental signs of the disease to aid in its diagnosis. A standardised method widely accepted and used today had been established by Hillson and colleagues (1998). Dental changes known to occur to the permanent dentition associated with congenital syphilis include (1) Hutchinson's incisor that primarily affects the permanent upper central incisors, and occasionally some lower incisors, (2) Moon's molars, (3) Fourier's molars which demonstrate a defect cutting into the base of the cups and (4) canines with a groove-like defect around the tip of the crown (Hillson., et al., 1998). Since enamel does not remodel, dental changes are important in archaeological and paleopathological collections.

Signs that are characteristic for a disease (pathognomonic) by definition cannot occur as a result of other diseases, thus their findings produce reliable diagnosis on their own. Re-examining the original works of Hutchinson (1859, 1863, 1887, 1888), Moon (1877, 1884), and Fournier (1886), it has turned out that they also documented a spectrum of variations among well diagnosed patients that was wider than Hutchinson's incisor, Moon's molar, and Fournier's molar as hitherto used. The

spectrum included notches on the edges of lateral and lower incisors and tips of canines, severe hypoplasia of their crowns, and hypoplastic patterns of nodules, groves and pits on the occlusal surfaces of first permanent molars. Recent paleopathological studies (Ioannou et al., 2015; Nystrom, 2011) of skeletal remains of 19th century individuals demonstrated this wide variation of dental changes related to congenital syphilis.

Among pre-antibiotic treatments, the most widely used for syphilis was mercury and its compounds (Fournier, 1889; Hutchinson, 1874, 1878, 1887; United States. Public Health Service. Division of Venereal Diseases, 1930). Mercury produced widespread severe enamel hypoplasia not only on the first permanent molars, but also on incisors and in some cases on canines (Hutchinson, 1878). Premolars were rarely affected. These changes were the result of disrupted amelogenesis that produced deep irregular pitting and irregular enamel with patches of exposed dentine. Dental abnormalities caused by mercury were so substantially different from those produced by congenital syphilis itself that Hutchinson (1878) and later Moon (1884) deemed them worthy to document. However, the effects of treatment, the "mercurial" changes, have never been used as a diagnostic method in paleopathological diagnoses until recently (Ioannou et al., 2015; Ioannou et al., 2016). The new approach of using jointly dental defects caused by congenital syphilis and its treatments as criteria of differential diagnosis can be now applied to assess the oldest paleopathological cases suggested in the literature to be those of congenital syphilis. Providing a strong diagnosis of congenital syphilis in these pre 15th century cases may contribute to the debate on the origins of the disease (Holcomb, 1935; Harrison, 1959; Cockburn, 1961; Hackett, 1963; Hudson, 1963; Goff, 1967; Harper et al., 2011), and the antiquity of the mercuric treatment. The aim of this study is to re-assess the dentition of the oldest cases attributed in earlier publications to congenital syphilis in order to determine whether their dental development processes have been affected by either congenital syphilis itself, its treatments (mercury) or a combination of both (syphilitic-mercurial).

2. Materials & Methods

A database search of PubMed and Google Scholar was conducted to find the oldest possible cases of congenital syphilis with dental abnormalities. Search criteria that were used included dates of cases prior to 1492, words: syphilis, congenital, dental,

treponemal, (and their equivalents in European languages other than English) and the requirement that a publication contained photographs of dental changes of sufficient quality to allow independent assessment of these changes.

This search has revealed three cases: one from North America, one from Central Europe and one from Anatolia in addition to our own earlier findings (Metaponto cases), totalling five cases (n=5). There were no cases found from Africa, Central and East Asia and the Pacific region. North American pre-Columbian case of congenital syphilis is B10-I11 from Yugüe, Oaxaca, Mexico (Mayes et al., 2009). The four cases from pre-Columbian Mediterranean/Europe published in peer-reviewed literature, claimed by their authors to have congenital syphilis are: STP 7315/3045 from St. Pölten, Austria (Gaul et al., 2015), ITK'90 56/6 from Nicaea, Turkey (Erdal, 2006) and individuals 306 and 320 from Metaponto, Italy (Henneberg et al., 1992, Henneberg and Henneberg, 1994, 1998).

Individual B10-I11, aged 5-6years, is from the site of Yugüe in the Mexican State of Oaxaca, dated to CE 100-250 (Mayes et al., 2009). The upper body has been represented by fragmented left and right humeri, left and right radii, and left and right ulnae. Lower limbs were missing. Dentition was the best preserved with both deciduous and permanent teeth present.

Individual STP 7315/3045 is approximately 6 years of age, of unknown sex, and comes from a cemetery located at St. Pölten, Austria dated to 1390-1440. Most of the skeleton is present. Cribra orbitalia are evident, but no other pathological changes are observable on the postcranial remains. Deciduous and permanent teeth have notable hypoplastic changes.

Individuals from graves numbered 306, and 320 are juveniles (age 15-19 years, no sex estimate possible), from a burial ground Pantanello within the ancient Greek colony of Metapontion (8-2 c BCE), now Metaponto, located in the Province of Matera, Italy. The individuals 306 and 320 were originally examined in 1985-87 by RH and MH and described in Henneberg et al. (1992) and Henneberg and Henneberg (1994, 1998). Skeletons of both individuals were fragmentary, juvenile 320 had thickened anterior border of the fragmentary tibia suggesting the sabre shin trait. Both individuals had preserved dentition.

ITK’90 56/6, approximately 14 to 15-year-old subadult, dated to 1222–1254 (13th century), was excavated in Nicaea, Iznik District of Bursa, Western Anatolia, Turkey. Most bones are present. According to Erdal (2006) the individual has Hutchinson’s incisor, radial scarring on the frontal bone, sabre shin, dactylitis, and gummatous, and non-gummatous osteomyelitis on most post-cranial bones.

Publications of all five cases were peer-reviewed.

The original works of Hutchinson (1859, 1863, 1874, 1878, 1887, 1888), Moon (1877, 1884) and Fournier (1886, 1889) were examined in order to determine the full range of dental characteristics that were noticed in patients with congenital syphilis (untreated and treated). The full range of dental characteristics described and illustrated by Hutchinson, Moon and Fournier in clinically diagnosed (untreated and treated) individuals (Fig 1, Fig. 2, and Fig.3) were compared to the dental abnormalities of these specimens to determine any similarities or differences. Permissions have been obtained to use original images from the publications discussed in this article.

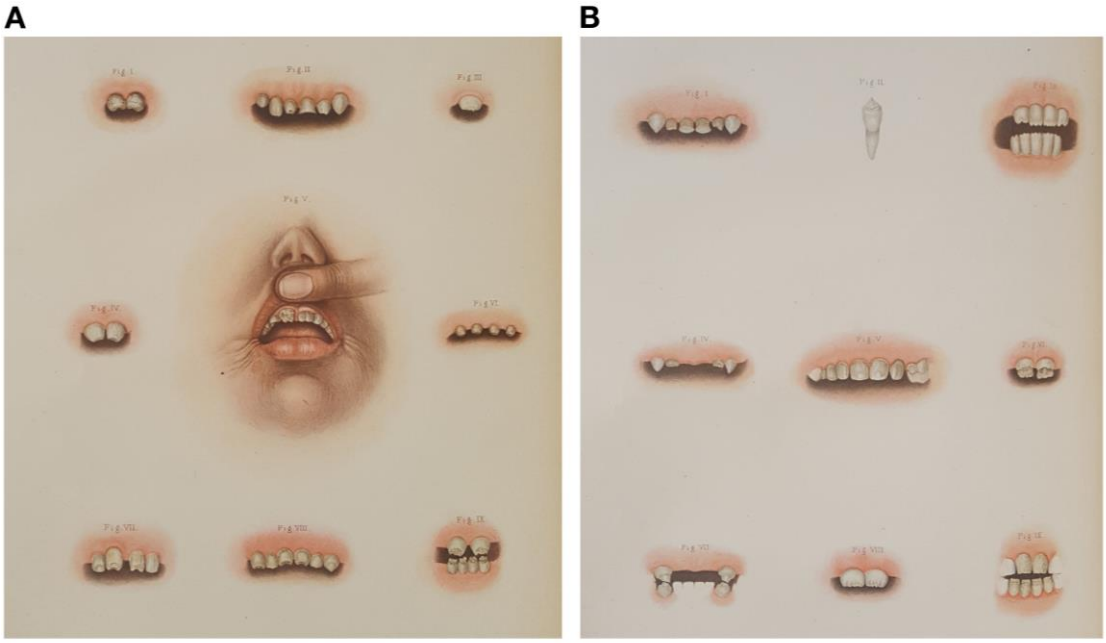

Figure 1. (A) Plate XLII: Variation of dental malformations in untreated patients with congenital syphilis observed by Hutchinson (1888: p. 9). (B) Plate XLIII: Figures I, II, IV, V and VII: variations of syphilitic teeth. Figure III: normal teeth with normal serrations. Figure VI: "craggy teeth", where enamel is missing on the lower half of the upper central incisors with distinct transverse demarcation separating healthy from affected enamel. Figure VIII: Malformations caused by scrofula. Figure IX: Mercurial teeth. Hutchinson, J (1888: p. 15)

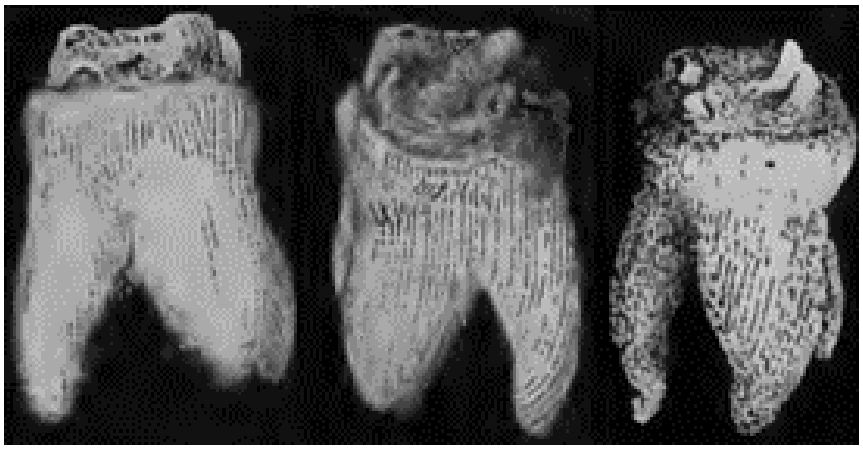

Figure 2. A variation of syphilitic molars observed by Alfred Fournier (1886: p. 84 & 85, Figures 7, 7A and 8).

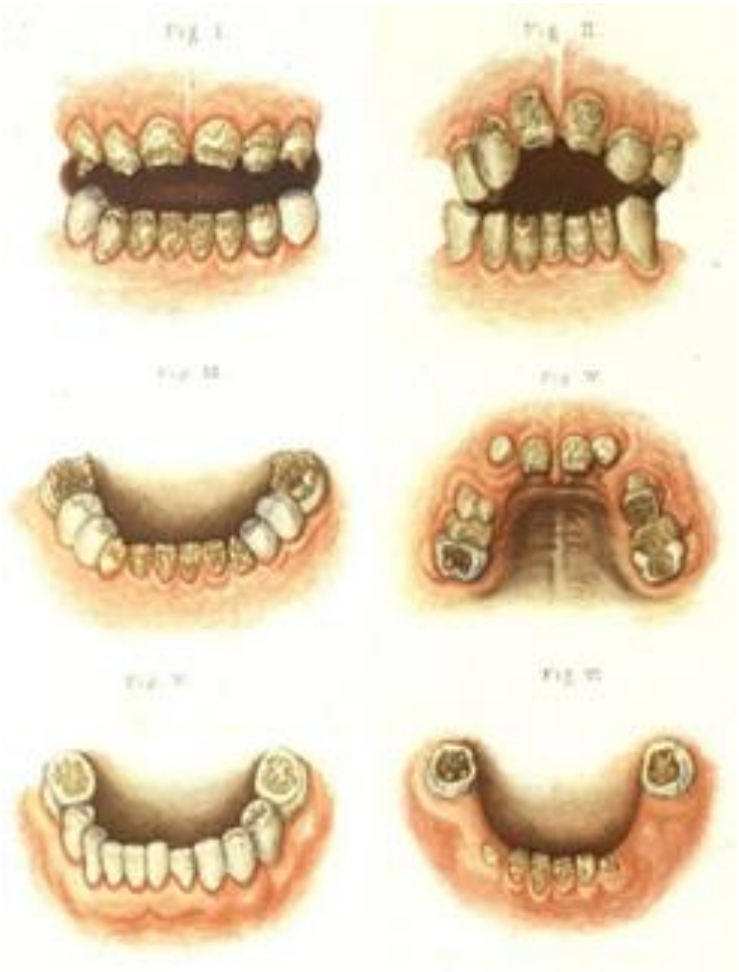

Figure 3. Dental malformations caused by mercuric treatments observed in patients aged between 11 and 28 years, by Hutchinson. Figure IV and VI complete jaw of an individual demonstrating syphilitic-mercurial teeth. Malformations caused by both syphilis and its treatments (mercury). Hutchinson, J (1878: p. 53), Plate XI.

3. Results

The pre-Columbian cases are described in the order of dental changes that they present, i.e. syphilitic, mercurial, and syphilitic-mercurial changes.

B10-I11, Yugüe, Oaxaca, Mexico, dated 150 BCE- CE 250

The left upper central incisor is missing the central mamelon, while the right incisor displays a large patch of hypoplastic enamel on the upper half of the incisal third and on the middle third of the crown. Left maxillary canine's tip is reduced in size, resulting in a pointy or fang like appearance. An impression is visible on the middle

third of its crown on the labial surface. The maxillary right first permanent molar has a reduced occlusal surface. No normal cuspal pattern is visible. Clear demarcation between diseased and healthy enamel is evident. Mandibular central incisors have strongly marked three mamelons, with a pit on the central third of the crown. The morphology of occlusal surfaces of the mandibular first permanent molars appears different from the maxillary molars. The occlusal surfaces are reduced but some normal cuspal patterns are visible. Minor pitting is present and clear demarcations between diseased and healthy enamel are evident.

STP 7315/3045, St. Pölten, Austria

In STP 7315/3045, from St. Pölten, the central mamelon of the maxillary central incisor is reduced in size and has multiple thin spines. The mesial and distal edges appear rounded. The canines are reduced and appear fang like in shape. The permanent first molars in STP 7315/3045 demonstrate multiple enamel tubercles. The occlusal surface demonstrates pitting and is reduced in size.

306 and 320 from Metaponto, Italy

Metapontine individuals 306 and 320 display hypoplastic first molars. The cusps on their occlusal surfaces are reduced in size and some dentin is exposed. Minor pitting is also present on the occlusal surface. Metapontine juvenile 320 displays minor notches on the incisive edges of the central and lateral incisors.

ITK'90 56/6: Nicaea, Iznik District of Bursa, Western Anatolia, Turkey

Byzantine individual ITK'90 56/6 demonstrates a notch on the incisal edge of the upper left central incisor. The upper right first permanent molar in ITK'90 56/6 has a reduced occlusal surface. Central areas of the occlusal surface are devoid of enamel resulting in some visible dentine.

4. Discussion

Four of the five cases presented here demonstrate variations in dental defects associated with congenital syphilis. No teeth affected by syphilis or its treatment are alike as Hutchinson (1878, 1888) demonstrated this abundantly (Fig. 1, Fig. 2, and Fig. 3). When modern standardised methods and 19th century illustrations of congenital syphilitic teeth are considered in their entirety, there are dental characteristics that are comparable to the individuals discussed in the present work.

The Yugüe case does not show “classic” Hutchinson or Fournier dental signs. The hypoplastic defects of the upper incisors do not resemble dental signs observed in congenital syphilis, however, this may be a variation. The lateral left canine does appear fang like in shape and this variant has been described in other cases of congenital syphilis (Jacobi et al. 1992). This fang like morphology is said to be due to cuspal hypoplastic lesions (Jacobi et al. 1992). While the upper and lower permanent molars present differently, they do resemble types of Fournier’s molars.

The dental signs observed in European/Mediterranean cases of congenital syphilis show closer similarity to typical signs of the disease.

STP 7315/3045, demonstrates dental abnormalities that could be the early stages which may lead to the characteristic notch. The appearance of the central mamelon of the maxillary central incisor, (reduced in size with multiple thin spines) (Fig. 4A), coincides with the Hutchinson’s descriptions and illustrations of how the development of a ‘typical” notched central incisor occurs in congenital syphilis. Whereby the central mamelon is “well marked out, and has not been cleared by the breaking of the thin and unprotected dentine” (Fig.4B & 4C) (Hutchinson, 1887). Once the central mamelon has broken away, the tooth will present with a notch on the incisal edge (Fig. 4D) (Hutchinson, 1887), resembling the characteristic “Hutchinson notch”. This malformation of the incisal edge does not occur in any other disease and is thus considered pathognomonic for congenital syphilis. The notch could, theoretically, occur as a result of mechanical abrasion of the centre of the incisal edge for cosmetic purposes (Scott and Turner II, 1988; Milner and Larsen, 1991). Were it so, however, the traces of rubbing an object against the enamel and dentine, or other traces of mechanical alteration would occur. These are not observable in STP 7315/3045 incisor. Also, no cosmetic dental modifications were reported from the sites where the described teeth were found. The permanent first molars in STP 7315/3045 (Fig. 5A and 5B), resemble Fournier’s noduled molar (Fig. 5C), whereby, multiple enamel tubercles and pitting are present and the occlusal surface is reduced in size (Fournier, 1886).

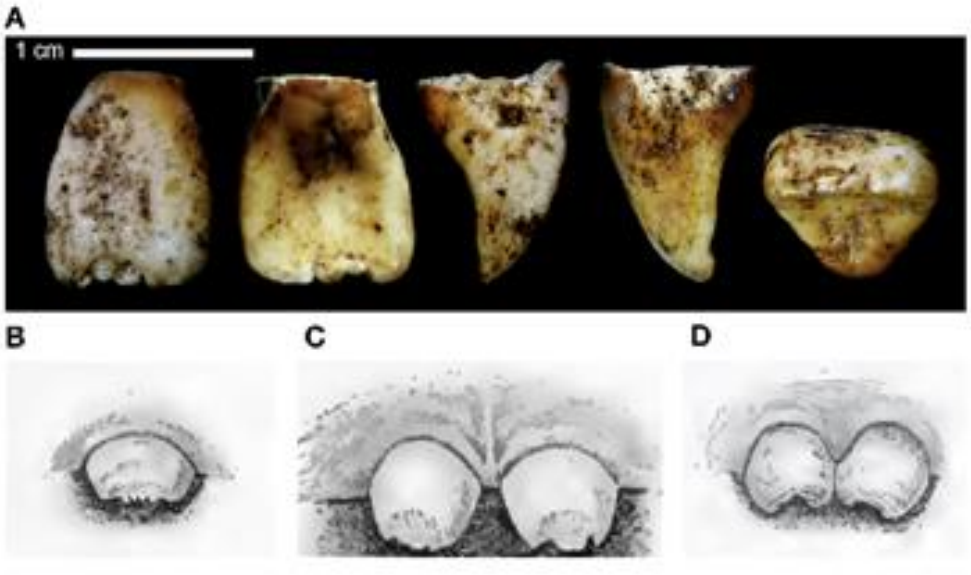

Figure 4. Changes to the central mamelon of the permanent upper central incisors, which will lead to the characteristic notch. Hutchinson, J (1863: p. 205), Plate II, Figs: 1, 2 and 3. (A) Labial, lingual, mesial, distal and occlusal views of central maxillary incisor in STP 7315/3045. Clinical evidence (Hutchinson, 1888): (B) Upper central incisor of a young boy shows a notch with small multiple spines. (C) Upper teeth of a girl are narrow at edges; the middle lobe is thin and surrounded by a crescentic line. (D) Upper central incisors of a boy aged 15 years are short, narrow and notched. Hutchinson observed that the thin middle lobe in the upper central incisors (marked out in B and C) would eventually break away leaving the "characteristic crescentic notch" seen in D. The upper central incisors of individual STP 7315/3045 resemble Hutchinson's descriptions and images. The thin mid lobe with multiple thin spines (seen in A) is present, and has not yet broken off to represent the "characteristic notch". This is only one of the variations of dental abnormalities seen by Hutchinson in patients with congenital syphilis.

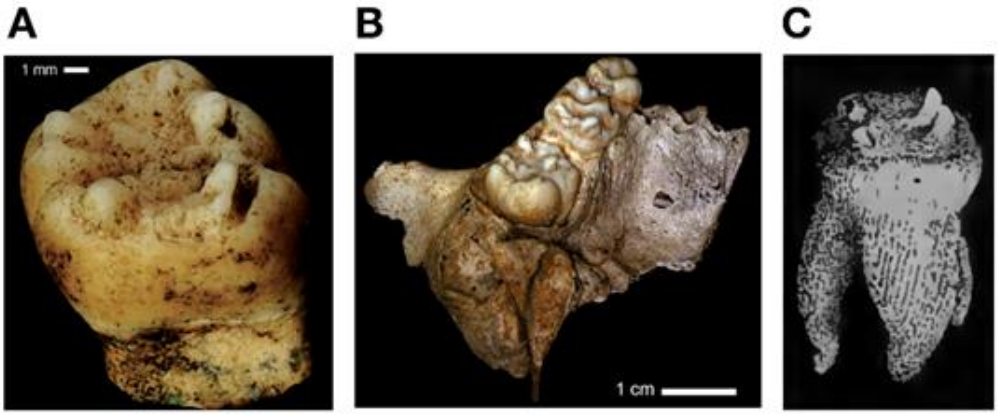

Figure 5. 14th century hypoplastic first permanent molars compared to Fournier's noduled molar. (A & B) Permanent molars from individual STP 7315/3045 display enamel hypoplasia which resembles Fournier's noduled molar seen in (C). The cusps of the permanent molars of Fournier's molar (C) undergo atrophy and separate into a series of cusps that become conical in shape.

Individual 306 demonstrates dental signs that fall within the wide range of dental abnormalities seen in patients with congenital syphilis. The hypoplastic first permanent molars of 306 (Fig. 6A) resemble those in syphilitic individuals observed by Jacobi et al. (1992) (Fig. 6B & 6C). The morphology and type of hypoplastic defects are extremely similar.

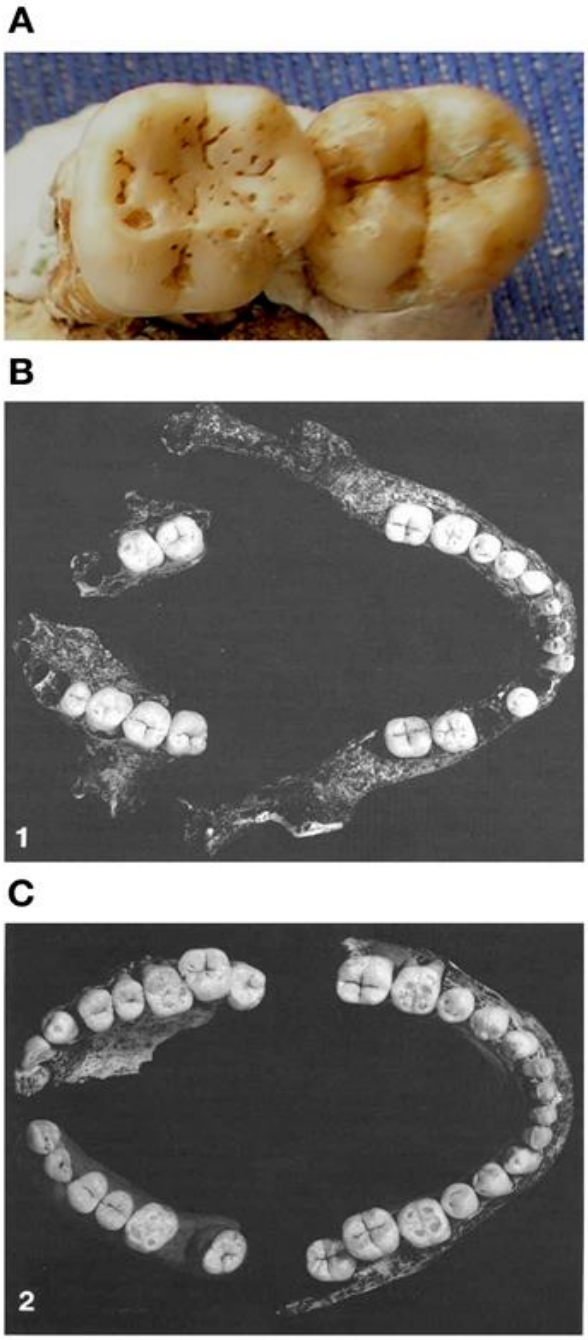

Figure 6. Syphilitic first lower left permanent molar of 306. Compare hypoplastic occlusal surface with that of the adjacent second molar. (A) Right lower first and second molars of juvenile individual 306 from Metaponto. The first molar displays occlusal hypoplasia similar to that observed by Jacobi in (B and C) describing them as Moon's molar (Jacobi et al., 1992: figure 1 and figure 2, pg. 149).

ITK’90 56/6 (Fig. 7A) and 320 from Metaponto (Fig. 7B), both demonstrate a notch on the incisal edges. Although these notches do not resemble the “classic” notch, they are similar to the types of variation of notches that occur in the upper central incisors in patients with congenital syphilis as observed by Hutchinson (Fig. 7C, see also Fig. 1A (Fig. II). The defect along the incisal edge of ITK’90 56/6 may be a carious cavity, however, caries rarely occurs in this area. Were the caries developing in this location, its development could be facilitated by the enamel defect resulting from the syphilitic sign. Individual 320’s incisor has a defect of the formation of the enamel not resembling in any way a carious lesion. This individual is also noted to have multiple linear hypoplastic defects on incisors and premolars and skeletal manifestations including tibial bowing, which indicates that this individual suffered from congenital syphilis.

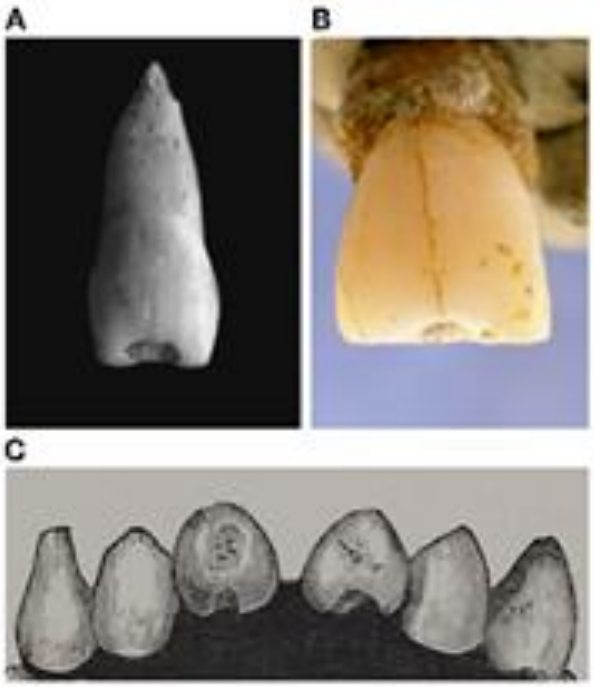

Figure 7: Notching of permanent upper incisors caused by syphilis. (A) A maxillary central incisor in ITK’90 56/6. (B) Central incisor from juvenile 320 from Metaponto. (C) Both ITK’90 56/6 and 320 display one of the types of variations in the middle lobe of individuals with congenital syphilis as observed by Hutchinson. The variations in the notch can also be observed in Figure 1.

The upper right first permanent molar in ITK'90 56/6 (Fig. 8A), resembles a documented 20th century case of congenital syphilis from London (Ioannou et al., 2016) (Fig. 8B). Both molars match Hutchinson's descriptions and illustrations of the types of abnormalities that can occur when affected by treatments that contain mercury (Fig. 8C). Mercury was used during the 13th Century for medicinal purposes; therefore, it is possible this tooth was affected (Buret, 1891; Goldwater, 1972). The notion that only the first permanent molars may be affected by mercury while the incisors are spared, has been described by Hutchinson, "Whilst the middle upper incisors are the test teeth of syphilis, it is to the first molars of both the upper and lower jaw that we must accord this rank in reference to mercury." (Hutchinson, 1878: p. 54 and Figure V p. 53 reproduced here in 8C). Variations in the types of abnormalities in permanent first molars can occur as a result of mercuric treatment (Figure. 3). This may be due to the amount of mercury administered, or the duration of treatment. Hillson and colleagues (1998, p.30) in their descriptions of syphilitic changes only, established that Fournier's molars demonstrate a "plane form hypoplastic defect, cutting sharply into the base of all the cusps". Therefore, the molars of ITK'90 and the case from London could either be the result of the disease itself or mercuric treatments, or both combined.

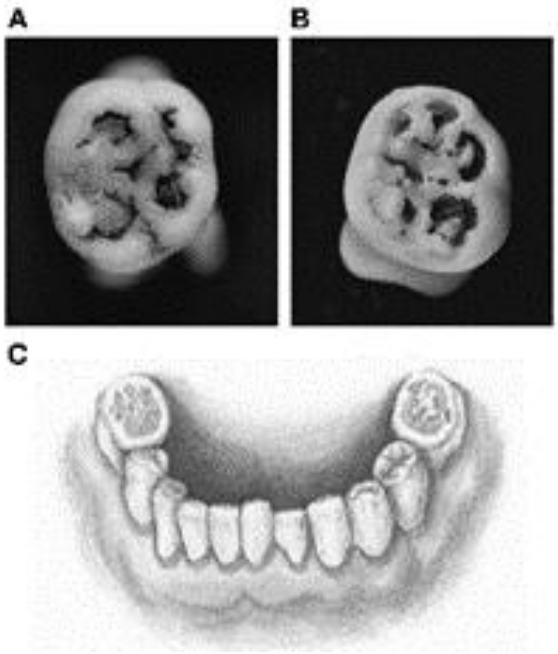

Figure 8. (A) ITK'90 56/6, 13th century (B) 8-year-old, 20th Century case of congenital syphilis from London (Ioannou et al., 2016) and (C) 23-year-old male thought to have been treated with mercury during childhood (Hutchinson, 1878). Similarities in enamel deficiencies are seen in the central areas of the occlusal surfaces

of the first permanent molars in all three individuals, A, B and C. More details required of occlusal surface.

The use of mercury for medicinal purposes to treat syphilis and congenital syphilis is well known (Weatherill, 1833; Hutchinson, 1874, 1878; Fournier, 1889; United States. Public Health Service. Division of Venereal Diseases. 1930; Waugh, 1982; Beers and Mousavi, 2013). Throughout Europe mercuric compounds were administered in various forms including pill, ointments, vapours and intramuscular injections. Mercuric treatments contained from 1 to 20 grains (1 grain is equivalent to 64798.9 μg) of solution (Hutchinson, 1887). This is significantly greater than the established tolerable weekly intake of methylmercury in 2004 of 1.6 μg per kilogram of body weight for children and pregnant mothers (to protect the fetus), and double (3.2 μg per kilogram of body weight) for adults (World Health Organization, 2004). The large quantities of mercury that were administered would be expected to interrupt odontogenesis and amelogenesis in children.

The dental defects observed in these individuals do not resemble those that are caused by other infectious diseases, genetic conditions, vitamin deficiencies or elemental toxicities (Cahn, 1925; Reichart, 1976; Formicola et al., 1987; Chaussain-Miller et al., 2003; Ortner, 2003; Zambrano et al., 2003; Chaudhary et al., 2004; Boldsen, 2005; Dabernat and Crubézy, 2010; Kar et al., 2012; Roffey and Tucker 2012; Sunny, 2013; Davit-Beal et al., 2014; Bedić et al., 2015; Gerdolle et al., 2015; Hlavenková et al., 2015; Rogers et al., 2016; Zhou et al., 2017).

The dental abnormalities described in the European/Mediterranean pre-Columbian cases match 19th century clinical cases better than those described in the case from the New World. The number of cases from the Old World available in the literature search is limited. In archaeologically recovered skeletal samples subadult remains are often missing (Henneberg, 1977; Buckberry, 2000; Lewis, 2007), and even if present, and recovered by meticulous excavation they may be fragmentary. In collections from older excavations curation of juvenile skeletal fragments has not been optimal (Henneberg and Henneberg, 2002). Many congenital syphilis patients did not survive to adulthood. Had they survived in conditions promoting significant tooth wear, syphilitic signs could have been obliterated fairly early in life. Moreover, crowns of

molars affected by syphilis or its treatments are prone to caries due to malformed enamel. Once destroyed by caries, the occlusal surface cannot be diagnosed. Even in populations widely exposed to infection congenital syphilis incidence is low because a fetus can only be infected when the mother is in the contagious stage of the disease, and infection of the fetus occurs in late pregnancy. Infections in early pregnancy usually end in miscarriage (Lindstrand et al., 1993; Wallace et al., 2015). Furthermore, not all babies infected with congenial syphilis develop characteristic dental signs. Therefore, the probability of recovering signs of congenital syphilis in archaeological samples is very low. The following calculation can be made to support this statement. The incidence of congenital syphilis in European countries (European Centre for Disease Prevention and Control, 2017) is 3-5 cases per 1000 patients with syphilis, which translates to approximately 4 cases per 10 000 population because prior to introduction of penicillin about 10% of adults could have syphilis (Corbett-Smith, 1914). Considering that only 10-65% (Švejda, 1952; Lipski and Przylipiak, 1959; Goens et al., 1994; Hillson, 1996) of congenital syphilis sufferers develop dental changes, and that only about 50% of subadult skeletons are represented in skeletal collections a probability of finding dental signs of syphilis in a collection of archaeologically recovered skeletons is approximately 0.0001 that is one case per 10 000 skeletons. Since not all dental signs present in skeletal collections were published, it is no wonder that only a few cases were found in the literature.

Despite this reservation, the number of cases may be greater since not all of the cases recovered are fully published. However, they are already known from conference presentations. For example, syphilitic-mercurial teeth of two juveniles from Oplontis who died in the 79 AD eruption of Vesuvius were presented at two conferences (Henneberg et al, 2006; Henneberg and Henneberg, 2008), and are now being prepared for a full publication (Henneberg et al., 2017 in preparation). Fragmentary skeletons of the two 12-14 years subadults from Oplontis had most of their dentition preserved. Maxillary and mandibular incisors were affected by severe hypoplasia consisting of deep horizontal grooves and irregular pitting. Tips of canines were narrowed, and first molars of both individuals had reduced upper third of the crown with abnormal occlusal surface covered by irregular cusps and pits. Although the number of congenital syphilis cases from the Mediterranean is limited, their close match to pathognomonic dental traits well documented in the 19th century is sufficient to

strengthen the view advocating the presence of the disease in the Old World. Including the effects of mercury as a diagnostic method is very important for paleopathologists, as it can add more diagnostic traits of the disease and thus gives the opportunity to continue the discussion on the origin of syphilis.

5. Conclusions

The dental signs in the Mediterranean pre-Columbian individuals correlate stronger to well-established dental signs of congenital syphilis than those from the New World, suggesting that syphilis in the Old World may have originated earlier than the 15th century. Dental abnormalities linked to congenital syphilis may occur as (1) signs of the disease only, (2) signs of treatment only or (3) the combination of both. All abnormalities caused by congenital syphilis and its treatments should be used when making a diagnosis of the disease since they do not occur in any other disease.

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Chapter 8

SUMMARY/DISCUSSION, CONCLUSION AND FUTURE DIRECTIONS

Summary and Discussion

The research undertaken in this thesis has focused on documenting the use of mercury and its use as a criterion in the diagnosis of congenital syphilis. Dental abnormalities are important criteria used to make a diagnosis of congenital syphilis. The types of dental abnormalities currently used are those commonly seen in the upper central incisors, first permanent molars and permanent canines. Dental abnormalities in these teeth were first described and illustrated by Sir Jonathan Hutchinson, Henry Moon, and Alfred Fournier during the 19th century (Hutchinson, 1859, 1863, 1887; Moon, 1877; Fournier, 1886). Since their descriptions/illustrations, dental abnormalities caused by congenital syphilis itself have been the topic of discussion for decades until a dental criterion was established by Hillson and colleagues (1998) to facilitate differential diagnoses of congenital syphilis in skeletal remains. Having documented these dental abnormalities caused by the disease itself, Hutchinson also described and illustrated dental abnormalities caused by treatments of syphilis containing mercury, and compared them to the types of dental signs and variations caused by the disease itself (Hutchinson, 1878, 1887). Despite the descriptions and illustrations of dental signs caused by both congenital syphilis and its treatments, dental signs caused only by the disease itself were recognised by physical anthropologists/ paleopathologists/researchers and applied in their studies of skeletal remains. The effects of mercury have not been explored or discussed further since the 19th century, even though its use and side effects were recognised for centuries (Goldwater, 1975; Swiderski, 2008).

Firstly, this work investigated the types of dental variations associated with treatments of congenital syphilis containing mercury (Chapter 2). The results of this study highlight that mercury's influence on teeth produced distinct variations in dental morphology, and more importantly, these variations were different from those produced by the disease itself. Once dental variations of mercuric treatments were established, the remaining studies applied knowledge of these dental variations to individuals predating the use of antibiotics in Australian, British and American skeletal collections who contained individuals documented as having suffered from, or died from syphilis or syphilis related issues to determine whether these dental varieties were present (Chapters 3-7). The evidence from these studies showed that dental signs attributed to mercury were distinct, and resembled mercuric dental signs documented

and illustrated by Hutchinson. The results also indicated that the approximate age at which mercuric treatment was administered, the length of time during which treatment was given, and the age treatment ceased could be determined, all by considering timing of dental development. These factors also influence the severity of abnormalities in the dentition. Their possible impact on the development of supernumerary molars has been explored. Thorough investigations demonstrated the historical use of mercury, pointing out that mercury was relied upon during the pre-antibiotic period to control the spread of syphilis throughout the United States. This highlighted that investigating dental abnormalities attributed to mercury was important in in skeletons from modern American populations.

Given that the focus of previous research by other authors was on dental signs attributed to the disease, the aim of this work was to determine whether dental abnormalities produced by mercury could be found in skeletal collections and whether the effects of mercury could be used as a way to diagnose congenital syphilis. The results of this thesis demonstrate that these aims were achieved. This work described a variety of dental abnormalities which can be attributed to both the disease and its treatment. Evidence from these studies indicates that (1) dental abnormalities produced by mercury are significantly different from those produced by congenital syphilis and (2) mercury was used and relied upon as a form of treatment to control syphilis/congenital syphilis in the Western medicine until the introduction of penicillin. While variation of dental signs is known to occur in cases of congenital syphilis, variation can also occur in dental abnormalities produced by mercury. Influencing factors can include the kinds of chemical compounds used, amounts of mercury administered, time of administration and period during which treatment was administered.

Conclusions and Future Directions

Dental abnormalities produced by mercuric treatments are clearly diagnosable with the range of variations documented in this study. They can be attributed to the use of mercury to treat congenital syphilis, and no other conditions, as the therapeutic use of mercury for no other reasons was justified. Even though mercuric dental signs are variable, they are distinct, and they do not occur in individuals who suffered from conditions other than syphilis. Therefore, it can be concluded that dental signs attributed to mercury can safely be used as a criterion to diagnose congenital syphilis

either in combination with the standard (congenital syphilitic) dental criteria used, or on its own as the standard dental criterion (as established by Hillson and colleagues, 1998) does not always occur in every individual.

Avenues that can be followed in further studies include exploring dental signs of mercury in larger skeletal samples and collections as this could reveal the extent of mercury's use in various populations. The issue of whether mercury can be detected in tissues of adult individuals who suffered from congenital syphilis and were treated with mercury early in life, needs to be further investigated. Theoretically, bones undergo turnover, but enamel does not undergo turnover. Thus, mercury levels in the enamel should be at the levels at which it was originally administered, however, if mercury completely disrupts amelogenesis when mercury levels are high in the blood stream of a child, then no enamel is produced. Only when mercury levels are low in the body, amelogenesis begins again producing enamel. This is something that could be investigated in an animal model to determine the best way to detect levels of mercury in skeletal remains of congenital syphilitic individuals.

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Appendices

Words that will looked for in ancient texts include those below. These words have been selected to determine whether descriptions using these words can be associated with syphilis or congenital syphilis. Also, leprosy has been said to be cofused for syphilis in the literature.
.
English / Ancient Greek:

- leprosy: λεπρα
- leprosy: λεπρος α ον
- leper: λεπρός
- leprous: λεπρός, λεπρώδης
- white leprosy: λευκή λέπρα
- white disease: νόσος της λευκής
- scale, shell: λεπις ιδος η
- make white: λευκαινω
- white paplar; white leprosy: λευκη ης η
- be white: λευκανθιζω
- white blossoming; white; bleached: λευκανθης
- white: λευκε
- vulva: αιδοιον

- ulcer: έλκος
- scabies: ψώρα
- skin disease: ψωρίαση

Passages that have been found in ancient texts that may be related to congenital syphilis are below but are quite vague.

Passages

***Hippocrates,* vol.2, p.323**
Translation by W. H. S. Jones, (1923), William Heinemann, London

Dentition
VII:
οποσοισιν επι οδοντοφυιη πυρετος οξυς επιγιγιγνεται ολιγακις σπωνται

Translation
Those who while teething are attacked by acute fever seldom suffer from convulsions

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VIII:
οποσα οδοντοφυευντα ευτροφα μενει καταφορικα εοντα κινδυνος σπασμον επιλαβειν.

Translation
Those who while teething are lethargic while remaining well - nourished run a risk of being seized with convulsions.

Hippocrates vol. 4 '*Heracleitus on the universe'*
Translation by W. H. S. Jones, Litt, D (1931) William Heinemann LTD, London

Humours*: p. 89*
XIV:
ελκεα μαδαρα, μαλιστα στομα, αιδοιον, και ταλλα. ην δε βορειον, βηχες, φαρυγγες, κοιλιαι σκληροτεραι, δυσουριαι φρικωδεες, οδυναι πλευρεων, στηθεων.

Translation
South winds cause deafness, dimness of vision, headaches, heaviness, and are relaxing. When such winds prevail, their characteristics extend to sufferers from diseases. Sores are soft, especially in the mouth, the privy parts, and similar places.

Aphorisms, II, p. 119
XLV:

των επιληπτικων τοισι νεοισιν απαλλαγην αι μεταβολαι μαλιστα της ηλικιης, και των ωρεων και των τοπων, και των βιων ποιεουσιν.

Translation
Epilepsy among the young is cured chiefly by change –change of age, of climate, of place, of mode of life.

Aphorisms, III, p. 129
XX:
του μεν γαρ ηρος, τα μελαγχολικα, και τα μανικα, και τα επιληπτικα, και αιματος ρυσιες, και κυναγχαι, και κορυζαι, και βραγχοι, και βηχες, και λεπραι, και λειχηνες, αλφοι, και εξανθησιες ελκωδεες πλεισται, και φυματα, και αρθριτικα.

Transation
In spring occur melancholia, madness, epilepsy, blood flux, angina, colds, sore throats, coughs, skin eruptions and diseases[1], eruptions turning generally to ulcers, tumours and affections of the joints.
1 It is not possible to translate the Greek terms for various skin diseases, as modern classification is so different from ancient.

Aphorisms, V, p. 163
XXII:

το θερμον εκπυητικον, ουκ επι παντι ελκει, μεγιστον σημειον ες ασφαλειν, δερμα μαλασσει, ισχναινει, ανωδυιον, ριγεων, σπασμων, τετανων παρηγορικον. των δε εν κεφαλη καρη βαριην λυει. πλειστον δε διαφερει οστεων κατηγμασι, μαλλον δε τοισιν εψιλωμενοισι, τουτων δε μαλιστα, τοισιν εν κεφαλη ελκεα εχουσι. και οκοσα υπο ψυξιος θνησκει η ελκουται, και ερπησιν εσθιομενοισιν, εδρη, αι δοιω, υστερη, κυστει, τουτοισι το θερμον φιλιον και κρινον, το δε ψυχρον πολεμιον και κτεινον.

Translation
When heat causes suppuration, which it does not do in the case of every sore, it is the surest sign of recovery; it softens the skin, makes it thin, removes pain and soothes rigors, convulsions and tetanus. It relives heaviness of the head. It is particularly useful in fractures of the bones, especially when they are exposed, and most especially in cases of wounds of the head. Also in cases of mortification and sores from the cold, of corroding herpes, for the seat, the privy parts, the womb, the bladder - for all these heat is beneficial and conduces to a crisis, while cold is harmful and tends to a fatal issue.

Aristotle, vol 1, *Problems*
Translation by W.S Hett, (1936) William Heinemann Ltd, London

Problems, X, 4, pg. 207

δια τι οι παιδες και αι γυναικες ηττον εχουσι λευκην των ανδρων, και των μεν γυναικων αι πρεσβυτιδες μαλλον; μ οτι η λευκη εστι πνευματος εξοδος, εστι δε τα μεν των παιδων ουκ ευπνοα σωματα, αλλα πυκνα, και τα των γυναικων ηττον η τα των ανδρων. εις τα καταμηνια γαρ τρεπεται. δελοι δε η λειοτης την πυκνοτητα της σαρκος. τα δε των πρεσβυτερων και των γραων ευπνοα. μονα γαρ, ωσπερ τα παλαια οικοδομηματα, διεστωσαν εχει την συνθεσιν των μοριων.

Translation
Why do boys and women suffer less from white leprosy than men, and old women more than young ones? Is it because leprosy is an escape of breath, and the body of boys are not well ventilated but are thick, and those of women are less well ventilated than those of men? For the breath is absorbed in the menses; the smoothness shows the thickness of the flesh. But the flesh of older men and of old women is well aired; for they alone like old buildings have gaps in the construction of their parts.

Problems, X, 33, pg. 225

δια τι λευκη ου γινεται τοις αλλος ξωοις; ποτερον οτι τοις μεν αλλοις νοσημα, τοις δε ανθρωποις γινεται διακευκα τα δερματα και αι τριχες αυτων; αλλ ομως απορησειεν αν τις δια τι υστερον ου γινεται, αλλ εκ γενετης η ποικιλια. η οτι τα δερματα των αλλων ζωων σκληρα, ανθρωβος δε φυσει λεπτοδερμοτατον; η δε λευκη πνευματος εστιν εκκρισις, ο κωλυεται δια την πυκνοτητα εξιεναι οις αλλοις ζωοις του δερματος.

Translation
Why does not leprosy occur in any animal except man? Is it that the disease does affect other animals, but that only in man does the skin and hair become white? Yet one might wonder why it does not only become so later on, but that the variation in colour takes place from birth. Or is it because the skin of other animals is hard, but man is naturally very thin skinned? Now leprosy is an expulsion of the breath, which is prevented by the thickness of the skin from escaping in other animals.

Problems, X, 34, pg. 225

δια τι δε εν μεν τη λευκη πολιαι γινονται, οπου δε πολιαι, ουκ αει λευκη; η διοτι αι τριχες εκ του δερματος εισιν, η δε πολια ωσπερ σαπροτης τις των τριχων εστιν; οταν μεν ουν το δερμα καμνη, αναγκη και την τριχα εξ εκεινου ουσαν καμνειν. οταν δε η θριξ, ουκ αναγκη το δερμα.

Translation
Why is it that in leprosy the hair turns grey, but that there is not always leprosy where there is grey hair? Is it because hair grows from the skin, but grey hair is a kind of decay of the hair? So when the skin grows weak, the hair that grows from it must also be weak, but when the hair is weak, the skin need not necessarily be so.

Words Searches (HB 2017)

Perseus/English (http://www.perseus.tufts.edu/)

illness (11x)
Pliny *Inquiry into Nature*
22.61 tendency to phthisis (emaciation) after a long illness; phthisis (27x, often related to lungs):
22.34 ruptures;
22.61 more useful when there is a tendency for phthisis after long illness;
28.67 the cure of phth. is wolf's boiled liver;
36.28 good for phth. and with honey it causes old sores to cicatrize, …

remedy (332): e.g.
in Pliny *Inquiry into Nature*
20.50; 20.53; 20.82; 22.21 (remedy for ulcers);
24.92 "the juice [of the Aron plant] is a marvelous cure for ulcers of every kind, whether phagedænic, carcinomatous, or serpiginous";
26.79 corrosive ulcers;
28.46 applied to ulcers of the head;
289.32 ulcerous sores;
29.39 ulcerations of the ears;
32.28 ulcerations of the mouth;

35.52 … heals ulcerations of the mouth, pimples and pruriginous erruptions

leprosy: Hdt. 1.138; Hippocrates Aph. 3.20; Prrrh. 2.43; Epid. 5.9 Morb. 1.3; Epid. 5.9

scale, shell: epithelial debris Hipp. Aphorisms 4.81; layer of skull Pmed in Arch pap. 4.270

syphilis?: *siphlos*: blemish, defect || *suphilos*: 'pig-lover' > siphlis (BHM 1955)

abscesses Pliny 23.24 signs of fever, for inveterate fluxes, ulcerations, ruptures, spasms, suppurated abscesses, debility of sinews, flatulency, cough, asthma 24.34; 26.79 cures for abscesses and hard tumors; 27.109, 113

cancer: (18) 20.33 cancer which is incurable by any other means; 22.72 … honey v. good for gangrenous sores; 73 arrests cancer of the nose …

Readings

TEMKIN, OWSEI. on epilepsy **Bulletin of the Institute of the History of Medicine; Baltimore, Md.** 1 : 277.

St Marys Cemetery

Burial No.	Age at Death (yrs)	Sex	Dentition
82	1.5	Male	Maxilla: Deciduous left and right central and lateral incisors, right first deciduous molar, left and right second molar germs in crypt. Mandible: Left and right central deciduous incisors, left and right canine germs in crypt, left and right first molars, left and right second molar germs in crypt, and first permanent molar germs in crypt just visible. Loose teeth: First permanent molar germ. No hypoplasia.
41	1.5	Male	Maxilla: Right canine germ in crypt, left and right first deciduous molars, left and right second molar germs in crypt. Mandible: Left first deciduous molar, second molar germ in crypt and left first permanent molar germ in crypt. Loose teeth: Two second deciduous molar germs, one central incisor, two deciduous lateral incisors, three canine germs, one permanent incisor germ. No hypoplasia.
40	1.5	Male	Mandible: Deciduous right and left canines in crypt, left and right deciduous first molars. Left second deciduous molar germ in crypt. Loose teeth: left and right central incisors, lateral left incisor. One first deciduous molar. One lower central incisor, left and right lower lateral incisors. Two canines. Three deciduous second molar germs. Three permanent incisor germs, three first permanent molar germs, and parts of a fourth first permanent molar germ present. No hypoplasia.
32	1.5	Female	Maxilla: Deciduous left and right central and lateral incisors, left and right canine germs, first deciduous molars, and second left deciduous molar germ in crypt. Mandible: Left and right central and lateral incisors, right canine germ in crypt, left and right first deciduous molars, left and right second deciduous molar germs in crypt. Left permanent molar germ in crypt. Loose teeth: Three permanent incisor germs, three permanent first molar germs. One canine germ split in half. No hypoplasia evident.

8	1.5	Male	Maxilla: Deciduous left and right central incisors, left and right canines and first molars. Second deciduous molar germs in crypt. Right first permanent molar germ in crypt. Mandible: Left and right central and lateral incisors, left and right deciduous canine germs in crypt. First deciduous molars. Second deciduous molar germs in crypts. Right first permanent molar germ visible. Loose teeth: Two permanent molar germs. No hypoplasia.
11	1.67 (20 mo)	Female	Maxilla: Deciduous left and right central and lateral incisors, left and right canines, and first molars. Mandible: Deciduous left and right central and lateral incisors, left and right canines, left and right first deciduous molars and left second molar germ nearly fully erupted. Left first permanent molar germ. Loose teeth: Two second deciduous molars, three first permanent molars germs. One isolated pit on the right canine. No other enamel hypoplasia.
58	1.5-2	Male	Maxilla: Deciduous left and right central and lateral incisors, left canine, right first deciduous molar, left and right second deciduous molar germs in crypt. Left and right first permane t molar germs in crypt. Morphology of right first deciduous molar is unusual. Mandible: Deciduous left and right central and lateral incisors, right canine, left and right first molars, left and right second molars. Left and right first permanent molar germs in crypt just visible. No hypoplasia.
27b	1.5-2	Male	Deciduous teeth: Maxilla: Left and right central and lateral incisors, left and right canines, right first molar, right second molar germ in crypt. Mandible: Only the right-side present. Lateral incisor, canine, first molar, second molar germ in crypt, first permanent molar germ in crypt. Loose teeth: Three first permanent molar germs, three permanent incisor germs, deciduous incisor, deciduous canine and a first deciduous molar and two deciduous second molars. No hypoplasia.
24	1.5-2	Female	Maxilla: Deciduous left and right central and lateral incisors, left and right canines, first

			deciduous molars and second deciduous molar germs. Mandible: Left and right central and lateral incisors, left and right canines, first deciduous molars, and second deciduous molar germs in crypt. First permanent molar germ in crypt. Deciduous maxillary first molars have unusual morphology. Loose teeth: Two first permanent molar germs. No hypoplasia.
31	3-4	Male	Maxilla: Deciduous left and right central and lateral incisors, left and right canines, left and right first and second molars. Left and right first permanent molar germs in crypt. Mandible: Deciduous left central incisor, left and right lateral incisors, left and right canines, left and right first and second molars, left first permanent molar germ in crypt. Loose teeth: First permanent molar germ. No forms of hypoplasia present, minor discolouration of teeth.
4	3-4	Male	Maxilla: Deciduous left central incisor, left and right lateral incisors, left and right canines, left and right first deciduous molars, right second molar. First left and right permanent molar germs in crypt. Mandible: Deciduous left and right central and lateral incisors, left and right canines, left and right first and second molars. Left and right permanent first molar germs in crypt. Crypt of permanent second molars are empty. No hypoplasia is present.
75	5-6	Male	Maxilla: Left and right first permanent incisor germs in crypt. Left deciduous canine, first and second deciduous molars, first permanent molar in germs in crypt not fully erupted. Left and right first permanent molar germs present. Mandible: Deciduous canines, left and right first and second molars, permanent left and right molar germs not fully erupted. Permanent second molar germs in crypt, just visible. No hypoplasia on deciduous teeth. Loose teeth: Deciduous upper central and lateral incisor, and deciduous lower incisor.
19	8	Indeterm	No maxilla. Mandible: Left central incisor, left and right lateral insicors, left and right canine germs in crypt, left and right first and second deciduous molars, left and right first permanent molars, right permanent second molar germ

			present. One isolated pit on the middle third of the lateral right incisor crown. No other forms of hypoplasia present or Hutchinson, Moon or Fournier teeth.
52b	10	Male	Maxilla: All teeth present except left lateral incisor and left and right M3. Mandible: Left and right central and lateral incisors, left and right canines, left and right first premolar germs, left and right second deciduous molars, first left and right permanent first molars. Second permanent molars nearly fully erupted. Loose teeth: Four deciduous first molars, and two deciduous second molars.
70	8-10	Male	Maxilla: Mixed dentition present. Only tooth missing is right central incisor. Left lateral incisor, partially erupted left and right lateral incisors, deciduous canines, left and right first and second premolars, first permanent molars, and second permanent molar germs. Maxillary left central incisor has rounded mesial and distal edges. Incisal edge is crescentic in shape. Both linear (three lines) and pitting hypoplasia is evident on the left central incisor. Enamel of incisal edge is thin. A round indentation is present on the lateral incisors. Left lateral incisor has a central pit 1mm in diameter. Deciduous canines are hypoplastic and discoloured. Premolars are normal. Permanent M1s are severely hypoplastic. There is a clear demarcation between healthy and diseased enamel. M1s appear dirty, pitted. Carious lesions present on mesial half of occlusal surface of right M1 and on occlusal surface of left M1. Pitting evident on palate stemming from right M1. Mandible: Central and lateral permanent incisors, deciduous canines and first and second deciduous molars, first permanent M1, and second permanent molar germs. All incisors have small mamelons and linear and pitting hypoplasia that appear at the same level. Canines are conical in shape and are hypoplastic 2/3rds of the crown. A distinct demarcation between diseases and healthy enamel is evident. Second deciduous molars demonstrate carious cavities. First permanent molars resemble maxillary M1s. Carious cavities evident in both M1s. Morphology of M2 germs appears normal.

51	10-11	Female	Maxilla: Left and right permanent central incisors, right lateral permanent incisor, right permanent canine, right first premolar, left and right M2. Mandible: Left lateral incisor, left first premolar, left M1, right deciduous molar. Loose teeth: Deciduous left and right central incisors, one lower incisor, one canine, and one second deciduous molar. Permanent teeth: Left lateral incisor, two canines, two lower incisors, four premolars, four permanent second molar germs.
28	12-13	Male	Maxilla: Left and right central and lateral incisors, left canine, left and right first and second premolars, M1s, and M2s. Hypoplasia on middle and cervical portion of anterior upper and lower teeth. Mandible: All teeth present (central, lateral incisors, canines, first and second premolars, M1s, and M2s). M3 not present. No Hutchinson, Moon or Fournier teeth.
79	16-18	Female	Maxilla: All teeth present except right M1. Left and right M3s in crypt. Looks like wholes have been drilled in between central right and lateral incisor and central left and lateral incisor. Mandible: All teeth present except left second premolar, and first M1. Left and right M2 germs in crypt. LEH evident on anterior teeth.
5	25-30	Female	No maxilla. Mandible: One left premolar only. Most of alveolar bone has completely healed. Loose teeth: Three mandibular incisors, one canine, one premolar. No LEH.
66b	30	Female	Maxilla: Left central incisor, left and right lateral incisors, left canine, right first and second premolars, left and right M2s. Mandible: Left and right central and lateral incisors, left and right canines, left and right first premolars, right second premolar. LEH is evident on the middle and cervical thirds of the central incisor crown. LEH and pitting hypoplasia evident on the anterior mandibular teeth.
53c	28-32	Female	Maxilla: Left and right canines. Mandible: Left canine and right M1. Loose teeth: Left and right central incisors, one lower incisor, one premolar, one permanent molar, and two roots

			with no crowns. Most of the alveolar bone has healed except where the anterior teeth would be.
73	30-35	Male	Maxilla: Left and right central and lateral incisors, canines, left second premolar, right M1 and left M3. Right M1 is severely worn. Mandible: Left and right ventral and lateral incisors, canines, and first and second premolars. Alveolar bone where other teeth would be is healed. No LEH. No Hutchinson, Moon or Fournier teeth.
9	38-40	Male	Teeth present: Maxilla: Left central and lateral incisor, canine, first and second premolar and M1. Right lateral incisor, and M1. Mandible: Only left side present. Lateral incisor, canine, first and second premolars, M1 and M2. M3 appears to have been extracted due to healed alveolar bone. Loose teeth: canine, lower incisor, root (possibly of lower incisor and enamel of what appears to be a lower incisor. No hypoplasia of any kind. No Hutchinson, Moon or Fournier teeth.
61	40-45	Female	Maxilla: Second left premolar. Mandible: Left canine and left second premolar. Alveolar bone has completely healed except for bone where anterior teeth would be. No hypoplasia, Hutchinson, Moon or Fournier teeth.
78	40-45	Male	No maxilla. Mandible: Most of alveolar bone has completely healed except bone where premolars and canines would be. Loose teeth: Two incisors, one premolar, one molar. Loose teeth have severe wear with dentine exposure.
6	45	Male	Maxilla: All teeth present except right central incisor and third molars. Severe wear on all teeth. Mandible: All teeth present except left second premolar, and left M1. No third molars. No hypoplasia, Hutchinson, Moon or Fournier teeth.
83	45-50	Male	Maxilla: Both central incisors, left and right lateral incisors, left canine, left and right first premolars, right second premolar, left M2, left and right M3s. Left and right M1s extracted as alveolar bone completely healed. Mandible:

			Right central and lateral incisors, right canine, first premolar, M2 and M3. Left canine, first premolar, M2 and M3. Severe wear on M2 and M3. LEH on left central incisor on cervical portion of crown. Pitting and LEH on the lower incisors, canines and first premolars on cervical portion of crown. No Hutchinson, Moon or Fournier teeth.
57	45-50	Male	Maxilla: All teeth present except left central incisor, premolars, canine and left M3. Mandible: All teeth present except central right incisor and right M3. No hypoplasia on any teeth, however there is extensive wear.
10	45-50	Female	No maxilla. Mandible present but no teeth. No teeth present at all.
59	48-52	Male	Only loose teeth present. LEH on middle third of maxillary central incisors and canines and on two mandibular incisors.
23	43-58	Male	No maxilla. Mandible: Central and lateral incisors, first premolars, left second premolar, and left M3. Loose teeth: Four incisors (possible but difficult due to severe wear), two premolars, four molars, 1 root of a molar with small portion of a crown, one root of an anterior tooth. LEH on cervical portion of mandibular anterior teeth. No Hutchinson, Moon or Fournier teeth.
72	45-50	Male	Maxilla: All teeth present except one M3. Mandible: All teeth present except right central incisor. Loose teeth: One upper M3. No hypoplasia, Hutchinson, Moon or Fournier teeth.
85	45-55	Male	Maxilla: No teeth. Mandible: Left lateral incisor and left canine. Both have wear.
68	55	Male	Maxilla: Right lateral incisor, left and right canines, left and right first premolars, left second premolar, right M2 and right M3. Right second premolar and M1 extracted during life as alveolar bone has healed to some degree but not completely. Mandible: All teeth present except right central incisor, left canine and left and right M1. Both M1s extracted during life, left side of alveolar bone healed more so than

			right side. No form of hypoplasia present and no Hutchinson, Moon or Fournier teeth.
63	50-60	Male	Maxilla: No teeth present. Mandible: Left and right central incisors, and left lateral incisor. No form of hypoplasia, Hutchinson, Moon or Fournier teeth.
14	50-60	Male	No maxilla is present. Mandible present but with no teeth. Only one loose premolar and root of what appears to be a lower incisor. No Hutchinson, Moon or Fournier teeth.

Smithsonian Institute, Washington, DC

CAT. NO.	SEX	AGE	YR BORN	YR DIED	PATH TYPE	CAUSE OF DEATH	HUTCHINSON'S INCISOR	MOON'S MOLAR	FOURNIER'S MOLARS	DENTAL OBSERVATIONS AND OTHER NOTES	SYPHILITIC/ MERCURIAL/ SYPHILITIC-MERCURIAL DENTAL
654					Congenital		N	N	N		
1207					Congenital		N	N	N		
1208					Congenital		N	N	N		
1215					Congenital		N	N	N		
1362					Congenital		N	N	N		
213	M	31	1893	24/05/1924	Treponemal Cong	Nephritis (with pus filled fistula in scrotum).	N	N	N	Right incisor incisal third of crown enamel is missing and LEH present. May be mercurial. Left incisor missing. Upper right M1 extracted (bone healed). Left M1 cusps completely worn down. Lower M1s extracted as bone has healed.	
679	F	33		26/12/1928	Treponemal Cong	TB	N	N	N	Maxilla: All teeth present except left M3. Central incisors have hypoplastic defects on middle third of crown (oval in shape) and pitting. LEH on cervical portion of crown. Lateral incisors peg like in shape with some pitting. Canines have pitting. Left and right M1s have some cuspal pattern visible but have abnormal enamel and are hypoplastic (pitted). Mandible: Left and right central and lateral incisors, and canines, left M2 and right M3 present. All incisors are notched and have linear enamel hypoplasia and pitting at the same level across all four teeth. The incisors of all incisors are notched. Canines and first premolar, left M2, and right M3 present with normal morphology. Second premolars, right and left M1s, right M2 and left M3 extracted, as alveolar bone healed.	Evidence suggests that dental signs are attributable to mercuric treatments.

707	M	26	1903	20/05/1929	Treponemal Cong	TB	N	N	N	Maxilla: Left and right central and lateral incisors, canines, fight and second premolars, left and right M1s, M2s, M3s. Mandible: Left and right central and lateral incisors, left and righ canines, first and second premolars, left and right M2s, left M3, right M3 represented by root only, and left M4. Incisal edges of maxillary central incisors are normal with isolated pits. Portion of iincisal third and middle third of central incisor crowns deomonstrate progressively severe defects and stop suddenly. Some black pits are evident. Cervical portion of crown is normal. Very clear demarcation between affected and healthy enamel. Similar type of hypoplasia on the left lateral incisor and left canine appear at the same level on both teeth. A portion of the crown of the right lateral incisor has broken off at the same level where the hypoplasia ends on the left lateral inisor. No enamel on right canine at all. Isolated pits on the second premolars but normal morphology. Maxillary M1s show some normal groove pattern but have a hypoplastic occlusal surface with pitting. Isolated pits on the second premolars. Crenulation on occlusal surface of M2s and isolated pits. Isolated pits on M3s. Mandibular incisors demonstrate hypoplasia on two thirds of the crown at the same level. LEH on the cervical portion of the crowns. Severe hypoplasia also evident on the lingual side of anterior teeth at the same level. Left and right M2s show crenulation. Left M3 appears large than other molars and is tilted. Left M4 has normal molar morphology, but is smaller in size.	Evidence suggests that dental signs are attributable to mercuric treatments.
286					Treponemal		N	N	N		
347					Treponemal		N	N	N		
969					Treponemal		N	N	N		
1024					TB		N	N	N		
1043					TB		N	N	N	Maxillary alveolar bone receeding above left central incisor. No LEH.	
1057					TB		N	N	N		
1093					TB		N	N	N	Has all teeth, and appear normal.	
1132					TB		N	N	N		
1185					TB		N	N	N		

1255					TB		N	N	N	Pitting on the palate, more extensive near secone premolar.	
1256					TB		N	N	N	Pitting in palate.	
1285					TB		N	N	N	No maxillary M1s. Mandibular right M1 has decay. No LEH.	
1604					TB		N	N	N	Alveolar bone resorbtion in maxilla where left lateral incisor and left canine would be.	
930					Rickets		N	N	N		
962					Rickets		N	N	N		
1029					Rickets		N	N	N		
1171					Rickets		N	N	N		
675					Periostitis		N	N	N		
706					Periostitis		N	N	N		
878					Periostitis		N	N	N		
938					Periostitis		N	N	N		
1437					Periostitis		N	N	N		
1531					Periostitis		N	N	N		
17R					Periostitis		N	N	N		
219398				Atopsied Howard University Medical College 1903.	Congenital	Not listed	May be early stage of Hutchinson incisor in right central incisor.	N	Y	Maxilla: left and right central and lateral incisors, canines, and first premolars. Left premolar is present, while right premolar represented by root. Left and right first M1s present and right M2. Left M2 extracted. Right central incisor has thin enamel along the incisal edge forming a cresentic pit which may be early stage of Hutchinson incisor. Left central incisor has some pittin galong incisal edge. Lateral incisors are peg like in shape. Carious lesion on distal portion of left first premolar. M1s have pitting hypoplasia, and grooves cut into the occlusal surface resembling Fournier's molars. There is some discolouration from the middle third of the crown to the cervical third of all teeth. Mandible: Left and right central, and lateral incisors, right canine, left and right first and second premolars, left and right M1s, M2s and root of right M3. Left M3 extracted, and alveolar bone nearly completely healed. Central incisors are hypoplastic with dentine exposure on the 1/4 of the crown from the incisal edge. Central and lateral incisors are incorrectly placed in mandible. Mandibular M1s have a reduced surface, are pitted and have multiple tuberclues resembling Fournier's molar.	Evidence suggests syphilitic dental abnormalities.

249552	F	Infant			Congenital	Macerated at Museum 1908, Baltimore, MD from F.P. Mall (J.	N	N	N	Mandible: Deciduous right central germ, left and right leteral incisor germs. Loose teeth: Deciduous incisor, canine and three molar germs. Incisor germ has LEH (two line) on the cervical third of the crown. LEH (one line) also appears on the cervical third of the canine germ.	
1207					Fracture		N	N	N		
161	F	45				Not listed				Maxilla: Left and right central and lateral incisors and canines, left and right first premolars, left second premolar, right first M1, left and right M2s and M3s present. All anterior teeth Left (canine to right canine) are severely hypoplastic. LEH is present on all anterior teeth that cross at the same level. Dark coloured pits also run along the crowns at the same level. Pitting hypoplasia also present on anteria teeth. LEH is also on lingual aspect of anterior teeth at the same level coresponding to labial surface of crown. Right M2 has large carious lesionon disto aspect of occlusal surface. Mandible: Left and right lateral incisors, and canines, left and right first and secons premolars, M2s and left M3. LEH and pitted hypoplasia on lateral incisors and canines on both labial and lingual surfaces at the same levels. Second premolar tilt inward. M3 has a carious lesion on the mesio-lingual aspect of occlusal surface.	Evidence suggests that dental signs are attributable to mercuric treatments.
11R	F	24			Syphilis	Lobar pneumonia	N	Y	N	Diagnosed with syphilis in 1930 and was institutionalised until her death, 11yrs and 2months later. Maxilla: Right canine, left and right first and second premolars, left and right M1s, M2s and M3s. Canine and premolars have normal morphology. Right M1 has a reduced occlusal surface, some pitting and is dome like in shape resembling Moon's molar. Left M1 is destroyed by caries. M2s and M3s have normal molar morphology but M3 has a carious lesion on the disto buccal portion of occlusal surface. Mandible: Left lateral incisor, left canine, left and right first premolar, left second premolar, left and right M2s and M3s. Left second premolar, left M2 and M3 are destroted by caries.	Evidence suggests Syphilitic dental abnormalities.

Cleveland Museum of Natural History, Cleveland, Ohio

SPECIMEN	CAUSEDEATH	SYNCLINK	Cadaver Age	Sex	Race	Skull	PC		Teeth present/ Dental Caries	Hutchinson Incisor	Moon's molar	Fournier's molar	Supernumerary teeth	Left humerus length	Right Humerus length	Right Femur length	Left Femur length	Carries sicca Y/N	Periosteal lesions	Other notes
HTH 1450	CONGENITAL LUES		0	F	W	N	N	n/a												
HTH 1867	CONGENITAL LUES		0	M	W	Y	Y	skull not in collection												
HTH 1963	SYPHILIS		0	F	B	N	N	n/a												
HTH 2124	SYPHILIS		0	M	B	N	N	n/a												
HTH 2131	CONGENITAL SYPHILIS		0	F	W	N	N	went back to family												
HTH 2008	CONGENITAL LUES		1	M	B	N	N	n/a												
HTH 0698	SYPHILIS		22	M	B	Y	Y		No dental caries in maxillary teeth. No linear or pitted enamel hypoplasia on incisors or other maxillary teeth or mandibular teeth. One central mandibular incisor missing as well as lower canines and one lateral incisor. Normal tooth morphology in mandibular teeth.	n	n	n	n					n		

HTH 1923	LUES		22	M	B	Y	Y		Maxilla: Anterior teeth broken or missing. One canine (loose) appears normal. Left first and second premolars present Left 1st molar and 3rd p molar present. Left 2nd molar missing. Right 1st molar missing, 2nd and 3rd molar present. All teeth present have normal tooth morphology. All mandibular teeth present but 1st and 2nd permanent molars. 3rd molars present. Central incisors have broken in half. No enamel hypoplasia and normal tooth morphology.	n	n	n	n					n		Thinning of vomer, ethmoid, orbits and temporal bone and maxilla.
HTH 2241	AORTIC INSUFFICIENCY		22	F	B	N	N			n	n	n	n					n		

HTH 1586	LUETIC MENINGITIS		23	M	B	Y	Y		All maxillary teeth present. All have normal tooth morphology. 2 lines of linear enamel hypoplasia present on central and lateral incisors and both left and right canines. First linear enamel hypoplasia line is 6.41mm from incisal edge of left central incisor, 2nd line is 9.30mm from incisal edge. Right c incisor 1st line is 6.14mm and 2nd is 8.79mm. Lateral left 1st, 7.19mm 2nd 8.81mm. Right lateral incisor 1st line is 6.86mm 2nd 9.11mm. Mandibular teeth present other than left and right first permanent molars and right second perm molar. Alveolar bone has healed. Right central and lateral incisor and half on canine teeth are broken. Left second molar has severe caries on three quarters of occlusal surface.	n	n	n	n					n		Extreme thinning of ethmoid and orbital bone, palate and vomer

HTH 0458	LEUTIC MYOCARDITIS		25	M	B	Y	Y		Maxilla: Central and right lateral incisor, right canine, roots only present for the first right and left premolar. All other teeth have normal tooth morphology. No linear or pitting hypoplasia. 3rd p molars don't appear to have erupted. No caries. Mandible: Right central and lateral incisors and left lateral teeth broken. Left central incisor, left and right canines and left and right premolars and second left premolar present. Morphology of all teeth are normal. Right second premolar, both 1st, and 2nd p molars extracted. Alveolar bone of 1st molar healed. Bone of 2nd molar still open. 3rd molars not erupted. No enamel hypoplasia's.	n	n	n	n					n

HTH 0933	LUES		28	F	B	Y	Y		Left first p molar has severe dental carie covering nearly the entire occlusal surface. Right 1st p molar has normal molar morphology. Left lateral premolar normal morphology is normal. All other maxillary teeth are broken. Both second molars extracted. Right side of alveolar bone healed, left side of alveolar bone not healed, very porous. Extracted later on in life. Third P molars possibly extracted also. Bone fully healed. Mandible: Central and lateral incisors, canines, left and right premolars and left 3rd molar present. All have normal tooth morphology. 3rd p molar has interproximal carie on distal side. Right side of alveolar bone, not fully healed.	n	n	n	n					n		

HTH 1059	LUES		28	F	W	Y	Y			n	n	n				n	Thinning of nasal bone and in orbital cavity.
								Maxilla: Right 1st P molar has 2 large caries one on the mesio buccal end approx. 5.21mm in length. Second carie on lingual buccal end of crown 6.80mm in length. Second right molar has caries in similar position as in first p molar. Second premolar missing. All molars have normal molar morphology. Other teeth have normal tooth morphology. No linear enamel hypoplasia on Central incisors. Left C incisor has one minor pit on left side. Left lateral incisor is peg shaped. Right c incisor is broken, most likely post mortem. Right lateral incisor is gold tooth. Mandible: All lower incisor present. two lines of linear enamel hypoplasia seen. First line approx. 4.43mm from incisal edge, second 6.68mm away from incisal edge. First and second Permanent molars missing, bone fully resorbed. 3rd right molar								

present with cavity B-D side. All teeth have normal tooth morphology.

HTH 1294	AORTIC INSUFFICIENCY		28	F	B	Y	Y		Maxillary central incisors missing. Hole in palate behind left central incisor measuring approx. 3.43mm wide. Only root present in left upper M1 and half of root of right M1. All teeth have normal tooth morphology. No pitting or enamel hypoplasia. All mandibular teeth present other than left and right first permanent molars and left second premolar. No enamel hypoplasia.	n	n	n	n			n	Thinning of ethmoid bone, vomer, orbits, maxilla, palate, temporal bone

HTH 2086	LUETIC MYOCARDITIS		28	F	B	Y	Y		Maxilla: All teeth present but lateral incisors. Left 1st premolar buccal enamel surface has come off post mortem. All tooth morphology of teeth is normal, however first central right incisor appears to have a crescentic notch along the incisal edge but may have been caused post mortem. No caries present. Linear enamel hypoplasia present on central incisors and canines 2/3rds up the crown approx. 7.81mm from incisal edge of both incisors and 6.58mm on left canine and 6.51mm on right canine. Mandible: All teeth present but third molars. Alveolar bone on left side (3rdmolar) not healed. Morphology of teeth are normal. No caries. Minor linear enamel hypoplasia on all incisors and canines on cervical 1/3rd of crown.	n	n	n	n					n		Thinning of ethmoid, orbits. Destruction of vomer.

HTH 2381	LUES		29	F	B	Y	Y		Maxilla: All teeth present but first left P molar. Left 1 and 2nd premolars broken. All teeth have normal tooth morphology. No enamel hypoplasia at all. Alveolar bone of missing 1st p molar has healed.	n	n	n	n					n	Unusual symmetrical holes in ethmoid bone approx. 6.02mm on right side. 6.76mm on the left side opposite right. 4 other holes on left side. Lyman says it may be extra foramina due to very thin bone. Bone on left thinner than on right.	Destruction of ethmoid, orbits, thinning of vomer and maxilla.
HTH 1270	PARALYSIS OF THE INSANE		31	F	B	Y	Y		Maxilla: Central and lateral incisors, left 3 molar and 3rd right p molars missing. 2nd right molar entire occlusal crown is missing. All teeth have normal tooth morphology. No linear or pitting hypoplasia. All mandibular teeth but 2nd and 3rdmolars present. Right side of alveolar bone healed, left has not fully healed. Tooth morphology is normal. Some wear on the buccal distal aspect of 1st p molars.	n	n	n	n					n		No

HTH 1876	LUES		31	M	B	Y	Y		All maxillary teeth present but right 2nd premolar and first premolar. All tooth morphology normal. Caries on 2nd left (disto-Lingual) and possibly 3rd right disto-lingual aspect. Left central incisor broken post mortem. Left lateral incisor is gold. Linear enamel hypoplasia on right central and lateral incisors on 2/3 of crown.M1s missing. All mandibular teeth present except for left 2nd premolar and 1st p molar. alveolar bone of 1st p molar healed. All teeth have normal tooth morphology. No enamel hypoplasia. Caries on 2nd premolar disto-lingual side and on 2nd p molar disto-lingual aspect.	n	n	n	n					n		Thinning and destruction of ethmoid bone and orbits and maxilla.
HTH 2516	LUES		31	F	B	Y	Y			n	n	n	n					n		No thinning of ethmoid, orbits, maxilla and resorption of maxilla.

HTH 0638	SYPHILIS	1M	33	M	B	Y	Y		Maxilla: All teeth have normal morphology. Central and right lateral incisor are broken, possible post mortem. Dental wear on left P molar is more extensive than on left 1st p molar. Second p molar has 3 cusps. No linear or pitted enamel hypoplasia. Mandible: all teeth, normal tooth morphology. Central left incisor broken, lateral incisor missing. Right canine broken.	n	n	n	n					n		
HTH 0990	GENERAL PARALYSIS OF THE INSANE		33	M	W	N	N			n	n	n	n					n		
HTH 1739	GENERAL PARALYSIS OF THE INSANE		33	F	W	Y	Y		No teeth at all. Upper and lower alveolar bone completely healed.	n	n	n	n					n		Thinning of palate, vomer, ethmoid, orbit, maxilla and spots of temporal bone.
HTH 1851	SYPHILIS		33	M	B	Y	Y			n	n	n	n					n		
HTH 2944	SYPHILIS		33	M	B	Y	Y			n	n	n	n					n		Destruction of vomer, thinning of ethmoid, orbits, maxilla, temporal bone.

HTH 1037	LUES		34	M	B	Y	Y		Maxilla: Lateral incisors and canines. Left and right M1s and M2s. All premolars and M3 extracted as alveolar bone completely healed where premolars were and reasonable healed where M3s were. Mandible: All teeth present except right M2 and M3 and left M3. Maxillia: Enamel on teeth removed so cannot tell if hypoplasia present. Mandibular: Minor linear enamel hypoplasia on anterior teeth of mandible towards cervical third of crown. M1 on left side looks mulberry in shape with a large interproximal carie.	n	n	n	n				n		Thinning of bone and bone destruction.

HTH 1053	LUES		34	M	B	Y	Y		Maxilla: All teeth present but left 2nd premolar, left and right M1. Mandible: Central and lateral incisors, right canine, right 2nd premolar, right M3, left canine, 1st and 2nd premolars, M2 and M3. Maxilla: Linear enamel hypoplasia on central incisors, pitting hypoplasia on lateral incisors, canines. Linear hypoplasia on the lingual aspect on anterior teeth resembling position of linear hypoplasia in labial surface. Mandible: Linear hypo on both labial and lingual surfaces correspondingly. Minor pitting on left M3.	n	n	n	n					n		Thinning of nasal bone and bone destruction. Thinning in side of orbits and symmetrically, palate and zygomatic bone.

HTH 1071	LUES		34	M	B	Y	Y		Maxilla: Teeth include right central incisor, canine and both premolars and M2. Mandible: Include all teeth but right M1 and M2 and left M2 and M3. No enamel hypoplasia at all. Alveolar bone fully healed in mandible and left and right M1 region in maxilla.	n	n	n	n					n		Bone thinning in nasal cavity and in palate, and temporal bone.
HTH 1085	GENERAL PARALYSIS OF THE INSANE		34	M	B	N	N			n	n	n	n					n		
HTH 2616	LUES		34	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid. Thinning and destruction of orbits. Thinning of maxilla.

HTH 0900	LUES		35	M	W	Y	Y		Maxilla: right and left canines, left and right 1st premolars, left and right M1 and M2 present. Central and lateral incisors missing. Right 2nd premolar not erupted. Left second premolar and left and right M1s extracted. Alveolar bone has healed in this area. Pit approx. 4.17mm long behind left incisor area. Mandible: Right lateral incisor left and right canines right 1st premolar left and right 2nd premolars present. Loose teeth: 1 Central and 1 lateral incisor and 1 premolar. Two roots also present. All lower molars extracted. Alveolar bone has healed.	n	n	n	n					n		
HTH 1864	LUETIC AORTITIS		35	M	B	Y	Y			n	n	n	n					n		
HTH 2391	THROMBOSIS		35	M	B	Y	Y			n	n	n	n					No but nodule on left parietal 8.93 wide by 7.98mm long		Thinning of ethmoid orbits and maxilla. Destruction of vomer.

HTH 2763	EMBOLUS		35	M	W	Y	Y			n	n	n	n					n		Thinning of ethmoid orbits, vomer and maxilla.
HTH 3011	TERTIARY SYPHILIS		35	M	B	Y	Y			n	n	n	n					n		
HTH 3332	SYPHILIS		35	F	B	Y	Y			n	n	n	n					n		
HTH 2125	LUES		36	F	W	Y	Y		Maxilla: Only teeth present include right 1st, 2nd and 3rd molars and left 2nd molar. Two loose teeth include one central incisor and one lateral incisor. No molars display any enamel hypoplasia. All 3 molars on the right-side display wear. Left 2nd molar has no wear and normal morphology. Mandible: Teeth present include half of right canine, 1st and 2nd right premolars, right 1st molar and 2nd left molar. Loose teeth include 3 incisors. Extensive caries in 1st right perm molar and 2nd left molar. right 2nd premolar has gold filling. Alveolar bone of left 2nd premolar, 1st left perm molar, left 3rd molar, and right 2nd perm molar has healed. Bone of	n	n	n	n					2 small possible healed gummatous lesions on the parietal bone at the back approx. 7.47mm wide.		Thinning of vomer, ethmoid and maxilla.

right 3rd molar has not healed.

HTH 2128	LUES		36	F	B	Y	Y		All teeth present except Central right incisor, 2nd right premolar, M1, 2nd and 3rd left perm molars. Alveolar bone of all missing teeth have healed except central right incisor. Left M1 has extensive wear. Carie on left first premolar on mesio buccal side. Mandible: Central and lateral incisors are broken in half. Both canines first premolars and first right M1 are present. Other teeth are missing. Second premolar, 1st and 2nd perm molar represented by roots only. Alveolar bone where 2nd right premolar, 2nd and 3rd molars has completely healed. There is wear on the lingual occlusal side of first permanent right molar.	n	n	n	n				n	

HTH 2289	AORTIC INSUFFICIENCY		36	M	B	Y	Y		Maxillary teeth not in alveolar bone except left canine. Loose teeth include right central incisor, right canine and two molars. Both molars have serious interproximal caries. One molar has a reduced occlusal surface. The interproximal carie takes away 1/4 of the lingual aspect of occlusal surface. No enamel hypoplasia present. Mandible: All teeth present except 3rd left permanent molar. No pitting or linear enamel hypoplasia. Half of right 3rd molar missing possibly due to caries. First M1 have and left M2 have some wear.	n	n	n	n					n		

HTH 3097	SYPHILIS		36	M	B	Y	Y		All teeth present but right canine and left M1. Minor pitting enamel hypoplasia on the 2nd third of central incisors and linear enamel hypoplasia on the cervical third of central incisors which corresponds to that which is on the lingual side also. Linear enamel hypoplasia on the middle third of lateral incisors and left canine which lines up straight with black markings (possibly caries) on the central incisors. LEH also corresponds to that on the lingual side also. M2, M3s and premolars have normal morphology. 2 isolated pits on the left M2. Mandible: LEH on the cervical third of the right central incisor, lateral incisors. Central incisors missing. LEH on the middle third of the canines. LEH on these lower teeth can be found on the lingual side also. Left and right 1st premolars and 2nd left premolar, left M1, M2 and right M2 have	n	n	n	n	303.97mm	304.46	434.17mm	433.99mm	n	right tibia 348.60mm, left 349.30mm. Long bones have nor pathological signs. No signs of pathology on ribs, scapula, hands or feet. Images have been take of hips, vertebrae, clavicle, sacrum.	Teeth possibly mercurial. Thinning of ethmoid, vomer and orbits, leading to some destruction.

normal morphology. Alveolar bone on right side has completely healed.

HTH 1131	LUETIC MYOCARDITIS		37	M	B	Y	Y		All teeth present but right 2nd premolar represented by roots only, left canine and left 2nd premolar reps by root only. Mandible: All teeth present but right central incisor, left and right M1s and right M3. No enamel hypoplasia. Dental wear and caries evident.	n	n	n	n					n		
HTH 0881	SYPHILIS		38	F	W	Y	Y		Maxilla: teeth present: left and right canines, right first premolar, right and left M2, left M3. M1s missing. Mandible: Lateral incisors, left and right canines and left and right M3. Loose teeth: 1 upper central incisor and 1 lateral incisor,2 premolars, lower teeth: 1 premolar.	n	n	n	n					n		
HTH 1189	GENERAL PARALYSIS OF THE INSANE		38	M	B	Y	Y		Most teeth present, no enamel hypoplasia at all.	n	n	n	n					n		Thinning of nasal cavity.
HTH 1880	LUES		38	M	W	Y	Y		7 upper teeth and all mandibular other than M2s. No signs of enamel hypoplasia.	n	n	n	n					n		Destruction of vomer, thinning of ethmoid and orbits.
HTH 2696	AORTIC ANEURYSM		38	M	B	Y	Y			n	n	n	n					n		

HTH 0883	GENERAL PARALYSIS OF THE INSANE		39	M	W	Y	Y		Teeth present: Maxilla: right canine and 2nd premolar. Right lateral incisor, 1st and 2nd premolar, M2. Mandible: lateral right incisor, left and right canines, 2nd premolar, left and right M2. Maxillary alveolar bone mostly healed. Large pit on palate behind the left central incisor area approx. 6.64mm long and on the right side approx. 2.48mm long. Normal tooth morphology of presented teeth. No signs of enamel hypoplasia.	n	n	n	n					n		
HTH 1100	GENERAL PARALYSIS OF THE INSANE		39	M	W	Y	Y		Maxilla: All teeth present but left M1 other than roots and right M3. Mandible: All teeth present but left M1. Left M3 did not erupt. No enamel hypoplasia on maxillary or mandibular teeth.	n	n	n	n					n		
HTH 1264	LUES		39	M	W	Y	Y			n	n	n	n					n		Thinning of nasal cavity

HTH 1279	GENERAL PARALYSIS OF THE INSANE		39	F	W	Y	Y		No maxillary teeth. Teeth on mandible have no enamel hypoplasia's	n	n	n	n					n		
HTH 2113	PARESIS OF THE INSANE		39	M	B	Y	Y			n	n	n	n					n		Destruction and thinning of vomer. Thinning of ethmoid, orbits, maxilla.
HTH 2305	GENERAL PARESIS		39	M	W	Y	Y			n	n	n	n					n		Destruction of vomer, ethmoid bone and orbits. Thinning of maxilla
HTH 2907	PARALYSIS OF THE INSANE		39	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid, maxilla, orbits, vomer, palate, parts of magnus foramina
HTH 3507	LUETIC AORTITIS		39	M	B	N	N			n	n	n	n					n		
HTH 0953	LUES		40	M	W	Y	Y		All teeth present but left M1 and right M2. Mandible: All teeth present but both M3s. Minor linear enamel hypoplasia on cervical third of anterior teeth and in middle third of crown on mandibular anterior teeth.	n	n	n	n					Lesion on the right parietal side of skull, approx. 19.90 long and 17.96 wide.		Thinning of the bone on the palate, zygomatic bone, nasal bone (ethmoid bone) and orbits.

HTH 1006	SYPHILIS		40	M	W	Y	Y		Maxillary teeth: left and right central and lateral incisors, left and right canines, left and right 1st premolars and right 2nd premolar. The rest of the alveolar bone has completely healed. Mandible: All anterior teeth present (central lateral, canines and first right and left premolars, right 2nd premolar and root of left 2nd premolar, and left M2 and M3. Alveolar bone of right and left M1 and left M2 has healed. M3 bone on right side is still porous. No enamel hypoplasia on maxillary or mandibular teeth.	n	n	n	n					Possible bone changes on left parietal bone.		Thinning of the bone on the palate, zygomatic bone, nasal bone (ethmoid bone).
HTH 1173	LUES		40	M	W	N	N			n	n	n	n					n		
HTH 1449	LUES		40	M	W	Y	Y		No signs of any form of enamel hypoplasia	n	n	n	n					n		Thinning of maxilla, vomer, orbits, ethmoid, temporal bone and magnum foramen.
HTH 1520	LUES		40	M	W	Y	Y		No teeth at all	n	n	n	n					n		Thinning of ethmoid, orbits, vomer bones.

HTH 1897	LUETIC MENINGITIS		40	M	B	Y	Y		All maxillary teeth, most mandibular. Upper M1s normal morphology. Linear enamel hypo on mandibular anterior teeth on cervical third on crown. Pitting enamel hypoplasia on middle third of right central incisor, Minor isolated pits on lateral incisors and canines.	n	n	n	n					n		Pitting on incisor. Thinning and destruction of vomer, ethmoid and thinning of maxilla.
HTH 2024	LUES		40	F	B	Y	Y		Only M1 in lower right. Normal morph. No M1s present. Left Central in with minor linear enamel hypo on 1/3 of crown.	n	n	n	n					n		Thinning of vomer, ethmoid and maxilla.
HTH 2252	GENERAL PARALYSIS OF THE INSANE		40	F	B	Y	Y			n	n	n	n					n		Destruction of vomer, thinning of ethmoid, orbits and maxilla.
HTH 2486	LUES		40	M	B	Y	Y			n	n	n	n					n		Complete destruction of vomer, thinning of maxilla, orbits, and ethmoid.

HTH 2580	PARESIS		40	M	W	Y	Y			n	n	n	n					n		thinning of skull temporal bone, ethmoid, vomer, maxilla
HTH 1088	GENERAL PARALYSIS OF THE INSANE		41	M	W	Y	Y		Maxillary Teeth present: central and lateral incisors, canines and 1st and 2nd right premolar. Root of left M1 and left and right M2s. Mandible: Central and lateral incisors, canines, and 1st and 2nd premolars and right M3. Dental wear evident by no enamel hypoplasia.	n	n	n	n					n		Nasal bone destruction and thinning of palate bone and in orbits.
HTH 2190	SECONDARY LUES		41	F	B	Y	Y			n	n	n	n					n		
HTH 1338	LUES		42	M	B	Y	Y		Most teeth present including M1. No signs of enamel hypoplasia.	n	n	n	n					n		Thinning of ethmoid, orbits, destruction of vomer
HTH 1749	GENERAL PARALYSIS OF THE INSANE		42	F	B	Y	Y		9 teeth in total, some have no enamel. Those that do show no form of enamel. Have normal tooth morphology. Cries in M3s.	n	n	n	n					n		Thinning and destruction of vomer, ethmoid, maxilla and orbits.
HTH 1788	PARALYSIS OF THE INSANE		42	M	B	Y	Y			n	n	n	n					n		

HTH 2082	PARALYSIS OF THE INSANE		42	F	W	Y	Y		10 teeth present. Normal tooth morphology. Minor linear enamel hypoplasia on cervical third of lower incisors.	n	n	n	n					n		Thinning of vomer, ethmoid and orbits
HTH 2920	SYPHILIS		42	F	W	Y	Y			n	n	n	n					n		Thinning of ethmoid, vomer and maxilla.
HTH 0925	LUES		43	F	W	Y	Y		Maxilla: No teeth. Mandible: left canine and right 1st premolar. Right canine, M2 and M3 present. Rest of teeth missing Alveolar bone on the left side from premolar region to molar is completely healed. Left side where M1 would be is also healed. Anterior region is porous. Loose teeth, one upper incisor and one root.	n	n	n	n					n		Nasal bones are very thin resulting in damage. Thin bone is also noted in the upper orbits and in spots near magnum foramen.
HTH 1176	LUES		43	M	B	Y	Y		Most teeth present. No enamel hypoplasia	n	n	n	n					n	n	
HTH 1866	LUETIC DEMENTIA	1M	43	M	W	Y	Y		11 teeth, mainly in mandible. Multiple lines f linear enamel hypoplasia on cervical third of mandibular anterior teeth	n	n	n	n					n		Thinning of vomer and maxilla and destruction of ethmoid and orbits.
HTH 1875	PARALYSIS OF THE INSANE		43	M	O	Y	Y			n	n	n	n					n		

HTH 2120	LUES		43	F	B	Y	Y			n	n	n	n					n		Thinning and destruction of vomer and ethmoid. Thinning of maxilla and orbits
HTH 2231	PARALYSIS OF THE INSANE		43	M	W	Y	Y			n	n	n	n					n		Thinning of bones, vomer, ethmoids, maxilla
HTH 2453	LUETIC AORTITIS		43	M	B	Y	Y			n	n	n	n					n		no Destruction of vomer, into ethmoid and thinning of orbits and maxilla.
HTH 2803	LUES		43	M	B	Y	Y			n	n	n	n					n		Thinning of Vomer, Ethmoid, Maxilla, Palate
HTH 0819	LUES, INSANITY, MENTAL DEFIC.		44	M	W	Y	Y		Maxilla: All teeth present but M3. Mandible: All teeth present but central and lateral incisors, left M1. Teeth have different levels of dental wear. Linear enamel hypoplasia on upper and lower central and lateral incisors on middle third and cervical third of crowns.	Slight notch on the right central incisor and on distal portion of left central incisor. Not typical Hutchinson incisor.	n	n	n					n		

HTH 1476	LUETIC AORTIC INSUFFICIENCY		44	M	B	Y	Y		Most teeth present. No form of enamel hypoplasia at all.	n	n	n	n					n		Thinning and destruction of vomer and ethmoid bone, thinning of palate
HTH 1962	DROPSY		44	M	B	Y	Y		Maxilla M1s Have dental wear and some no enamel most likely post mortem. No lower M1s. Very minor linear enamel hypo on lower anterior teeth. Minor linear enamel hypo on central incisors and an isolated pit.	n	n	n	n					n		Thinning and destruction of vomer and ethmoid bone, thinning of palate

HTH 2266	AORTIC INSUFFICIENCY		44	M	B	Y	Y		Maxilla: All teeth present except right M1. Second premolar represented by root only. Both M3 have serious caries (nearly entire occlusal surface and into the pulp cavity. Minor LEH (2 lines) on the middle third of the central incisors. Minor LEH can just be seen on the lateral incisors. Possible minor notch on both central incisors but could be minor wear or post mortem (images have been taken).	n	n	n	n	330.16mm	327.73mm	442.09mm	443.06mm	n	No pathologies on femori, possible pathology on right side of pelvis, see images. No pathologies on vertebrae. No pathologies on any long bone, ribs, scapula, sternum, left or right feet or hands.	Minor notch in central incisors. Possible pitting on parietal left side. Clavicle with the hole is the right one. Thinning of the back of the palate, ethmoid, vomer and orbits. Some destruction of ethmoid bone and bottom of vomer. Very minor pitting on the occipital bone just below lambdoid suture, this may just be normal.
HTH 3330	SYPHILIS	1M	44	M	B	N	N			n	n	n	n					n		
HTH 1144	LUES		45	M	B	Y	Y		Maxilla: All teeth present except left central and lateral incisor and left M3. Mandible: All teeth present except left and right M1 and M2. Central and left lateral incisor represented by root only. No enamel hypoplasia at all. Some dental wear.	n	n	n	n					n		Thinning of bone of nasal cavity, orbital bone and spots on temporal bone and bac of palate and spots near magnus foramen.

HTH 1192	LUES		45	M	B	Y	Y		No enamel hypoplasia at all.	n	n	n	n					n		Thinning of bone of nasal cavity
HTH 1212	GENERAL PARALYSIS OF THE INSANE		45	M	W	Y	Y			n	n	n	n					No carries sicca. Blow in skull on left parietal bone (55.26mm long, 25.31 wide).		Nasal cavity thinning of bone.
HTH 1659	SYPHILIS OF THE AORTA		45	M	B	Y	Y			n	n	n	n					n		Thinning of nasal bone, orbital bone and palate
HTH 1756	GENERAL PARALYSIS		45	M	W	Y	Y		some teeth present. Most have no enamel/ Those that do display very linear enamel hypoplasia.	n	n	n	n					n		Pitting on parietal. Thinning of orbits, destruction on vomer, ethmoid, temporal and part of frontal bone.
HTH 2176	SYPHILIS		45	M	W	Y	Y			n	n	n	n					n		
HTH 2499	TABIO PARESIS		45	M	W	Y	Y			n	n	n	n					n		Thinning of ethmoid, vomer, maxilla and orbits.

HTH 2716	LUES		45	M	B	Y	Y			n	n	n	n					n		Thinning and destruction of ethmoid, vomer, and orbits. Thinning of orbits
HTH 0975	LUES		46	M	W	Y	Y			n	n	n	n					n		
HTH 1603	GENERAL PARALYSIS		46	M	W	Y	Y		No enamel hypoplasia at all.	n	n	n	n					n		Extreme thinning of nasal bone, zygomatic bone and orbital bone.

HTH 2263	LUES		46	M	B	Y	Y		All teeth present! Tooth morphology of upper central incisors is normal but pitting evident on middle third of both crowns. Similar pitting evident on lateral incisors and canines. May be signs of mercury. Similar pitting noted on all lower incisors and left canine. Entire crown of right canine appears to have broken off (post mortem perhaps). Morphology of all M1s appears normal but with dental wear.	n	n	n	n	337.46mm	328.45mm	448.92mm	421.09mm	no	Left femur: thickening of bone (periosteal reaction) and curvature of superior portion of left femur. Length difference between both femurs also. Tibia (right) 384.57mm. Left tibia 384.50mm. Some bone remodelling on spine (see image). Bone changes on ilium right side (see image) more than left. Sacrum has some changes. Minor changes on sternum. Ribs towards spinal end feel bumpy on inferior ends on left and right ribs.	Thinning of ethmoid, orbits and maxilla. Destruction of vomer. Nasal bride intact. Thinning of entire skull noted when shining light in it.
HTH 2543	GENERAL PARALYSIS OF THE INSANE		46	F	B	Y	Y			n	n	n	n					No but 2 depressions one on left and right of frontal bones.		Thinning of ethmoid, orbits and maxilla. Thinning of vomer.
HTH 2638	LUES		46	M	W	Y	Y			n	n	n	n					n		Thinning of vomer, ethmoid, maxilla

HTH 1165	PARETIC DEMENTIA		47	M	W	Y	Y		Maxilla: All teeth present but M3s. Right premolars represented by roots only. Anterior teeth, central, lateral incisors and right canine broken post mortem. Mandible: All teeth present but left M1. Left M2 is has root and half of crown and right M2 represented by roots only. No enamel hypoplasia.	n	n	n	n					n		Thinning bone in nasal cavity, orbits and temporal bone.
HTH 1858	PARALYSIS OF THE INSANE		47	M	O	Y	Y		3 M1s and 1 central incisor. M1s have severe dental wear. Incisor has normal morphology. Minor linear enamel hypo on cervical third of incisor crown.	n	n	n	n					n		Thinning of ethmoid, orbits and vomer.
HTH 2019	PARALYSIS OF THE INSANE		47	M	W	Y	Y			n	n	n	n					n		Destruction of vomer, thinning of ethmoid, orbit and maxilla.
HTH 2290	AORTIC INSUFFICIENCY		47	M	B	Y	Y		No central incisors, M1s normal morphology just have dental wear.	n	n	n	n					n		Thinning of ethmoid and maxilla, thinning and destruction of vomer, orbits.

HTH 2348	GENERAL PARALYSIS		47	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid and maxilla, thinning and destruction of vomer, orbits.
HTH 3040	CEREBRAL SYPHILIS		47	M	A	Y	Y			n	n	n	n					n		
HTH 3521	GENERAL PARESIS		47	M	W	N	N			n	n	n	n					n		
HTH 0943	LUES		48	M	W	Y	Y		Maxilla: both Central and lateral incisors, and canines present. Right 1st premolar and left M1, M2 and M3 present. Dentures are also present. Mandible: All incisors and canines present. Right 1st premolar present. Right M2 present. Dentures of lower teeth 2 premolars and m1 and M2 on left and 2 premolars and M1 on right. No enamel hypoplasia on any teeth.	n	n	n	n					n		Thinning of the back of palate, thinning and destruction of nasal cavity, upper orbital bone, left and right temporal bones, some spots near foramina magnum.
HTH 2733	CENTRAL NERVOUS SYSTEM, LUES		48	M	B	Y	Y			n	n	n	n					n		Destruction of vomer and some of ethmoid due to thinning of bone and parts of temporal bone.

HTH 3205	SYPHILIS		48	M	W	Y	Y			n	n	n	n					n		Thinning of ethmoid, maxilla, orbits. Complete destruction of vomer and some of ethmoid.
HTH 3289	GENERAL PARESIS		48	M	B	Y	Y			n	n	n	n					n		Ethmoid and vomer thinning and destruction.
HTH 3367	GENERALIZED SYPHILIS		48	F	B	N	N			n	n	n	n					n		
HTH 3454	SYPHILIS		48	M	B	N	N			n	n	n	n					n		
HTH 1045	LUES		49	M	W	Y	Y		No teeth present all. Maxillary bone and most of mandibular bone completely healed.	n	n	n	n					n		Thinning and destruction of nasal cavity and gummatous lesions.
HTH 2459	LUES		49	M	B	Y	Y			n	n	n	n					n		Destruction of vomer and orbits. Thinning of ethmoid and maxilla (palate).
HTH 2965	CEREBRAL SPINAL SYPHILIS		49	M	B	N	N			n	n	n	n					n		

HTH 0029	SYPHILIS		50	M	W	Y	Y		Maxilla: teeth present include right and left lateral incisors, right canine, right second premolar, left second premolar, right first and second permanent molars. All teeth have wear especially premolars and permanent molars. Lingual disto caries on 1st perm molar, interproximal carie on 2nd molar. Alveolar bone resorption observed. Holes in alveolar bone exposing roots of 2nd perm molars. Approx. 6.55mm on left and 4.11mm on right. Mandible: All incisors, left canine, left 2nd premolar, 1st and 2nd right and left molars present. Cusps considerable worn down. No form of hypoplasia observed. No skull cap available to see.	n	n	n	n				No skull cap		

HTH 0097	AORTIC INSUFFICIENCY	1M	50	M	B	Y	Y		Maxilla: right side: 2nd premolar, M1, M2, M3. Left side, Central and lateral incisors, canine both premolars, M1, M2. Loose teeth, Upper right central and lateral incisor. Mandible: All teeth present except left 2nd premolar and M1, right M3. Considerable wear on teeth. No enamel hypoplasia on any teeth.	n	n	n	n					n		
HTH 0183	AORTIC ANEURYSM		50	M	W	Y	Y	missing	All anterior teeth present (central, lateral incisors) right premolar, left M1, M2. Mandible: All teeth present except central left incisor. Dental wear observed. No signs of any enamel hypoplasia.	n	n	n	n					n		
HTH 1512	LUES		50	M	W	Y	Y		No enamel hypoplasia on teeth present, some enamel missing off teeth.	n	n	n	n					n		Destruction of vomer, thinning and pitting of ethmoid bone, thinning and destruction of orbits and maxilla.
HTH 2588	SYPHILIS		50	M	W	Y	Y			n	n	n	n					n		Thinning of vomer, ethmoid, maxilla.
HTH 2684	LUES		50	M	B	Y	Y			n	n	n	n					n		

HTH 3244	SYPHILIS		50	F	W	Y	Y			n	n	n	n					n		
HTH 3312	GENERAL PARESIS		50	M	B	Y	Y			n	n	n	n					n		
HTH 3444	PARESIS		50	F	B	N	N			n	n	n	n					n		
HTH 3574	GENERAL PARESIS		50	M	W	N	N			n	n	n	n					n		
HTH 1132	GENERAL PARALYSIS OF THE INSANE		51	M	W	Y	Y			n	n	n	n					n		Nasal cavity destroyed due to thinning.
HTH 2110	GENERAL PARALYSIS OF THE INSANE		51	M	B	Y	Y			n	n	n	n					n		
HTH 0890	SYPHILIS		52	M	W	Y	Y		Only teeth: second premolar and Right M1. Both teeth severely worn. Alveolar bone of maxilla completely healed. Left side of mandible healed. Left and anterior sides still porous. Loose teeth: 2 incisors.	n	n	n	n					n		
HTH 1065	GENERAL PARALYSIS OF THE INSANE		52	M	W	Y	Y		Maxilla: Central and lateral incisors, 1st and left and right 2nd premolars and right M3. Alveolar bone has healed. Mandible: central and lateral incisors, both canines 1st and 2nd premolars, M2. Some linear enamel hypoplasia on anterior teeth near cervical third.	n	n	n	n					n		Thinning of bone in nasal cavity, orbital bone, zygomatic arch, palate, temporal bone
HTH 3612	THROMBOSIS OF THE AORTA	2M	52	M	B	N	N			n	n	n	n							

HTH 2088	LUES		53	M	W	Y	Y			n	n	n	n					no but a lesion on the right frontal bone. Loos puss like, 9.34mm wide by 11.37mm long.		Thinning of ethmoid and orbits and maxilla. Destruction of vomer.
HTH 3140	GENERALIZED ARTERIOLARSCLEROSIS	1M	53	F	W	Y	Y			n	n	n	n					n		Thinning of vomer, ethmoid
HTH 1394	RUPTURED AORTIC ANEURYSM		54	M	B	Y	Y		No form of enamel hypoplasia at all on teeth.	n	n	n	n					n		Destruction of vomer, thinning and destruction of ethmoid and orbits
HTH 2559	LUETIC AORTIC INSUFFICIENCY		54	M	W	Y	Y			n	n	n	n					n		Destruction of ethmoid, parts of orbit due to thinning. Thinning of maxilla (palate).
HTH 3113	THROMBOSIS		54	M	B	Y	Y			n	n	n	n					n		
HTH 0270	GENERAL PARALYSIS OF THE INSANE		55	M	W	Y	Y		No teeth at all.	n	n	n	n					no, however, skull cap very thin.		

HTH 1386	AORTIC ANEURYSM		55	M	W	Y	Y		Minor linear enamel hypoplasia on anterior teeth of maxilla in third cervical third of crown.	n	n	n	n					no, however, skull cap very thin.		Thinning of vomer, ethmoid and orbits and some spots in maxilla.
HTH 2682	AORTIC INSUFFICIENCY	1M	55	M	W	Y	Y			n	n	n	n					no, however, skull cap very thin.		Thinning of vomer, ethmoid and orbits and some spots in maxilla.
HTH 2682	LUES	1M	55	M	W	Y	Y			n	n	n	n					n		
HTH 2748	SYPHILIS		55	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid, orbits, maxilla and vomer.
HTH 2918	THROMBOSIS		55	M	W	Y	Y			n	n	n	n					n		Destruction of vomer, parts of ethmoid due to thinning, thinning of maxilla.
HTH 3505	CARDIO VASCULAR DISEASE		55	M	W	N	N											n		
HTH 2375	LUETIC AORTITIS		56	M	B	Y	Y			n	n	n	n					n		Destruction of vomer, thinning of ethmoid, maxilla and orbits.

HTH 2498	GENERAL PARALYSIS OF THE INSANE		56	M	W	Y	Y			n	n	n	n					n		Inferior portion of vomer destroyed. Thinning and destruction of ethmoid, orbits and thinning of maxilla parts of temporal bone and palate.
HTH 2924	PARESIS		56	F	W	Y	Y			n	n	n	n					n		Thinning of ethmoid, vomer, maxilla.
HTH 2018	PARALYSIS OF THE INSANE		57	M	B	Y	Y		No M1s or incisors.	n	n	n	n					n		Thinning of ethmoid, vomer, maxilla palate
HTH 2874	SYPHILIS		57	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid, vomer, maxilla palate.
HTH 3566	GENERAL PARESIS		57	M	B	N	N													
HTH 2001	LUES	2M	58	M	B	Y	Y		Most teeth present. Nothing abnormal with M1s. No incisors. No enamel hypoplasia of any kind.	n	n	n	n					n		Destruction of vomer, thinning of ethmoid, orbits and maxilla palate.

HTH 1111	LUES		59	M	W	Y	Y		Maxilla: right and left lateral incisor, right 1st premolar and left M1. All teeth but molar is broken. Alveolar bone has healed. Mandible: central and lateral incisors, canine and 1st premolars, left and right M3. Alveolar bone has healed.	n	n	n	n					n		Thinning of nasal cavity, orbital bone.
HTH 1217	CEREBROSPINAL SYPHILIS		59	M	W	Y	Y		Three teeth in total with no enamel.	n	n	n	n					n		
HTH 3142	HYPER-CARDIO VASCULAR DISEASE		59	M	W	Y	Y			n	n	n	n					n		Thinning of bones.
HTH 3615	SYPHILIS		59	M	B	N	N											n		
HTH 0346	PARALYSIS OF THE INSANE		60	F	W	Y	Y		No teeth. Alveolar bone of maxilla and mandible fully healed.	n	n	n	n					n		
HTH 0924	LUES		60	M	W	Y	Y		No teeth at all. Upper anterior portion of alveolar bone healed while molar region still somewhat porous. Lower alveolar bone completely healed.	n	n	n	n					n		Nasal bone very thin and broken. Thin bone moves into the orbital region.

HTH 1452	LUES		60	M	B	Y	Y		Most teeth present. Only signs of enamel hypoplasia on mandibular teeth, central left incisor approx. 2.18mm, right central 2.39mm, right lateral 3.47mm away from cemeto enamel junction.	n	n	n	n					n		Extreme thinning and destruction of ethmoid, vomer and orbital bone, some thinning of upper maxilla and magnum foramen
HTH 1464	SYPHILIS	1M	60	M	W	Y	Y		Few teeth. No hypoplasia of any kind.	n	n	n	n					n		Extreme thinning and destruction of nasal and orbital bone, some thinning in temporal and magnum foramen
HTH 2633	VASCULAR ACCIDENT		60	M	B	Y	Y			n	n	n	n					n		Thinning of ethmoid, vomer.
HTH 3491	CENTRAL NERVOUS SYSTEM, LUES		60	M	B	N	Y											n		
HTH 1463	LUES		61	M	B	Y	Y		No form of enamel hypoplasia on any teeth.	n	n	n	n					n		Complete destruction of vomer, orbits, upper maxilla and ethmoid bone.
HTH 2130	LUES		61	F	W	Y	Y			n	n	n	n					n		Destruction of vomer. Thinking of ethmoid, orbits, maxilla palate.

HTH 0567	LUETIC MYOCARDITIS	1M	62	M	W	Y	Y		Only mandible present. Only teeth are lateral left incisor and root of left canine. Alveolar bone has completely healed.	n	n	n	n					no skull		
HTH 3010	TUBERCULOUS PNEUMONIA		62	M	W	Y	Y			n	n	n	n					n		Thinning of palate, maxilla, orbits, destruction in vomer and ethmoid due to thinning.
HTH 3245	SYPHILIS		62	M	B	Y	Y			n	n	n	n					n		Thinning vomer, ethmoid, maxilla palate.
HTH 3555	GENERAL PARESIS		62	M	W	N	N											n		
HTH 0234	GENERAL PARALYSIS OF THE INSANE		65	F	W	Y	Y		No teeth.	n	n	n	n					n		
HTH 0464	AORTIC INSUFFICIENCY		65	M	W	Y	Y		Maxilla: All teeth present but right M1 and M3 and left canine and second premolar. Central and lateral incisors and right canine are broken. No enamel hypoplasia on premolars or molars, but dental wear is evident. Mandible: All teeth present except M1 and M3. Loose teeth: 2 perm molars and an incisor. No	n	n	n	n					n		

									incisors missing so not sure if it belongs with individual. No enamel hypoplasia evident on any teeth. Some dental wear present.											
HTH 1408	SYPHILITIC DEMENTIA	1M	65	M	W	Y	Y		Few teeth. No enamel hypoplasia evident at all.	n	n	n	n					n		Thinning and destruction of palate, orbits and ethmoid. Thinning of vomer and magnus foramen.
HTH 2043	ANEURYSM		65	M	W	Y	Y		Most teeth present. C incisors and M1s normal morpho, minor linear hypo on cervical third of crown corresponding to lingual side.	n	n	n	n					n		Destruction of vomer, thinning of ethmoid, maxilla palate and orbits.
HTH 2686	DIFFUSE VASCULAR SCLEROSIS		65	M	W	Y	Y			n	n	n	n					n		thinning and palate, orbits and ethmoid. Thinning of vomer

HTH 3225	SYPHILIS		65	M	W	Y	Y			n	n	n	n					n		Thinning vomer, ethmoid, maxilla palate.
HTH 3338	EDEMA		66	F	W	Y	Y			n	n	n	n					n		Some destruction of vomer and ethmoid due to thinning of bone.
HTH 1930	LUES	2M	67	M	W	Y	Y		4 mandibular teeth present. Right 2nd premolar rotated 90 degrees. Alveolar bone of mandible healed, most of maxilla healed.	n	n	n	n					n		Destruction of vomer, thinning of ethmoid, maxilla and orbits.
HTH 2379	LUETIC AORTITIS		67	M	B	Y	Y			n	n	n	n					n		Thinning of vomer, destruction of ethmoid. Thinning of orbits
HTH 3572	GENERAL PARESIS	1M	68	F	W	N	N											n		

HTH 1001	SYPHILITIC MYOCARDITIS		69	M	W	Y	Y		Maxilla: all teeth present except right M1 and M2 and left M1. Mandible: All anterior teeth (central and lateral incisors, left and right canines (right broken) and 1st and 2nd right premolars. Loose teeth: one premolar. Other teeth missing. Alveolar bone on right side healed. Linear enamel hypoplasia on the middle third and cervical third of crowns of anterior teeth in maxilla and in same position on mandibular anterior teeth however not as deep as on maxilla.	n	n	n	n					n		Thinning of bone in palate, orbits and nasal bone resulting in destruction.
HTH 2468	LUES	1M	69	M	W	Y	Y			n	n	n	n					n		Thinning of vomer, ethmoid, maxilla and temporal bone.
HTH 3579	GENERALIZED ARTERIOSCLEROSIS		69	M	W	N	N											n		

HTH 0838	GENERAL PARALYSIS		70	M	W	Y	Y		No teeth present in maxilla. Mandible: left canine and 1st left premolar present. Loose teeth: 1 incisor and 3 roots. Maxillary alveolar bone porous. Mandibular alveolar bone healed in molar region and porous where anterior teeth were. No molars present at all.	n	n	n	n					n		
HTH 1153	PARETIC DEMENTIA		70	F	W	Y	Y		Maxilla: No teeth. Alveolar bone nearly completely healed. Mandible: Left lateral incisor, left canine and 1st premolar. Alveolar bone completely healed.	n	n	n	n					n		Thinning bone in nasal cavity.
HTH 2177	SYPHILIS		70	M	B	Y	Y			n	n	n	n					n		Thinning of orbits, ethmoid and vomer, maxilla. Destruction of vomer
HTH 1838	ARTERIOSCLEROTIC GANGRENE OF THE RIGHT FOOT	1M	71	F	B	Y	Y		Maxillary teeth (5) represented by roots only. 8 mandibular teeth only. No enamel hypoplasia at all.	n	n	n	n					n		Complete destruction of vomer. Thinning and some destruction of ethmoid, orbits. Thinning of maxilla and temporal bones.

HTH 3508	CEREBRAL SPINAL LUES		71	M	W	N	N											n		
HTH 1413	SYPHILIS OF THE AORTA		72	F	W	Y	Y		No teeth, only dentures. Found mandibular incisor enamel in box with no enamel hypoplasia at all. In very good condition.	n	n	n	n					n		Destruction of vomer, ethmoid, maxilla, orbits
HTH 2982	DIFFUSE VASCULAR SCLEROSIS		72	M	B	Y	Y			n	n	n	n					n		Thinning of vomer, maxilla, ethmoid, palate.
HTH 1032	GENERAL PARESIS	1M	73	M	W	Y	Y		Maxilla: All teeth present except left M2, M3 and right M3. Mandible: All teeth present except right premolars and M1 and M2. Linear enamel hypoplasia (2 lines) present on anterior teeth on cervical third of crowns. Cannot see LEH on mandibular teeth due to discolouration. Severe dental wear on molars. No signs of any hypoplasia.	n	n	n	n					n		Thinning of the bone on palate, nasal bone, orbital bone and zygomatic bone.
HTH 2593	LUETIC AORTITIS		73	F	B	Y	Y			n	n	n	n					n		Thinning of ethmoid, maxilla, orbits, destruction of vomer.

HTH 1451	GENERAL PARALYSIS OF THE INSANE		75	F	W	Y	Y		Three teeth present in mandible only, right central and lateral incisor, and left canine. Max and mandible alveolar bone mostly healed.	n	n	n	n					no but depression on each side symmetrically on sagittal suture approx. 28.68mm from lambdoid suture on left side and 25.70mm on right.		Complete destruction of vomer, some of ethmoid and orbits. Resorption of maxillary alveolar bone.
HTH 2319	SYPHILIS		75	M	B	Y	Y			n	n	n	n					n		Thinning of vomer, ethmoid, maxilla and orbits.
HTH 1166	PARETIC DEMENTIA		76	M	W	Y	Y		Maxilla: No teeth. Mandible: root of canine and 1st premolar.	n	n	n	n					n		Thinning of nasal bone and orbital bone.

HTH 0834	GENERAL PARALYSIS		77	M	W	Y	Y		Right central incisor root in maxilla. Only teeth present are loose teeth. 1 incisor and 1 premolar. Alveolar bone in maxilla still porous. Some of mandible alveolar bone in right molar area has healed. The rest of mandible is porous. Large pit in palate behind left incisor approx. 4.13mm long. No Permanent molars.	n	n	n	n					n		
HTH 1767	SYPHILIS		77	F	W	Y	Y		No teeth at all. Upper and lower alveolar bone completely healed.	n	n	n	n					n		Thinning and destruction of vomer, ethmoid, orbits, maxilla palate.
HTH 2650	AORTIC ANEURYSM		78	M	B	Y	Y			n	n	n	n					n		
HTH 3220	AORTIC ANEURYSM		80	M	W	Y	Y			n	n	n	n					n		
HTH 1195	PARESIS		84	M	B	Y	Y		No teeth. Alveolar bones upper and lower have healed.	n	n	n	n					n		
HTH 0713	GENERAL PARALYSIS OF THE INSANE			M	W	Y	Y		All adult upper and lower teeth present except upper right lateral incisor, right 1st premolar and right M3 and left M2. Lower right M3 missing. All teeth considerable worn down. Very minor linear enamel	n	n	n	n					n		

									hypoplasia on cervical third of incisor crowns.											
HTH 2118	PERICARDITIS		13	F	B	Y	Y		Maxilla: Central incisors, left and right lateral incisors, canines not fully erupted, left and right 1st premolars, left 2nd premolar, right 2nd premolar not fully erupted (still in crypt), right M1, left M1 not fully erupted (still in crypt), right and left M2 still in crypt. Mandible: central and lateral incisors, canines, right 1st premolar, missing left 1st premolar. Second premolar not fully erupted (still in crypt). Right and left M1 and M2s still in crypt. Enamel hypoplasia on teeth looks mercurial.	n	n	n	n	Not present.	211.90mm	274.71mm	278.27mm	n	n	Clavicle appears normal.

Presence of dental signs of congenital syphilis in Pre-modern specimens

Supplementary Information

Hutchinson, Moon and Fournier's observations in patients with congenital syphilis

Having examined thousands of patients with congenital syphilis, Hutchinson noticed that there were distinct dental changes caused by the disease itself, and by the use of mercury. In patients that did not receive any treatment, the disease would primarily affect odontogenesis. However, in patients treated with mercury, dental abnormalities were seen to affect amelogenesis. As a result of these distinct differences in dental abnormalities among patients, Hutchinson defined these changes into classes, although he recognized that variation could occur within these classes. The three classifications of dental anomalies included syphilitic, mercurial and syphilitic-mercurial.

The main type of dental characteristics observed in patients with congenital syphilis that were not administered any treatment (syphilitic) includes the central maxillary incisors which are short and narrow with crescentic notching and rounded edges[1.] It is these teeth that were regarded as the "test teeth"[1]. Other characteristics comprised of the other incisors demonstrating rounded incisal edges and look peg-like in shape[2]. These dental abnormalities described by Hutchinson are recognized and accepted as pathognomonic characteristics by paleopathologists and are used as a method to make a differential diagnosis of congenital syphilis in skeletal remains.

Other dental anomalies observed in cases of congenital syphilis include Moon's molar and Fournier's molar, however, these are not considered as pathognomonic signs of the disease. Moon's molar has a reduced occlusal surface, becoming dome like in shape[3] while Fournier's molar has multiple cusps, rough and conical in shape and are separated by grooves[4].

In patients treated with mercury, the enamel of the first permanent molars of the maxilla and mandible are affected and considered the "test teeth"[5]. The enamel on the surface of the crown is deficient and "dentine grows through, presenting a number of tubercles and spines"[5]. If the pitting is deep, they can appear as black points. In some cases the whole surface of the first molar will be involved, while in other only central areas and in severe cases the whole tooth will be dwarfed. It was also noted by

Hutchinson, that it was common to find in treated patients, dental characteristics caused by both syphilis and mercury which may have caused confusion among physicians[5]. The notched upper central incisors would present with pitting and discolouration as a result of the treatment containing mercury. It is this significant characteristic that has not been used by paleopathologists as a diagnostic tool for congenital syphilis.

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Research Article

Diagnosis of Mercurial Teeth in a Possible Case of Congenital Syphilis and Tuberculosis in a 19th Century Child Skeleton

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Without the presence of "*caries sicca*," "sabre shins," and nodes/expansion of the long bones with superficial cavitation, differential diagnosis of venereal syphilis and tuberculosis (TB) may be difficult as various infections produce similar responses. However, congenital syphilis has distinctive features facilitating a diagnosis. A case study of remains of a juvenile European settler (probably male, 8–10 years old) (B70) buried in the 19th century and excavated in 2000 from the cemetery of the Anglican Church of St. Marys in South Australia is presented. B70 demonstrated that the two diseases might have been present in the same individual, congenital syphilis and TB. Widespread destruction of vertebral bodies and kyphosis-related rib deformations indicate advanced TB. Severe dental hypoplasia is limited to permanent incisors and first molars; there is pitting on the palate, periosteal reaction on the skull vault, and thinned clavicles. Dental signs are not limited to "screwdriver" central incisors and mulberry molars. Apical portions of the crowns of permanent upper, lower, central, and lateral incisors have multiple hypoplastic-disorganized defects; deciduous canines have severely hypoplastic crowns while possibly hypoplastic occlusal surfaces of lower deciduous second molars are largely destroyed by extensive caries. These dental abnormalities resemble teeth affected by mercurial treatment in congenital syphilitic patients as described by Hutchinson.

1. Introduction

In the past, the presence of numerous diseases and the lack of an effective form of treatment meant individuals could have suffered from more than one disease. This is especially the case in relation to chronic afflictions that could be combined with congenital diseases or acute infections. Syphilis and tuberculosis (TB) were two of these diseases. Significant in the past, both diseases continue to be an important public health problem. Syphilis, caused by the spirochete *Treponema pallidum* is typically transmitted through sexual contact. It can also be transmitted via the placenta from an infected mother to the fetus while she is in the most infectious stages of the disease (early primary or secondary stage). It is known as congenital syphilis [1]. Syphilis affects more than 12 million adults [2–4] and a million pregnancies each year [4–6]. Tuberculosis, a chronic infectious disease caused by *Mycobacterium tuberculosis,* is usually transmitted through the inhalation of airborne droplets filled with bacteria produced by infected individuals usually when coughing [7, 8]. Approximately 9 million new cases were registered and 1.5 million people died from tuberculosis in 2013 [9].

In most palaeopathological studies, skeletal signs of diseases are diagnosed to one nosological unit. This finds some justification in the fact that only a small portion of diseases leave recognizable signs on hard tissues of the body (bones and teeth). It is, however, possible to find signs of more than one affliction on a single skeleton [10]. When this is the case, study of skeletal involvement should not be the only method applied when making a differential diagnosis.

The differential diagnosis of syphilis and tuberculosis in palaeopathological specimens remains difficult as both diseases rarely affect or leave any signs on hard tissues of the body. In syphilis, only 1/3 of individuals suffering from the tertiary stage of the disease will develop any bone lesions [10] while only about 3% to 5% of individuals with active TB will have skeletal changes [11–13]. The diagnostic characteristic of syphilis include "caries sicca," sclerosis, and pitting of the outer table of the cranial vault resulting from accumulation of stellate scarring [11, 14] creating a "worm eaten" appearance

[14], tibial bowing, known as sabre shin [11, 15, 16], and the expansion of the long bones with nodes with superficial cavitation [14]. In tuberculosis diagnostic elements include osteolytic lesions on the thoracic and lumbar vertebral bodies [10, 13, 17]. Rib involvement including new bone formation, particularly periosteal reactions on the visceral surface [18–21] is now considered in the diagnosis of tuberculosis [22].

Lesions of congenital syphilis can also be difficult to identify in skeletal samples as many pregnancies can result in stillbirths, abortion, or death [15, 23] and those skeletons are not often preserved. However, in those patients that do survive, the disease causes a disturbance in dental development producing abnormalities that are distinguishable features of the disease. The most recognisable are Hutchinson's incisors, while others include Moon's molars and Fournier's "mulberry" molars [15, 16, 24–30]. It is this characteristic that can support a differential diagnosis of the disease.

However, in cases where these diagnostic changes are not present, differential diagnosis of a specimen can be difficult. Our knowledge of the type of treatments used to combat syphilis and tuberculosis throughout history is well known. They used natural remedies, chemical compounds, and recently penicillin; however, our knowledge of the effects of these treatments on hard tissues has not been explored in depth.

Mercury has been used as early as the 27th century BC in China [31]. It was recognised as a form of treatment for venereal diseases [31–33] prior to the introduction of salvarsan [34–37] and penicillin in the 20th century [38]. Mercury was provided to mothers during pregnancy [39] children, and infants in the form of ointments, calomel teething powders [24, 40, 41], and injections [41, 42]. Mercurial poisoning was noted by Sir Hutchinson [24, 25, 40] to grossly influence tooth development producing abnormalities of enamel formation (Figure 1). These may interfere with the expression of "classic" dental signs of congenital syphilis. When salvarsan was introduced, replacing mercury early in the 20th century, American military physicians recommended the use of mercury for the treatment of tuberculosis in adult patients [43, 44], but it is unclear how widespread this method of TB treatment became. There is no mention of its effects on dentition.

This paper presents a case study of the pathological lesions observed on a European subadult dated from the mid-19th to early 20th centuries who died during the early European colonization of South Australia, Australia [45]. The influences of mercury are considered in this case. In order to understand variation in skeletal lesions it is useful to consider the treatments used and their possible effects on the hard tissues of the body. This method may assist in a differential diagnosis.

2. Materials and Methods

The juvenile in this study (B70) was among a sample of 70 individuals excavated in 2000 from the cemetery of the Anglican Church of St. Marys, located at 1167 South Road, in St. Marys, Adelaide, South Australia. Many of those buried at the cemetery were in unmarked graves in a section of the grounds dating from 1846 to 1927, preventing individual identification [46]. These unmarked graves were considered colloquially as "paupers" graves due to their low socioeconomic status. Written records of burials can be found at the Church's Office. Signs of various infections were found on paleopathological analysis among the skeletal sample excavated including acquired syphilis, tuberculosis, pulmonary, and systemic infections. Some of these were also listed as causes of death in parish records [46]. Two thirds of the skeleton survives (Figure 2). Bone tissue is fragile and poorly preserved with some bones missing and others in fragments. The individual was aged by dental development, eruption, and formation using the Ubelaker chart [47] and primary ossification centres [47, 48]. Sex of a subadult is difficult to estimate [49–51] and the methods proposed do not produce highly reliable results. Using the morphology of the symphyseal region of the mandible [52] and the shape of the mandible [53] in combination with the robusticity of long bones [54], the shape of the sciatic notch would have been used to aid in determining sex; however, the majority of the pelvis is missing. To determine the effects of mercury on hard tissues and possible pathologies, a search of the literature was conducted and compared to B70.

3. Results

B70 is probably a subadult male. According to dental eruption and formation, the child is between eight and ten years of age. An osteoblastic lesion approximately 15 mm in diameter is present on the cranial vault (possible periosteal reaction) on the posterior portion of the left parietal bone close to the lambdoid suture (Figure 3). Pitting is present on the maxillary alveolar process (Figure 4) and on both sides of the palate; however, it is stemming from the root of the right first upper molar (Figure 5).

3.1. Dentition. B70 demonstrates mixed dentition. The maxillary upper right central incisor is the only tooth missing postmortem. The dentition consists of a left central incisor, partially erupted lateral right and left incisors, deciduous canines, first and second premolars, permanent first molars, and second permanent molar germs. The maxillary left central incisor demonstrates narrow and rounded medial and distal edges and is slightly crescentic in shape. It is hypoplastic. Its incisive edge is slightly narrowed with minute mamelons and multiple notching. The incisal 1/3 of the labial surface has thinner, discoloured (darker) enamel with pitting hypoplasia. This part of the crown forms a few months after birth [55]. The remainder of the labial surface has three transverse hypoplastic lines (Figure 4). On the lingual surface, the incisal 1/3 of the crown has thinner enamel. It is separated from the remainder of the crown by a distinct hypoplastic grove that extends to the mesial and distal surfaces. The lateral right incisor is narrow and hypoplastic. The right and left maxillary lateral incisors on the labial view, approximately a third of the distance from the apical point of the crown, are a round indentation in the enamel. The lateral left incisor has a central pit about 1 mm in diameter and is notched mesially. Crowns of the upper deciduous canines have wide hypoplastic discoloured (darker) areas beginning below

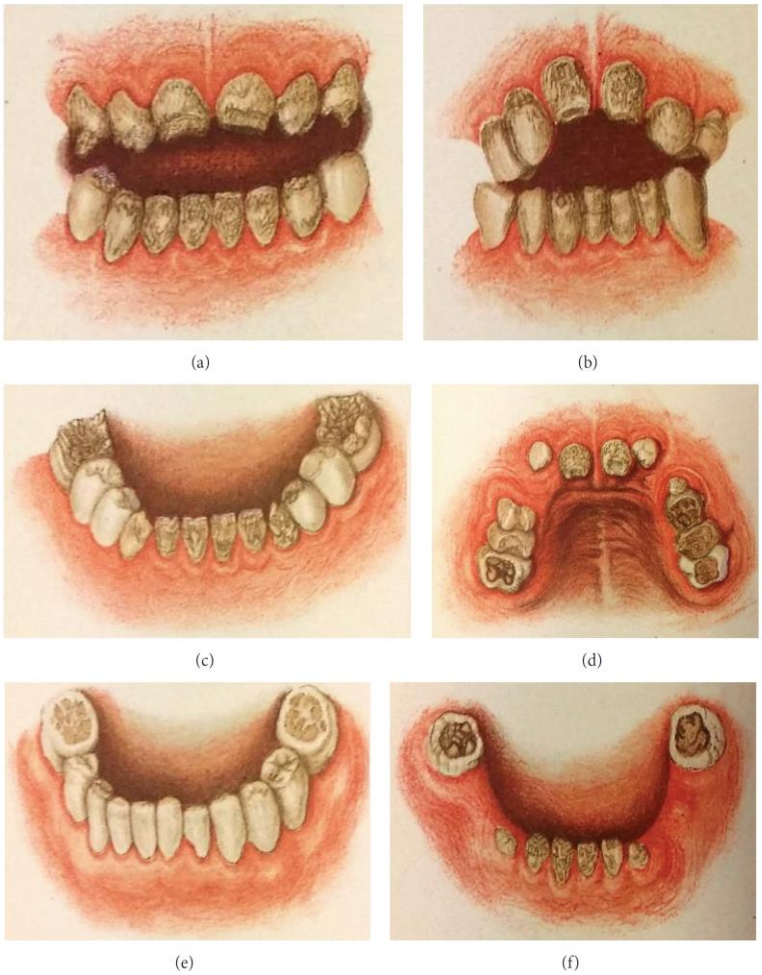


FIGURE 1: Diagrams of mercurial teeth seen in mercurial treated congenital syphilitic patients by Hutchinson. Hutchinson, J. 1878. Illustrations of clinical surgery consisting of plates, photographs, woodcuts, diagrams, and so forth: illustration of surgical diseases, symptoms and accidents, also operative and other methods of treatment, with descriptive letterpress, London, J. & A. Churchill.

the tip of the crown and extending down to about 1/3 of the crown indicating that the changes occurred after birth (Figures 4 and 5). All maxillary premolars appear normal. Both first permanent upper molars have grossly abnormal crowns. Their occlusal surfaces have widespread hypoplastic defects (Figures 6(a) and 6(b)). Extensive carious lesions are present on the mesial half of the occlusal surface of the right upper first permanent molar and small carious lesions on the occlusal surface of the left first permanent molar. Distinctive lines of thinner enamel are present on both permanent molars, separating the upper part of the crown (occlusal surface) from the rest of the crown. Areas constricted by the lines are smaller than the extent of the lower parts of the crowns. This indicates that the changes occurred shortly after birth [55]. The crown morphology of the second permanent molar germs is normal.

Mandibular dentition includes all permanent incisors, deciduous molars, canines, first permanent molars, and second permanent germs. The permanent incisors are hypoplastic with small mamelons and linear and pitted hypoplasia on the crowns (Figure 7(a)). Distal 2/3 crowns of lower deciduous canines are very narrow with thinner hypoplastic enamel and appear conical in shape (Figure 7(a)). The remaining proximal 1/3 has rather normal enamel. The proximal 1/3 of deciduous canine crowns has normal enamel. First deciduous molars show discolouration but no caries.

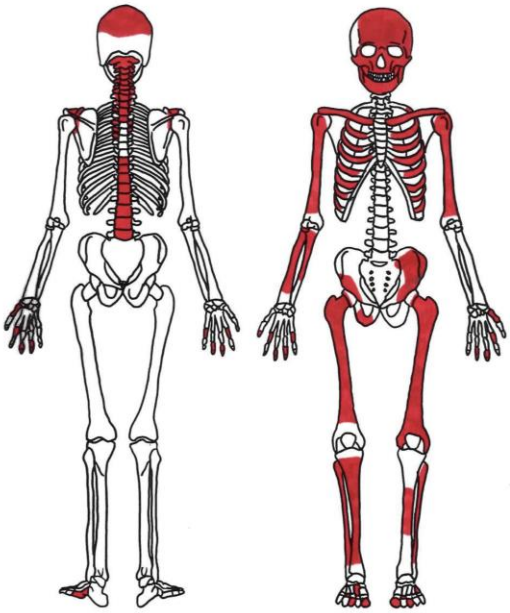


Figure 2: Shaded areas represent bones present.

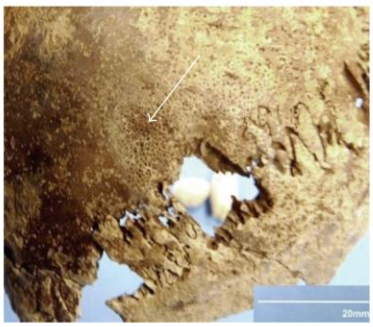


Figure 3: Periosteal reaction approximately 15 mm in diameter on posterior portion of the left parietal bone close to the lambdoid suture. On close inspection there is no erosion of the cortical bone (Lamina externa).

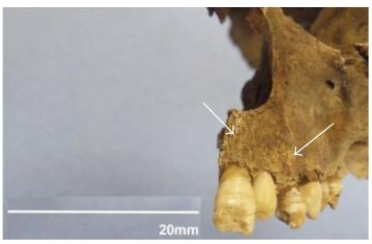


Figure 4: Pitting on maxillary alveolar process due to inflammatory response.

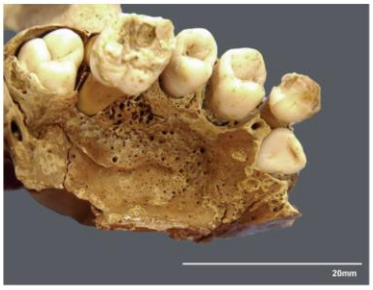


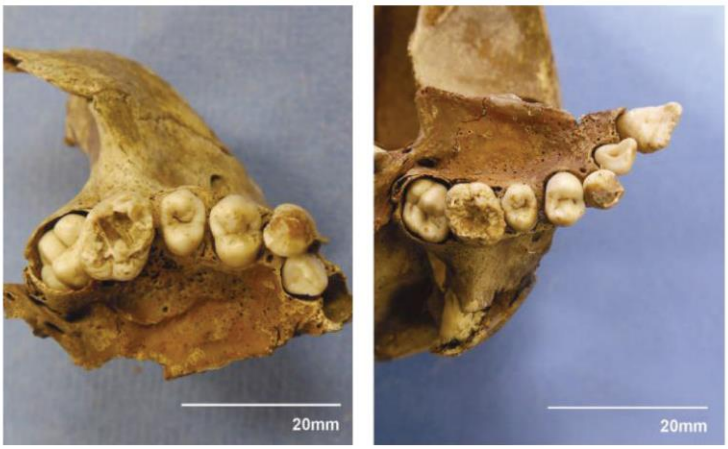
Figure 5: Pitting on palate stemming from permanent first molar due to inflammatory response.

The second deciduous molars and canines have extensive carious cavities. The first permanent molars occlusal surfaces are grossly hypoplastic (Figure 7(b)). Similarly to the maxillary dentition, hypoplastic changes indicate that they have occurred within the first few months after birth. The right lower permanent molar has an extensive carious lesion extending through most of the centre of the occlusal surface. A small carious pit in the centre of the mesial half of the occlusal surface is present in left (Figure 7(b)). The crown morphology of both lower second molar germs is normal. Resorption of the alveolar bone is observed (Figure 7(a)).

3.2. Clavicle and Ribs. Morphology of the clavicle and several ribs appears abnormal. Thinning of the sternal end of the clavicle is evident (Figure 8). There is a small proliferative change on the upper portion of the 3rd rib. Localised inflammatory reaction is present on the right side, superior surface on the 4th or 5th rib (Figure 9). Added grooving is evident on the superior surface of several ribs.

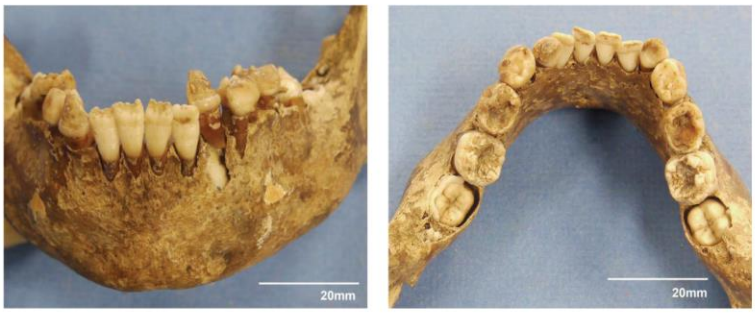
3.3. Vertebral Column. There are extensive pathological changes on the vertebral column. The vertebral bodies of C5-Th3 show damage to their anterior parts. Signs of remodelling on C6 and C7 could indicate signs of healing (Figure 10). Cervical vertebrae C1–C4 show no pathological signs. Vertebral bodies of Th3-Th4 are largely destroyed, Th4 more so than Th3. Bodies of all other thoracic vertebrae, except Th10 and Th11, are absent, but it cannot be ascertained whether this was due to taphonomic processes or due to actual pathological destruction. Zygapophyseal joints between what are likely to be Th5-Th6 are completely fused on both sides and there are no vertebral bodies (Figure 11(a)). The left zygapophyseal joints of Th6-Th7 are also fused, while the right side is missing. Th9 is possibly in fragments. Vertebral body of Th10 is partially destroyed. Th11 and Th12 are represented by small fragments.

Two bodies and two arches of the lumbar vertebrae are preserved. One body has two deep pits on its anterior surface, which appear lytic (Figure 11(b)). The other body and the arches show no pathological signs. The body and right lateral mass of the first sacral segment are preserved without obvious pathological signs. The left lateral mass of the sacrum



(a) (b)

Figure 6: (a) Right permanent upper first molar showing signs of dysplastic occlusal enamel. (b) Left permanent upper first molar with hypoplastic defects characteristic of dysplastic occlusal enamel.



(a) (b)

Figure 7: (a) Angled lower border of mandible, similar in shape to male juvenile mandible A.668 studied by Loth and Henneberg [52, Figure 2]. (b) Lower first permanent molars grossly hypoplastic.

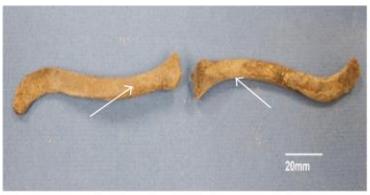


Figure 8: Thinning at sternal ends of clavicles.

Figure 9: Inflammatory reaction of inferior surface on 4th or 5th rib.

is completely fused with the left ilium at the sacroiliac joint. There are no clear signs of any inflammatory processes. Right sacroiliac joint appears normal. The first sacral segment has a normal body. Bodies of other sacral segments are preserved in fragments and no pathological signs were observed. No pathological signs were noted on the long bones.

4. Discussion

4.1. Differential Diagnosis. In this case, it is possible that B70, a mid-19th to early 20th century specimen, suffered from multiple conditions. Differential diagnosis of B70 includes

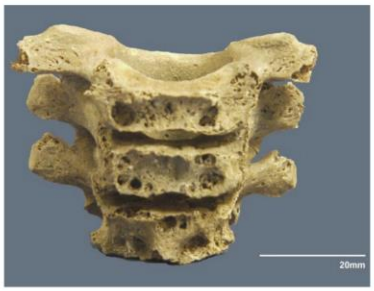
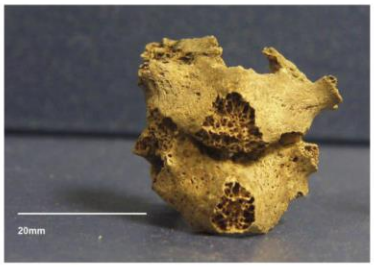
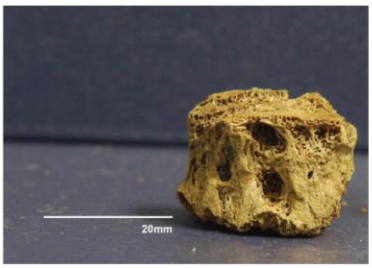


Figure 10: Destruction of anterior bodies of lower cervical vertebrae.



(a)



(b)

Figure 11: (a) Fusion of zygapophyseal joints between Th5 and Th6 completely fused with no vertebral bodies. (b) Lumbar vertebral body with deep pits.

infectious and noninfectious diseases including congenital syphilis, tuberculosis, brucellosis, rickets, and fluorosis.

Lesions in congenital syphilis can vary from periosteal reactions and osteomyelitis in the early stages [56–58] and cranial gummatous lesions and frontal bossing of the bone, destruction of the nasal bridge, a high arch palate, sternoclavicular thickening, and tibial bowing (sabre shin) in the late stage of the disease [15, 16, 59–61]. With the exception of a possible localised periosteal reaction on the cranial vault of B70, there is minimal skeletal evidence to support the differential diagnosis of congenital syphilis.

The dental changes in B70, although not "typical" (Hutchinson's incisors, Moon's molars, or Fournier's mulberry molars), may still be a result of congenital syphilis through the mercurial treatment of the disease. Hutchinson recognised that mercury produced enamel defects in particular pairs of teeth. In severe cases it would affect dentine, too. With the tooth enamel deficient, the tooth would appear rugged, pitted, and dirty [40]. The first permanent upper and lower molars are the "test teeth" for mercurial influence, similar to the upper central incisors considered to be the "test teeth" in congenital syphilis. The crown enamel is deficient, with dentin growing through and revealing numerous discoloured tubercles [40]. A distinct demarcated line separating healthy enamel from diseased enamel was also evident on the sides of the molars. In severe cases, the tooth could appear dwarfed. Upper and lower incisors and canines were usually affected, with enamel deficiencies occurring below a line that would cross them at the same level; however, premolars usually escape all damage [40]. Hutchinson also noted that it was common for both syphilitic and mercurial teeth to be present at the same time which may have caused confusion among physicians [40]. He did not specify, however, exact ages or developmental stages of dentition at which the changes occurred.

B70's dentition closely resembles the descriptions and images (Figure 1(c)) of congenital syphilis patients treated with mercury as provided by Hutchinson. The first upper and lower permanent molars demonstrate enamel deficiency across the occlusal surface exposing multiple tubercles, appearing rugged, pitted, and dirty. There is a clear distinction between diseased and healthy enamel on all four molars and all three canines. All upper and lower incisors exhibit enamel deficiencies apical to the linear enamel hypoplasia. All upper premolars appear normal. Taking into account individual variation in formation of deciduous and permanent tooth crowns, the most likely age at which the changes in B70's dentition occurred is shortly after birth. The cervical ends of enamel on all teeth appear normal, suggesting that ameloblasts were disturbed during the early years of life [62]. Tips of deciduous canine crowns seem to be normally formed, but the crown area below them is hypoplastic in contrast to first deciduous lower molars whose morphology is normal. Permanent tooth changes affected apical or occlusal portions of specific crowns that form in the first few months of life. It is possible that the type of enamel damage to the first permanent molars in B70 could be classified as cuspal enamel hypoplasia [62]; however, to confirm this, scanning electron microscopy would need to be performed.

Clinical presentations of congenital syphilis present similar dental features to those seen in B70. These include multiple notching or serrated edges which were seen in five patients [63] pitted enamel hypoplasia of the upper central and lateral incisors and primary and secondary dental caries on numerous teeth [64]. Narrowing and a reduction of the dentinoenamel junction of the permanent incisors and first molars, with a reduction in the size of the crowns and constriction of mamelons, was also noted by Sarnat and Shaw [27].

In comparison to palaeopathological specimens, similarities to B70 include the round indentation in the enamel on the maxillary right and left lateral incisors [65–67] and pitted enamel hypoplasia in the lower right incisors. Others include linear enamel hypoplasia in all four incisors with a deficiency

in enamel above (apically) a hypoplastic line [67, 68], the distinct demarcation between healthy and diseased enamel, and severe enamel deficiencies exposing multiple tubercles in molars [67].

The lack of skeletal lesions on limb bones of B70 could be supported by clinical cases of late congenital syphilis, which found no periosteal lesions or perichondritis [69, 70]. This may be related to the stage of infection in maternal syphilis and transmission [69]. The later stages of the disease in the mother produce lesser risk of infection [15] and possibly less severity.

Tuberculosis is typically diagnosed by osteolytic skeletal lesions in the vertebral bodies and in large joints of palaeopathological specimens [11]. The most common manifestations of skeletal tuberculosis in children are spondylitis, osteomyelitis, and involvement of the joints [11, 71]. In children, common areas affected by the disease included the knee [72, 73], lytic circumscribed lesions of the cranium [7, 74, 75], spine [71, 76], hip [73, 77], elbow [78], and ribs [76]. There is no documentation with regard to dental abnormalities found in juvenile tuberculosis [7, 79]. Dental changes briefly mentioned include linear enamel hypoplasia [80, 81], carious lesions, and decreased enamel thickness [80].

Comparing B70 to skeletal signs of tuberculosis, osteolytic lesions evident on the thoracic and lumbar vertebrae resemble few juvenile specimens [81, 82]. A circumscribed periosteal lesion on the superior surface of rib four or five in B70 is similar to that found in the case of TB in the Hamann-Todd Osteological Collection [83]. However, no lytic lesions were apparent on the cranial vault of B70, neither was there involvement of the joints as in the cases mentioned above. Linear enamel hypoplasia and dental abnormalities as seen in B70 have not been noted in clinical cases of primary tuberculosis [84–86]. There are no documented palaeopathological cases of congenital tuberculosis. This may be due to the rarity of the disease and the low survival rates of infants born with the condition [87–89]. Therefore, congenital TB is not known to produce extensive hypoplastic defects on incisal edges nor on occlusal surfaces of teeth. It is likely that B70 suffered from TB acquired during childhood.

While we know that mercury has been used in the treatment of tuberculosis, its descriptions and suggested use begin from 1908 and they do not seem to be widespread. B70 was buried in a cemetery dating from 1846 to 1927, so it is unlikely that mercury's use in treatment of tuberculosis would be the cause of described dental changes.

Brucellosis affects different areas of the skeleton in adults and in children. In adults the spine or sacroiliac joint is more commonly affected, whereas in children, the knee, hip, and ankle joints are more common [90–94]. While the left sacroiliac joint is fused in B70, who is a child, there do not appear to be any signs of inflammation and there are no other pathologies that resemble those seen in brucellosis; therefore, it is difficult to make a confident differential diagnosis. However, the sacral segments that are present do not show any pathology. There are also no lesions present on the knee joint or the rest of the appendicular skeleton, and thus brucellosis is unlikely.

Rickets is a vitamin D deficiency, affecting the metabolism of calcium and phosphorus and the mineralization of bone. Skeletal changes include bending deformities [95, 96], metaphyseal flaring, and porosity of cortical bone [11, 95, 97]. These changes can affect the cranial vault, long bones, pelvis, ribs, and vertebrae. In conjunction with the skeletal pathologies of rickets, abnormalities in dentition are common, particularly linear enamel hypoplasia, pitting, dental opacities, and caries [98–100]. Considering that there are no bending deformities, flaring, porosity of the cortical bone, and dental opacities and while hypoplasia is not limited to linear defects, rickets in B70 is unlikely.

Fluorosis is a disturbance of dental development resulting from ingestion of large quantities of fluoride [11, 101]. These dental abnormalities include opaque white patches in the enamel. This can result in pitting, striations, and widespread brown staining [101–104]. Skeletal pathologies include abnormal bone formations on the appendicular or axial skeleton, mostly linked with the insertions of tendons and ligaments [11]. In clinically diagnosed cases of fluorosis in children, skeletal manifestations included osteopenia, growth lines, and sclerosis [105–107]. Considering that there is no widespread dental staining nor skeletal lesions relating to fluorosis, it is unlikely that B70 suffered from fluorosis.

5. Conclusion

B70 was excavated from St. Marys cemetery, from a section of the grounds dating from 1846 to 1927, when European settlers colonized South Australia. B70 was buried at the expense of the Government in a section of the cemetery referred to as the "paupers" graveyard [108]. Burial records of St. Marys indicate that treponemal diseases and tuberculosis were present among the skeletal sample B70 originated from and other skeletons (B10, B6, and B53c), demonstrated possible cases of treponemal disease [46]. Considering that B70 was excavated from the pauper's section of the graveyard and multiple diseases were present in the sample (syphilis and tuberculosis), it is probable that B70 suffered from multiple diseases in congenital syphilis and tuberculosis. The significance of this skeleton is that it displays dental signs that are not typically seen in congenital syphilitic cases. It is possible that this specimen displays the effects of mercury that was used to treat the disease. It is possible that chemical elements or compounds have not been considered in paleopathology to have an effect on hard tissues. Hopefully, this paper will reintroduce an interest in the work of Hutchinson who noted that mercury, used to treat syphilis, plays a role in the disruption of enamel formation. Mercury's effects are separate from tooth development (size and shape), caused by the disease and yet they are indicative of the disease through its treatment. Therefore, Hutchinson's incisors, Moon's molars, and Fournier's molars are not the only dental abnormalities that should be considered in the diagnosis of syphilis when examining specimens from antiquity up to the introduction and usage of modern treatments.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Five Cases of Dental Anomalies Attributable to Congenital Syphilis from Early 20th Century American Anatomical Collections

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ABSTRACT Specific dental abnormalities are considered pathognomonic of congenital syphilis (CS); however, European physicians recognized their variation during the late 19th to mid 20th centuries. Observations of syphilis-related dental abnormalities in American individuals from similar time periods are made to determine types of variation among the American population.
From a survey of the Smithsonian Institution's National Museum of Natural History anatomical human skeletal collection, five individuals demonstrated dental characteristics consistent with CS (P00011R, P219398, P000707, P000679, and P000161). Hutchinson's three categories of dental anomalies were used to describe variations among syphilitic individuals.
Previously identified pathological dental characteristics related to CS were present in the analyzed individuals. P00011R, 24-year-old Black female, has a maxillary right Moon's molar. P219398, approximately 20-year-old Black female, has Hutchinson's incisors and Fournier's molars. P000707, 26-year-old Black male, displays severe hypoplasia on all incisors, canines and maxillary first molars. P000679, 33-year-old Black female has "screwdriver" shaped maxillary central incisors, altered occlusal morphology of first maxillary molars and hypoplasia. P000161, 45-year-old Black female, demonstrates severe hypoplasia on incisors and canines (molars lost).
"Classic" dental characteristics of CS are not ubiquitous to all identified cases. This study exemplifies that dental anomalies associated with CS do not all have to be present for diagnosis. Although other causes for some of these anomalies are possible, observations in these five cases are most consistent with CS.

Prior to the introduction of penicillin in the 1940s, syphilis was a public health problem in the United States (Lancet, 1930; Lancet, 1937a). The prevalence of syphilis in the United States at that time is difficult to determine, as data collection for syphilis by state health departments did not begin until the early 20th Century, and the Venereal Disease Division of the U.S. Public Health Service was not created until 1918 (Nakashima et al., 1996).

To control venereal disease, various states implemented programs (free treatment, and clinics that offered free, pay, and part pay clinics) (Lancet, 1937a), and legislation (marital examination law and prenatal law) (Lancet, 1917; Prebble, 1938; Lancet, 1940; DePorte, 1941). In cases of medical intervention, mercury was used to treat congenital syphilis in the 19th and early 20th centuries throughout the United States (Conrad and McCann, 1922; Cole et al., 1929; Scheer and Fraser, 1930; Cole et al., 1933; Chargin and Saunders, 1939). Treatments of syphilis also included chemotherapies of arsenic and bismuth compounds (Lee, 1878; Cole et al., 1929; Eller and Maloney, 1929). The chemotherapies most favored in the treatment of congenital syphilis included mercury, arsphenamine and potassium iodide (United States. Public Health Service. Division of Venereal Diseases, 1930).

The effectiveness of mercury as a treatment for syphilis has been questioned (Miller, 1858: Weatherill, 1833); although, the treatment remained popular with some physicians. In some cases, syphilitic lesions completely healed and patients became seronegative (Wakerlin, 1934). In syphilitic women treated with mercury during their pregnancy, 91.5% were efficient in completing their pregnancies successfully by live birth, while 47.6% non-treated women experienced fetal death (United States. Public Health Service. Division of Venereal Diseases, 1930). Mercury and its compounds were seen to

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have antibacterial properties that actually reduced, or cured infections with *Treponema pallidum* (Smith, 1844; Hare, 1858; Warner, 1881; Wakerlin, 1934). Despite their possible curative effects on syphilis, mercurial treatments yield serious side effects including scarlatiniform rashes, stomatitis, pyrexia, bleeding of the rectum, and death in some cases (Chopping, 1899; French, 1909). Therefore, the use of mercury was abandoned later in the 20th century when other effective forms of treatment (i.e., penicillin) became available and mercuric treatments were dropped from clinical practice.

In paleopathology, the diagnosis of congenital syphilis (CS) is based on skeletal and dental signs. However, when skeletal signs are not present specific dental abnormalities caused by a disturbance in odontogenesis are associated with the disease (Hillson et al., 1998). Signs include Hutchinson's crescentic notched or screwdriver incisors (Hutchinson, 1859; 1887), Moon's dome-shaped molar (Moon, 1884), and Fournier's molars of "upset appearance" (Bouleversée d'aspect) (Fournier, 1886:84). These changes occur when odontogenesis is affected during the early stage of the disease. During the 19th century, Jonathan Hutchinson, was the first to note that syphilitic treatments containing mercury also affected dental development, disrupting amelogenesis. Hutchinson described that these mercury-induced dental malformations were significantly different from those caused by congenital syphilis alone, and in some cases, patients exposed to a treatment regimen involving mercury could manifest dental signs associated with the disease and treatment (Hutchinson, 1888; Moon, 1884; summarized in - Ioannou et al., 2015, 2016). It should be noted that 10-30% of patients clinically diagnosed with congenital syphilis do not manifest changes associated with disturbed odontogenesis (Švejda, 1952; Lipski and Przylipiak, 1959). It is clear that these inconsistencies caused confusion among physicians in the past (Hutchinson, 1878) and with diagnoses in both clinical and paleopathological settings.

During late 19th and early 20th centuries, various institutions produced collections of skeletons for future research purposes. These collections included skeletons of individuals who suffered from various diseases including treponemal diseases. Today such collections provide hard evidence of the disease and its treatments, independent of government records and the literature. For some individual skeletons, there is medical documentation stating the cause of death, while others have been given differential diagnosis based on the skeletal evidence by the curator. Such diagnoses were based on paleopathological knowledge of the curator at the time.

While previous studies have focused on "typical" dental characteristics associated with congenital syphilis, this paper will also assess the possibility of some of the dental anomalies being from the medical treatments. Therefore, the aims of this paper are: (1) to describe the variation and similarities in dental abnormalities associated with congenital syphilis in individuals either medically diagnosed with the disease or who were posthumously diagnosed by skeletal pathological conditions or dental anomalies to have been afflicted with congenital syphilis, and (2) to evaluate whether there are any indications of dental features that could be the result of treatments for congenital syphilis. Differential diagnoses of other diseases or genetic conditions that could have effects on dental characteristics are reviewed, including tuberculosis, leprosy, amelogenesis imperfecta, rickets, fluorosis, and some of the chemicals used to treat these diseases are also considered, such as mercury, arsenic, bismuth, lead and cadmium.

MATERIALS AND METHODS

As stated above, 10-30% of patients clinically diagnosed with congenital syphilis do not manifest dental anomalies (Švejda, 1952; Lipski and Przylipiak, 1959). To assess the range of expression of the dental anomalies attributed to congenital syphilis, those conditions as described by Jonathan Hutchinson (1859, 1863, 1878, 1887, 1888), Henry Moon (1877, 1884), Alfred Fournier (1886), and Hillson et al. (1998) are used as the criteria for the cases observed here to evaluate the likelihood of congenital syphilis in the anatomical collections and to see if comparable dental abnormalities are present. The criteria are reviewed and described by Ioannou et al. (2016).

A review of dentition in the early 20th century Robert J. Terry anatomical skeletal collection and cadaver room skeletons from the Howard University Medical School was made at the Smithsonian National Museum of Natural History (NMNH) in Washington DC. The survey focused on individuals listed as having pathological conditions related to the following: congenital syphilis, treponemal disease, lues disease, syphilis, tuberculosis, and rickets. These pathological identifications came from death certificate records, reports from the morgue records, or diagnoses made by observations of the cadavers or the skeletal elements in dissection or after skeletonization. Some of the observations made by curators were independent from the cause of death of these individuals.

Out of 38 individuals that were narrowed down from the initial survey, five individuals exhibited various dental malformations consistent with those in patients diagnosed with congenital syphilis (Excel file with data is available from SI upon request). The five individuals were P00011R, P219398, P000707,

P000679 and P000161, of which only P00011R was clinically diagnosed with congenital syphilis while living. The dentition of these individuals was analyzed to document the types and range of malformations in tooth morphology. Since human variation and their effects from disease are individualistic and often do not present the "typical" pathological manifestations of a particular disease.

To evaluate the possibility of mercury treatment of any of these subjects, portable x-ray fluorescence (pXRF) spectrometry was conducted to determine whether mercury could be detected in the enamel and bone in each of the individuals.

Dental Malformation Criteria for Evaluation of Treponemal Disease

Hutchinson (1859, 1863, 1878, 1887, 1888) recognized that dental malformations observed in children with congenital syphilis varied so considerably that he deemed it necessary to create various categories to distinguish kinds of anomalies in dental formation. His three categories of dental malformations were - syphilitic teeth, mercurial teeth, and syphilitic-mercurial teeth.

In the syphilitic category, the maxillary central incisors are the "test teeth". The central incisors can appear "peg like" or screwdriver in shape, are dwarfed and display a crescentic notch on the incisal edge (Hutchinson's incisors). Some of these features can also be observed in the maxillary lateral incisors and mandibular incisors (Hutchinson, 1887; Hillson et al., 1998). Other characteristics within the syphilitic category include malformations observed in the first permanent molars (Hutchinson, 1887) labeled as Moon's molar and Fournier's molars. Moon's molar is "smaller than usual and dome-shaped" (Moon, 1877), while Fournier's molars either have several nodules and tubercles or have a flat surface (Fournier, 1886). Both varieties of Fournier's molars have a clear demarcation between healthy and diseased enamel.

Mercurial teeth demonstrate severe enamel hypoplasia, caused by treatments containing mercury. The first permanent molars are the "test teeth". The enamel is deficient and appears rugged, pitted, and dirty with a honeycomb appearance (Hutchinson, 1878; Ioannou et al., 2016). Dentine is affected in severe cases with the appearance of multiple spines or tubercles. The entire occlusal surface or a central area can be affected. Incisors and canines are also affected with severe linear enamel hypoplasia that crosses these anterior teeth at the same level. The enamel between the linear enamel hypoplasia and the tip of the crown is deficient (Hutchinson, 1878), and pitting hypoplasia is also common. Premolars in most cases appear normal. However, the characteristic notch observed in syphilitic incisors is not mimicked in mercurial conditions only (Hutchinson, 1878). Syphilitic-mercurial teeth demonstrate a combination of both syphilitic and mercurial dental malformations (Hutchinson, 1878; Moon, 1884; Ioannou et al., 2016). The upper central incisors can have a peg-like or screw-driver shape (outline), the incisal edges appear characteristically notched, and any part of the enamel surface can be hypoplastic, pitted and discolored. The first permanent molars can show an absence of enamel on the occlusal surface of the crown but have healthy enamel on its sides (Hutchinson, 1878).

RESULTS

Terry Collection P00011R (Fig. 1) is an African American female, born in 1918 and died in 1942, at 24 years old. The primary cause of death was attributed to lobar pneumonia, but was clinically diagnosed with congenital syphilis in 1930 and was subsequently institutionalized until her death, 11 years and 2 months later. This is the only individual that was diagnosed with congenital syphilis during the life of the individual.

All maxillary incisors and left maxillary canine were lost many years before death (Fig. 1A). The first right upper molar has a clearly narrowed occlusal surface with pitting hypoplasia resembling a dome shape (Moon's molar) (Fig. 1B & 1C). The left first upper molar has a narrowed occlusal surface, and is largely destroyed by dental caries. All the premolars and right canine have normal morphology. The second and third permanent molars have normal molar morphology. The left third molar has a single carious lesion on the disto-buccal aspect. Upper alveolar process shows periodontal changes on both sides.

The mandibular teeth present include the left and right lateral incisors, left canine, left and right first premolars, left second premolar and left and right second and third permanent molars. The lateral incisors appear peg like in shape (Fig. 1D & 1E). Both first permanent molars were lost many years before death, and the alveoli are completely healed (Fig. 1F). The occlusal surface of the left second premolar and second and third permanent molars are destroyed by caries. Bone resorption suggests periodontal disease (Fig. 1D & 1F). Cranial morphology is normal, no 'saddle nose' is present, and the nasal cavity and palate are normal. The molars in P00011R are syphilitic.

Howard Collection P219398 (Fig. 2) is an African American female who died in 1903 in Washington, DC with no recorded cause of death and was autopsied at Howard University School of Medicine. There is not a reported age at death, but dental and skeletal development indicators suggest this individual died between 20 and 25 years of age. Previous evaluation

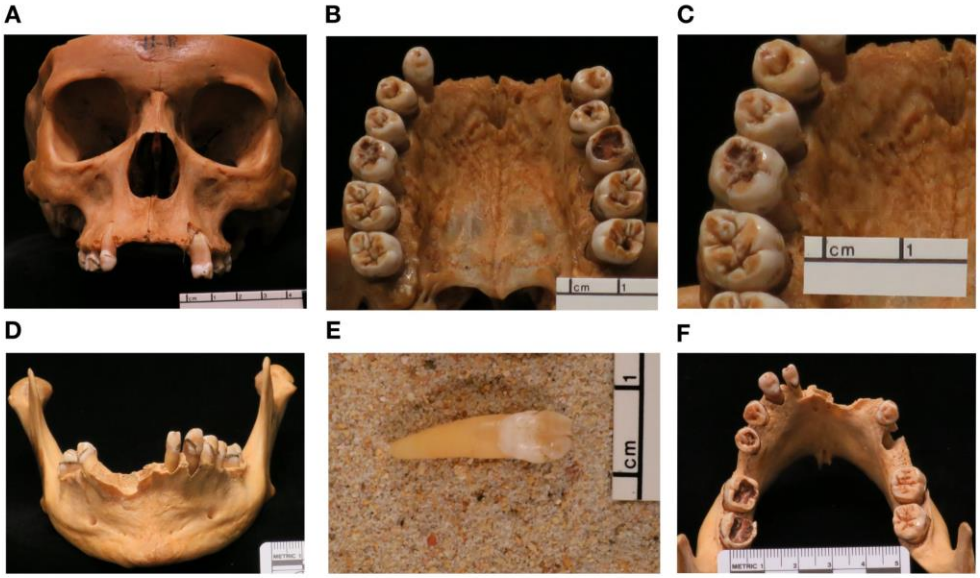

Figure 1. Individual P00011R, 24yrs old female. (A) Anterior view of maxilla: Central and lateral incisors, and left canine missing. No saddle nose. (B) Occlusal view: Most teeth have normal morphology. Carious destruction of the left first molar does not allow precise observation, but it seems that the crown has a narrow occlusal surface. (C) First right permanent molar has a narrow and reduced occlusal surface resembling Moon's molar. Pitting is also present. (D) Anterior view of the mandible. Periodontal disease is evident. (E) Loose anterior tooth of mandible; lateral right incisor. (F) Occlusal view of mandible: No first molars, most likely lost to caries.

by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All maxillary teeth are present, except the left second and third permanent molars. The maxillary central incisors are marked by rounded mesial and distal incisal edges. The labial aspects of the incisal one-third of both crowns have centrally located hypoplastic defects. On the right central incisor, this hypoplasia resulted in a smooth crescentic pit, while on the left central incisor there is irregular hypoplastic pitting in the same location (Fig. 2A). Multiple short lines of hypoplastic enamel are also apparent on the lingual surface of both teeth. The mesial and distal edges of the right and left lateral incisors are also rounded off, giving both teeth a peg-like shared crown. Multiple pits are present on the lingual surface of both lateral incisors. The tips and lingual aspects of the canines display hypoplastic pitting. The occlusal surfaces of the first permanent molars have diminished areas compared to the dimensions of the rest of the crown (Fig. 2B & 2C). There are also scattered hypoplastic pits and various areas of the occlusal surfaces have irregular grooves (Fig. 2C). The molars resemble both types of Fournier's molars. The second right permanent molar has normal molar morphology. The left second molar was lost during life, as the alveolar bone has healed.

The mandibular dentition is nearly complete. The left canine was lost post-mortem, while the alveolus of the lower left third molar is healed. The central incisors are affected by severe enamel hypoplasia and exposed dentine on the incisal one-fourth of the crown (Fig. 2D). The morphology and enamel of all other teeth, except the first permanent molars, appears normal. The occlusal surfaces of the crowns of the first permanent molars are reduced in size and severely hypoplastic (Fig. 2E & 2F). The cusps appear to be reduced in size and multiple tubercles are visible (Fig. 2F). This appears similar to Fournier's nodule-type molar. The dentine is also exposed in places. The morphology of the second permanent molars appears normal, with the left demonstrating signs of crenulation. The entire crown of the third right permanent molar is missing with only the root present while the left was lost during life as indicated by

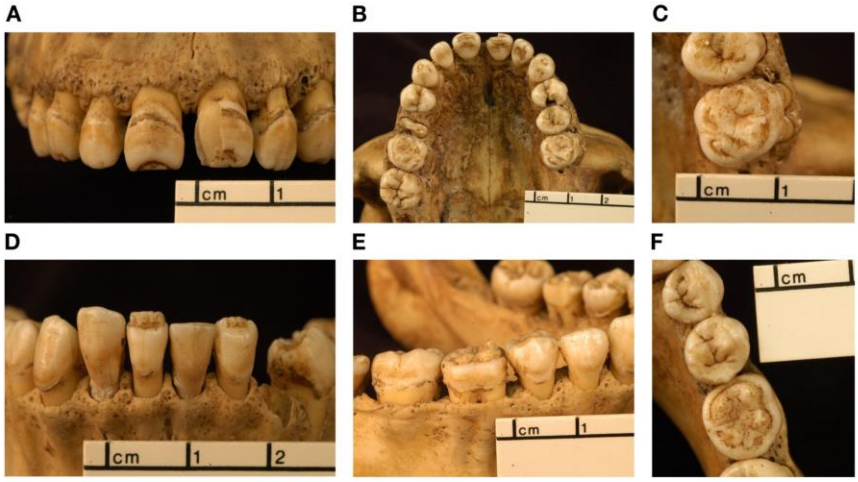

Figure 2. P219398, 20yrs old female. (A) Anterior view of maxilla: Labial aspect of permanent central incisors. Right incisor has thin enamel along incisal edge forming a crescentic pit. Irregular pitting is noted in the same location on the left incisor. Lateral incisors are peg-like in shape. (B) Occlusal view of maxilla: Occlusal surfaces of the first permanent molars are reduced and demonstrate scattered hypoplastic pits and irregular grooves. (C) Occlusal view of the left first permanent molar of maxilla demonstrates pitting and grooves in enamel. The occlusal surface is also reduced. (D) Anterior view of mandible: Central incisors demonstrate enamel hypoplasia and exposed dentine on the 1/4 of the crown. Note, the central and lateral incisors appear to be incorrectly inserted into mandible post mortem. (E) Lateral view of right side of mandible: First permanent molar resembles that in the maxilla. (F) Occlusal view of right mandibular first permanent molar: it has reduced surface, multiple tubercles and pitting hypoplasia.

healed alveolar bone. The morphology of the alveolar bone suggests some periosteal inflammation was present at the time of death. The dental abnormalities in P219398 are most consistent with syphilitic malformations.

Terry Collection P000707 (Fig. 3) is an African American male, aged 26 years at the time of his death in 1929 in St. Louis, Missouri from pulmonary tuberculosis. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All permanent teeth, including the third molars, are present. The central incisors are marked by minor notches and isolated pits along the incisal edges. Enamel adjacent to the incisal edge appears healthy with minor pitting, however, the middle third of the crown shows progressively more severe pitting hypoplasia that ends with extremely deep defects that likely penetrate the pulp cavity (Fig. 3A). The cervical portion of the crowns appears normal. The left lateral incisor is affected by a similar progressively pitted enamel defect on the incisal third of the crown (Fig. 3A). The incisal third of the right lateral incisor has been lost at a point where the pitting morphology appears like that observed in its left-side antimere. A similar enamel defect affects the left canine (Fig. 3B). The enamel of the right canine appears to have broken off postmortem. The lingual surfaces of these anterior maxillary teeth are affected by irregular hypoplastic defects, demonstrating a mottled like appearance. The premolars have normal morphology. The occlusal two thirds of the crown of the first permanent molars are hypoplastic, with pitting hypoplasia and reduced surfaces in comparison to the other permanent molars present (Fig. 3C). However, some normal groove patterns of the occlusal surfaces are preserved. Minor pitting is present on the second and third permanent molars. The second left and third right permanent molars demonstrate crenulation. The alveolar bone suggests some periosteal inflammation was present.

The mandibular dentition consists of all permanent teeth, except the left and right first molars. Two thirds of all incisors and canines are affected by severe hypoplastic defects (Fig. 3D). The left and right first molars were lost antemortem. The alveoli for the first molars are healed but not completely resorbed (Fig. 3E). The second permanent molars and the left third permanent molars have normal molar morphology but demonstrate crenulation (Fig. 3F). The third left molar appears larger than the second permanent molars. A supernumerary fourth molar is present on

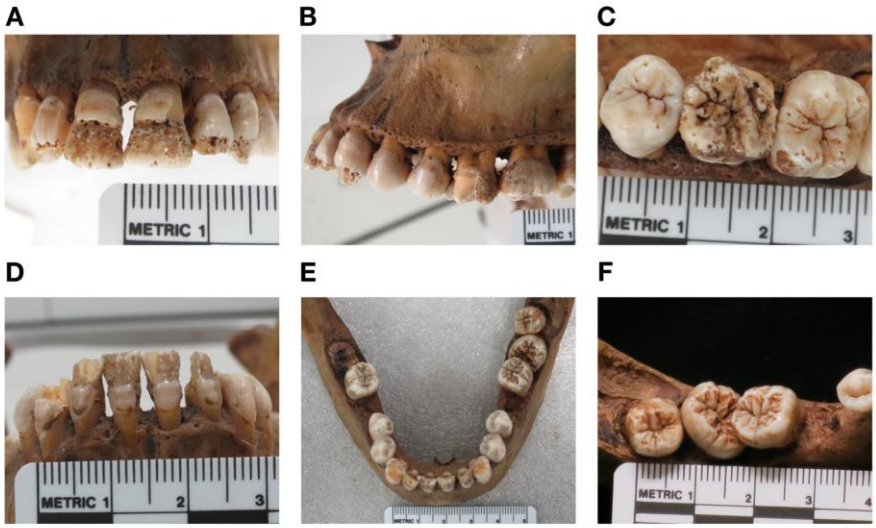

Figure 3. P000707, 26yrs old male. (A) Anterior view of maxilla: Incisal edges of the maxillary central incisors appear healthy with isolated pits. The middle third of the crown demonstrates progressively severe enamel hypoplasia. Similar enamel hypoplasia is evident on the lateral incisors and canines. (B) Lateral view of the left side of maxilla: The lateral incisor and canine display enamel defects similar to the central incisors. (C) Occlusal view of upper right first permanent molar, note unusual configuration of enamel on the occlusal surface. Two thirds of the occlusal surfaces of the first permanent molars are severely hypoplastic, although some normal groove patterns are preserved. (D) Anterior view of the mandible: Two thirds of all incisor and canines crowns are affected by severe hypoplastic defects. (e) Occlusal view of mandible, note both first molars are missing. (F) Close up of supernumerary fourth molar. Note crenulation on occlusal surfaces of other molars.

the left side (Ioannou & Henneberg, 2016). It is smaller in size in comparison to the other molars and has normal molar morphology (Fig. 3F). P000707 demonstrates dental signs that are suggestive of mercuric treatments.

Terry Collection P000679 (Fig. 4) is an African American female, who died of tuberculosis at 33 years of age in St. Louis, Missouri in 1928. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. The maxillary dentition is complete, except for the left third molar. It is unclear whether the absence of this tooth was due to agenesis or antemortem tooth loss. The maxillary central incisors have narrowed incisal edges with rounded corners. Located at the midcrown on the labial surface are hypoplastic defects that consist of an approximately oval-shaped area of thinner enamel, which is surrounded by pitting that extends distally to the one -third of the crown from the incisal edge (Fig. 4A). Shoveling is apparent on the lingual aspects, as is one linear hypoplastic line on the cervical third of the crowns (Fig. 4B). The lateral incisors appear peg like in shape with round mesial and distal edges. A couple of isolated pits are evident on the right lateral incisor. One hypoplastic line runs at the same level on both lateral incisors on the labial aspect. The left canine has isolated pits on the tip of the crown. Pits and grooves are present on the lingual aspect of the canines. Pitting is on the occlusal surface and lingual aspect of the first premolars. The right second premolar has a deep groove on the lingual surface. Maxillary first molars have occlusal surfaces that are reduced in size and have abnormal enamel formation (Fig. 4C). There is a demarcation between diseased and healthy enamel by pitting hypoplasia (Fig. 4D). The second molars and third right molar have normal morphology.

The mandibular dentition is represented by a full set of anterior teeth from the left first premolar to the right first premolar. The right third molar and the left second molar are present. All other posterior teeth were lost antemortem as indicated by complete alveolar remodeling (Fig. 4E). The incisors are marked by multiple notches on their incisal edges. Shallow indistinct furrows are present about one-third the length of the crown (Fig. 4F). Isolated pits are present on the lateral incisors. Part of the enamel on the labial

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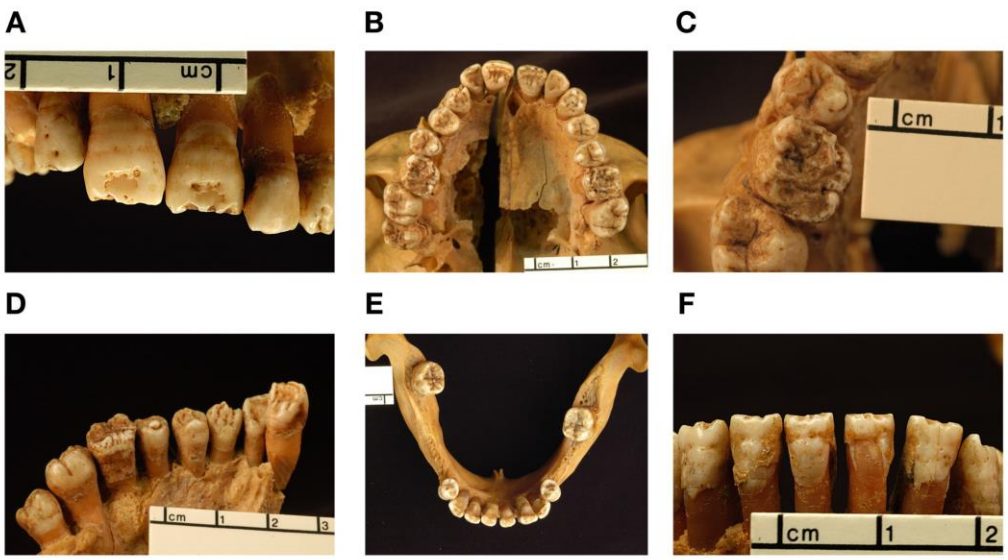

Figure 4. P000679, 33yrs old female. (A) Hypoplastic defects on labial surface of central incisors. Those that are in the incisal third of the crown are large and oval in shape and are centrally located with small-scattered pits. Some other teeth also display pitting. (B) Occlusal view of maxilla: occlusal surfaces of first permanent molars have abnormal formation of the enamel. (C) Close up of upper right first molar. (D) Palatine view of the right maxillary dentition: Note demarcation between diseased and healthy enamel in the first permanent molar. (E) Occlusal view of mandible. (F) Anterior view of mandible: Incisors are marked by multiple notches on their incisal edges while shallow indistinct furrows are present about one-third the height of the crown.

surface of the left central incisor has broken off postmortem. The first premolars have isolated pits on their surfaces. All other remaining mandibular teeth have normal morphology. The dental defects in P000679 are comparable to Hutchinson's dental observations for CS and suggestive of mercurial teeth morphology.

Terry Collection P000161 (Fig. 5) is an African American female who was approximately 45 years of age at the time of death and added to the skeletal collection in 1925. No cause of death is recorded in the morgue records. Previous evaluation by researchers and curators identified the dental anomalies and considered them to be the product of congenital syphilis and this was noted in the Smithsonian pathology files. All maxillary teeth are present, except the right second premolar and the left first molar. The incisal margins of the central and lateral incisors are notched. The labial surfaces of crowns of anterior teeth have malformed enamel, featuring irregular pitting and a deep furrow located about one-third of the crown height proximal to the incisal edge (Fig. 5A). A second furrow appears on the left central incisor on the cervical third of the crown. The furrows of the anterior teeth appear approximately at the same level. Some enamel was lost postmortem on the cervical third of the right central incisor and parts of the mesial aspect of the left central incisor. Numerous dark colored pits run horizontally along the middle third of the crown of the central incisors and the incisal third of the lateral incisors and tip of canines. (Fig. 5A). Similar pitting and linear hypoplastic defects occur on the lingual surfaces of these teeth (Fig. 5B). The morphology of the premolars and other molars still present appears normal. A fragment of the occlusal surface of the right first permanent molar is marked by irregular enamel and pitting. A large carious lesion is present in the disto-lingual area of the right first permanent molar, while an interproximal carious lesion is evident towards the mesio-lingual end of the crown. The left first molar has been lost most likely due to dental caries. The alveolar bone has not healed completely, so it is possible the loss occurred shortly before death. The morphology of both second molars and third molars appears normal. On the palate anteriorly on the right side there is a circular bony depression surrounded by elevated bone. There is a large perforation on the right side of the palate. There is also some pitting in the palate that is more apparent near the right first permanent molar.

The mandibular dentition consists of the left and right lateral incisors, canines, first and second premo-

lars, second molars and the left third molar. The central incisors were lost post mortem, while both first molars and the right third molar were lost antemortem. The alveoli for both first molars are completely remodeled, but the alveolus for the left has been less remodeled than the right. The third right molar alveolus is healed. Similar to the maxillary dentition, severe linear and pitted enamel hypoplastic defects are present on the lateral incisors and canines (Fig. 5C). The multiple hypoplastic lines run along at the same level of the crown of these teeth on both labial and lingual surfaces (Fig. 5C & 5D). The tops of the crowns of the first premolars appear hypoplastic. Pitting and two small carious lesions are present on the occlusal surface of the left first premolar. The crowns of both second premolars appear normal. The abnormalities seen in the dentition of P000161 are consistent with Hutchinson's description of patients with CS and possibly some features suggestive of mercury effects.

Mercury testing using pXRF

An exploratory, qualitative analysis using a portable x-ray fluorescence analyser (pXRF) was performed to see if any of the individuals above might have mercury or other chemical elements possibly related to treatment for CS and the cause of the dental abnormalities. The analysis was conducted using a Bruker Tracer III-V handheld analyser on portions of hypoplastic enamel on the central and lateral incisors for all of the individuals, except individual P00011R, which lacked central incisors - instead, a lateral incisor and canine were tested. The analysis was conducted with settings optimized for mercury (0.001" Cu, 0.001" Ti, 0.012" Al filter at 40 keV/16 micro amps for 300 seconds, without vacuum). Bone testing was done on the femur of the same individuals to test for contamination if high readings of any particular elements were found. No mercury was detected. The lack of mercury in these individuals most likely can be attributed to amounts of mercury that may be too minute for the instrument's detection capabilities (see Zuckerman, 2016:50 for discussion on mercury detection with pXRF).

Differential Diagnosis

Diseases that interfere with odontogenesis and amelogenesis are considered for a differential diagnosis.

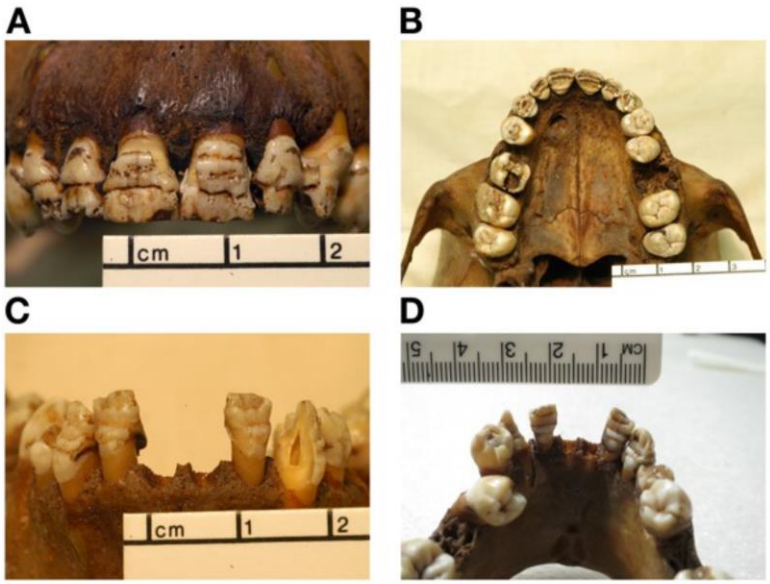

Figure 5. P000161, 45yrs old female.(A) Severe hypoplastic enamel of the maxillary incisors and canines. Incisal thirds of the central and lateral incisors' and canines' crowns are hypoplastic with deep furrows. Dark colored pits run horizontally across the crowns. (B) Occlusal view of maxilla: Linear and pitting hypoplasia noted on the lingual surface of anterior teeth. (C) Anterior view of mandible: Severe linear and pitted enamel hypoplasia on the lateral incisors and canines. (D) Lingual view of mandible: Pitted and linear enamel hypoplasia evident on lateral incisors and canines corresponds to that on labial surface.

These include tuberculosis, leprosy, amelogenesis imperfecta, rickets and fluorosis, as well as elements that have been used as treatments or are known to affect tooth development such as mercury, arsenic, lead, bismuth, and cadmium.

Tuberculosis is a chronic disease that predominately affects the ribs, vertebrae, and the large joints of the body. In adult onset of tuberculosis, there would be no effect on the dentition. In cases of childhood tuberculosis, the most common dental abnormalities are associated with developmental stress - linear enamel hypoplasia (Dabernat and Crubézy, 2010; Bedić et al., 2015); carious lesions (Formicola et al., 1987; Hlavenková et al., 2015); and decreased enamel thickness (Formicola et al., 1987). Since dental signs observed in childhood tuberculosis do not resemble the dental abnormalities or the severity observed in the five cases, tuberculosis is not likely and would be ruled out as a differential diagnosis.

Leprosy is a chronic disease that affects the skin and peripheral nervous system with skeletal loss by resorption in the latter stages of the disease. It is a slow and progressive disease, signs of the disease can start to develop from six months to 30 years (World Health Organization. 2012). Dental abnormalities that have been reported in skeletal cases with evidence of leprosy include linear enamel hypoplasia (Boldsen, 2005) (which might be correlated to possible frailty in the individuals, rather than leprosy itself), and constriction of the roots of the upper permanent central incisors (leprogenic odontodysplaia) (Roffey and Tucker, 2012) that might be related to the resorption of the alveolus rather than development effects of dental formation (Roberts 2011). These observations are not common or diagnostic of the disease. If a child were to be infected with leprosy, since its macroscopic expression would be long-term, it is assumed that the disease would not severely affect dental development, possibly only producing linear enamel hypoplasias from insults to development. It is unlikely that there would be the severity of dental pathology similar to those in the described cases here. Since leprosy is predominately an adult disease, if in children it would not have the severe effects as seen in CS, therefore, leprosy is ruled out as a differential diagnosis.

Amelogenesis imperfecta (AI) is a hereditary condition characterized by enamel defects. Phenotypic expression of the condition is caused by a disturbance in ameloblasts secretions producing hypoplasia, hypocalcification, hypomaturation and hypomaturation-hypoplasia with taurodontism (Gadhia et al., 2012; Prasad et al., 2016). Amelogenesis imperfecta also manifests in enamel discoloration, enamel pitting, and thin enamel (Kar et al., 2012; Gerdolle et al., 2015; Rogers et al., 2016). The prevalence of AI varies between populations from 43:10,000 in Turkey to 1.25:10,000 in Israel (Gadhia et al., 2012). Amelogenesis imperfecta is an unlikely differential diagnosis for the described cases since AI tends to affect amelogenesis in most all or all teeth – this is unlike congenital syphilis where only specific teeth are affected.

Rickets is a disorder caused by either a lack of vitamin D or phosphorus. These metabolic deficiencies affect tooth mineralization and bone development. Rickets may cause some non-severe linear or pitting-type enamel hypoplasia and in cases discoloration and enamel opacities (Zambrano et al., 2003; Davit-Beal et al., 2014). Like AI, rickets more uniformly affects the teeth. Therefore, with the severity of hypoplastic defects described and the specific tooth involvement, this is not consistent with rickets and their differential diagnosis can be ruled out.

Consumption of large amounts of fluoride can lead to fluorosis, and specifically in developing dentition will cause disturbance of amelogenesis. Enamel will appear discolored (yellow to dark brown), demonstrate white opaque patches or lines, or pitted or mottled hypoplasia (Sherwood, 2010; Munñoz et al., 2013). Similar to AI and rickets, fluorosis does not affect selected teeth, and its hypoplastic effects are less severe than those described in the five cases presented here. Thus, the diagnosis of fluorosis is unlikely.

Mercury was used for medicinal purposes throughout the United States to treat syphilis and congenital syphilis (Cole et al., 1929; United States. Public Health Service. Division of Venereal Diseases. 1930). Mercury was administered in various forms but was most commonly injected intramuscularly or rubbed onto the skin. Treatments containing mercury ranged from one and a half to fourteen grams of solution or ointment (Cole et al., 1929; Cole 1933). Since some of the malformations observed in P000707, P000679 and P000161 could be suggestive of the mercurial or syphilitic-mercuric category set by Hutchinson (1878) and Moon (1884), it is possible that mercury might have caused the dental malformations. There is no proof that any of these individuals may have had treatments and the one clinically diagnosed case (P00011R), was diagnosed at an age that would have excluded the severe effects of dental malformation if mercury were administered after her diagnosis.

Arsenic was also used to treat syphilis/congenital syphilis; however, its effects on enamel development in children with congenital syphilis are limited. Arsenical poisoning has been found to cause tooth sensitivity and tooth abrasion in children (Sunny, 2013), but nothing in the way of severity of the anomalies caused by mercury. Thus, the possibility of arsenic poisoning or treatment is an unlikely differential di-

agnosis.

Bismuth was introduced later than mercury and arsenic, and was used in conjunction with these to treat syphilis and congenital syphilis. Bismuth was noted to cause pigmentation of gums and the enamel, most frequently seen on the labial surfaces of the lower and upper central incisors and in prolonged acute cases, loosening of the teeth (McCarthy and Dexter 1935; Dean, 1943). The common factor observed in bismuth poisoning is that the cervical portion of the incisors was the most constant location for pigmentation (McCarthy and Dexter 1935; Dean, 1943). We see none of this pigmentation, and these individuals would have been too young to have received bismuth treatments, thus, excluding this as a differential diagnosis.

Lead was considered a possible cause in dental development, but previous studies have not found lead to cause enamel abnormalities. High levels of lead only result in a decrease in microhardness of enamel (Gerlach et al., 2002; Youravong et al., 2005) coupled with increases in abrasion and discoloration (Gil et al., 1996). Normal enamel morphology has been observed in cases where high levels of lead were present (Gerlach et al., 2002; Youravong et al., 2005).

Cadmium, although not used to treat syphilis or congenital syphilis, is known to accumulate in enamel; however, its effects on enamel development are limited in the literature. Wilson and Deeds (1939) noted that cadmium toxicity caused bleached white enamel discoloration. Since that is not observed in the discussed individuals, cadmium is unlikely diagnosis.

DISCUSSION AND CONCLUSIONS

Syphilis was a disease that caused serious problems in the United States during the late 19th and early 20th centuries, with various measures taken to control its spread (Lancet, 1930; Lancet, 1937a; Lancet, 1917; Prebble, 1938; Deporte, 1941). While various programs and legislations were initiated, treatments (including mercury) were of primary importance to reduce prevalence rates (Lancet, 1921; Lancet, 1937a; Lancet, 1939). Even though mercury was known to produce side effects, similarly to other chemotherapies (arsenic and bismuth), it was still considered the most effective, being used on its own or in combination with other pharmaceuticals (Lancet, 1937b). However, the healing nature of mercury has also been called into question due to non-systematic recording of treatments and outcomes in the 19th century, as well as misdiagnosis of the decades-long quiescence of the disease as "cured" (Zuckerman, 2016).

Individual P00011R was diagnosed in life with congenital syphilis. The only detectable manifestations of this diagnosed condition are visible in her teeth. While some of her teeth are missing, those that are present, especially the first permanent molars, are highly consistent with the anomalous condition found in cases of congenital syphilis. The dome-shaped and reduced occlusal surface of her first permanent molars is obviously a consequence of developmental disruption caused by congenital syphilis. They resemble those described by Moon (1884), but due to developmental variability, are not not identical to the description.

While congenital syphilis was diagnosed and recorded only in this one individual, the other four individuals display dental changes that fit the broad range of changes described by Hutchinson (1859, 1863, 1878, 1887, 1888), and Moon (1877, 1884). Individual P219398 demonstrates tooth morphology that fits the syphilitic category described Hutchinson. The right central incisor displays a crescentic groove towards the incisal edge. Hutchinson (1863) describes that once this thin enamel has broken off, the characteristic notch is present.

The hypoplastic lesions in the dentition of individuals P000707 and P000161 are of significant severity. In P000707, enamel malformations in the maxillary central incisors begin approximately 2mm from the incisal edge and a normal groove pattern is visible on the very occlusal surface of the first permanent molars, indicating malformation in amelogenesis in the first months of the infant's life. The lateral incisors and canines demonstrate similar enamel defects but are located at different crown heights that correspond to the differences in the timing of formation of these teeth. Crown development of first permanent molars begins perinatally, permanent central incisors begin to form at approximately 3-4 months of age, lateral incisors at approximately 10-12 months and canines at six months (Nelson & Ash, 2010). The crown of first molars is completed at about 2.5-3 years of age, both incisors at approximately 4-5 years of age, and at about 6-7 years of age for canines (Nelson & Ash, 2010). Judging from the position of hypoplastic defects (reflecting the mercurial category features by Hutchinson) these changes would occur at about 2.0-2.5 years of age.

The pathological changes in the dentition of individual P000161 follow similar interpretation for development and hypoplastic events similarly to individual P000707. However, hypoplastic defects are positioned somewhat earlier in the individual's life and ceased later than in individual P000707. The severe enamel abnormalities observed in individual P000161 are changes that are more similar to the examples of the mercurial category as described by Hutchinson. But as presented above, no record of this treatment can be attributed to this individual.

Individual P000679 has enamel defects of the maxillary central incisors that are much like the mercurial

category described by Hutchinson. Whatever disturbances caused the anomalous formations of the teeth would have to have started not long after birth or from treatment to the mother - the abnormal enamel occurs much closer to the incisal margin than that seen in either individual P000707 or P000161. But again, there is no record of this treatment attributable to this individual.

In skeletal collections when medical information is not available, paleopathologists make differential diagnoses from the skeletal/dental evidence using the knowledge available at that time. During the turn of the last century and into the 20th century R. Terry, D.S. Lamb, A. Hrdlicka, T.D. Stewart and JL Angel made diagnoses of pathological conditions and anomalies on the anatomical and archaeological remains using their familiarity with the pathological understanding from their medical experience, and their knowledge of medical treatment for various diseases. For the individuals studied here, notations of the dental and skeletal observations related to or attributable to "treponemal disease" were made in the Smithsonian records from these scientists based on their observations and knowledge of the disease. In these records, differential diagnoses were often not listed, and thus in some cases, the labeling of a disease may have been from the observations, not from the clinical record of cause of death. From what has been observed in this study, these individuals encompass a range of variation in the dental abnormalities that have occurred in syphilitic patients. The findings of this study provide examples of this range of manifestations, discussing the basis for the malformations, and provide additional insight into identifying CS in future studies.

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A Rare Case of Congenital Syphilis and a Supernumerary Fourth Molar in an Early 20th Century African American Woman

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Keywords: disease; mercury; mandibular distomolar; morphology; supplemental teeth

ABSTRACT Congenital syphilis is a disease recognized for interfering with odontogenesis, producing specific dental characteristics including Hutchinson's incisor, Moon's molar, Fournier's molar and mulberry molar, while its past treatments including mercury are known to affect amelogenesis. Supernumerary teeth, mainly associated with syndromes, are not commonly found in cases of congenital syphilis. A rare case of congenital syphilis in an individual (P000707) treated with mercury and a mandibular left fourth molar with normal morphology is presented.
Materials and Methods: During a systematic examination of 28 skeletons with treponemal disease at the Smithsonian museum in Washington, DC, a supernumerary mandibular distomolar in one individual (P000707) was revealed.
Results: P000707 was an African American female, 26 years of age. Dentition showed severe enamel hypoplasia of the maxillary and mandibular incisors, left canine, and upper first molars, consistent with the effects of treatment of congenital syphilis by mercurial compounds. Crown of the left mandibular distomolar has typical molar morphology but is smaller in size than other permanent molars. Arrangement of grooves resembles the +4 pattern, but is complex due to crenulation. Oblique x-ray revealed that the fourth molar had one root with a pulp chamber extending towards the apex, suggesting taurodontism. No other distomolar teeth were present.
Conclusions: Congenital syphilis and treatment containing mercury may not influence the development of supernumerary teeth due to: (1) the age at which the development of the fourth molar takes place, (2) the stage of the infection at the time of development and (3) the age at which treatments containing mercury are administered to patients with congenital syphilis.

Congenital syphilis is a disease caused by the transmission of *Treponema pallidum*, from the mother to the fetus during pregnancy or at birth. In the neonate, various systems are affected. Pathological signs appear in two stages of the disease. During the early stage, skeletal manifestations include periosteal reactions, osteochondritis, and osteomyelitis (Hira et al., 1985; McLean, 1931) while during the late stage, signs can include frontal bossing, short maxilla, high palatal arch, saddle nose, Higoumenakis's sign, diaphysitis, metaphysitis and sabre shins (Fiumara and Lessell, 1970; Rasool and Giovender, 1989). However, the disease is most recognized for interfering with tooth formation (odontogenesis), producing certain characteristic teeth including Hutchinson's incisors, Moon's molar, Fournier's molar and the mulberry molar (Fournier, 1886; Hutchinson, 1863; Karnosh, 1926; Moon, 1884). Even though these characteristic dental signs in congenital syphilis are seen in the permanent teeth (upper central incisors and first molars), which erupt approximately at 6-8 years of age, the dental abnormalities in these teeth are produced during the early stages of the disease, that is, once the infection and fever set in around the time of birth affecting initial crown formation. However, these dental abnormalities do not occur in all cases of congenital syphilis. The incidence of Hutchinson's incisors ranges from 30 to 50% (Putkonen and Paatero, 1961), while changes in first permanent molars range between 3 and 37% (Berfield, 1971).

In the past, mercury was used to treat congenital syphilis due to its antibacterial effects (Hutchinson, 1874, 1878; Warner, 1881). Even though mercury was seen to benefit infected individuals, it was also seen to produce dental abnormalities that were different from

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those caused by the disease. Hutchinson recognized that mercury affected amelogenesis resulting in severe enamel hypoplasia (Hutchinson, 1878). Treatments containing mercury were given to infants soon after birth, the time which enamel formation in permanent teeth begins. First permanent molars and incisors begin their formation around birth and this is when they are exposed to disease. Mercury used to treat syphilitic infants continued for months after birth, severely affecting other tooth formation, depending on the length of time the treatment was administered (Hutchinson, 1878). The abnormalities produced by congenital syphilis can be combined with the effects of treatment containing mercury (severe hypoplastic effects) (Hutchinson, 1878; Moon, 1884). Treatment with mercury was commonly used in cases of congenital syphilis until the early 20th century. The whole suite of changes caused by congenital syphilis and treatments containing mercury have been discussed in detail (Ioannou et al., 2016).

Supernumerary teeth have been associated with various syndromes and disorders including Down's and Gardner's, cleidocranial dysostosis, and cleft lip and palate (Kumar and Gopal, 2013; Menezes and Vieira, 2008; Millhon and Stafne, 1941; Panjwani et al., 2011; Sandler, 1951); however, they have not been described in detail in cases of congenital syphilis. Supernumerary teeth are observed when more than 20 deciduous or 32 permanent teeth are present in an individual. They can erupt, remain unerupted, or become impacted (Kara et al., 2012; Mali et al., 2012). Their appearance can be unilateral, bilateral, as a single tooth or in multiples (Brinkmann et al., 2012; Cavalcanti et al., 2011; Harris and Clark, 2008). The morphology of supernumerary teeth can vary in each individual from normal in shape and size, normal shape and reduced in size, conical in shape and abnormal in shape and reduced in size (Harris and Clark, 2008; Kumar and Gopal, 2013; Rahnama et al., 2014).

This paper presents a case of congenital syphilis in an African American woman dating from the early 20th century with a fourth mandibular molar. A focus will be made on the development of the fourth molar in the presence of a disease, which primarily affects dental development.

MATERIALS AND METHODS

During a systematic examination of 28 skeletons held at the Smithsonian museum in Washington, DC, whose documentation stated that they had "treponemal or treponemal congenital" disease, a case of a supernumerary mandibular distomolar in one individual (P000707) was revealed. This individual was an African American female, who was born in 1903 and died of pulmonary tuberculosis in 1929, at 26 years of age. Occlusal and oblique X-rays of the mandible were taken using a Frankenstein unit to see whether a fourth molar was present on the right side. Chemical analysis was performed to detect any levels of mercury. A Bruker Tracer III-V handheld analyser was used on hypoplastic portions of the central and lateral incisors. The initial analysis used an all-elements setting. The settings for the following test were elevated to (0.001" Cu, 0.001" Ti, 0.012" Al filter at 40 keV/16 micro amps for 300 seconds, without vacuum) (Ioannou et al., In press).

RESULTS

All maxillary permanent teeth were present, the central and lateral incisors, canines, premolars and all three molars. The enamel of the central incisors from the incisal third to the middle third of the crown appears mottled and thin (Figure 1). The incisal third of the lateral incisors and left canine demonstrate the same mottled appearance and pitted enamel hypoplasia. Deep pits are apparent toward the middle third of the crown of the central incisors and incisal third of the lateral incisors and canines. In addition to signs caused by mercury on the incisors and canines, other teeth display isolated hypoplastic pits. Maxillary premolars are not affected. First permanent molars have abnormal occlusal surfaces, with cusps reduced in size and pitting hypoplasia, which is also consistent with the side effects of mercury (Figure 2). Diseased enamel is clearly demarcated from the healthy enamel on the cervical third of the crown. The morphology of the second and third permanent maxillary molars is normal with normal groove patterns, but there is some enamel pitting on the occlusal surface.

Mandibular permanent teeth include the central and lateral incisors, left and right canines, first and second premolars, second and third molars and the

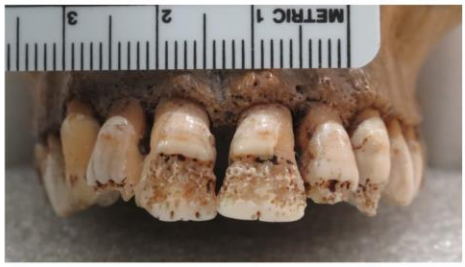


Figure 1. The maxillary central and lateral incisors and left canine display hypoplastic enamel seen in patients with congenital syphilis treated with mercury. Signs include thin enamel, pitted enamel hypoplasia (in some places very deep), and distinct demarcation separating diseased from healthy enamel.

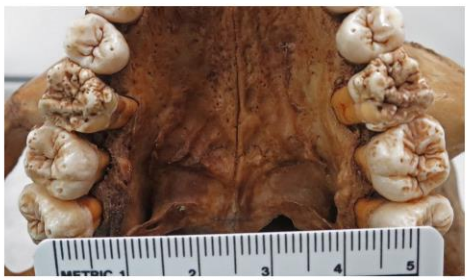


Figure 2. Occlusal view of the maxilla. First permanent molars have abnormal surfaces with small cusps and pitting hypoplasia

distomolar. The first permanent molars were lost ante-mortem, possibly by extraction and their alveoli are completely healed. All mandibular incisors have mottled enamel (Figure 3). The left and right second molars and the third left molar do not display severe hypoplasia, save for minor pitting. Their occlusal surfaces are crenulated. The third permanent molar on the right side is represented by its roots only. The crown has broken off probably after its destruction by dental caries. On the left side, in the mandible, there is a fully erupted fourth molar (distomolar). Its crown has normal molar morphology, but is smaller in size in comparison to the other permanent molars present. The arrangement of groves resembles the +4 pattern. However, the groove pattern is complex because of crenulation. Entoconid, metaconid, hypoconid and protoconid are present, and it appears that there may be a narrow metaconulid, but crenulations make it difficult to determine (Figure 4). An oblique X-ray of the mandible shows that the distomolar only has one root with a large pulp chamber extending far down towards its apex, suggesting a taurodont condition (Figure 5). The third molar on the left is large and crowded between the distomolar and adjacent second molar. Its crown is rotated approximately 10 degrees and tilted mesially. Inspection of the X-ray

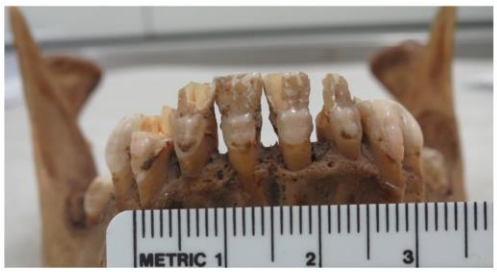


Figure 3. The anterior view of the mandibular incisors displaying enamel defects

does not reveal the presence of the antimeric distomolar (Figure 6). All molar crowns appear crenulated.

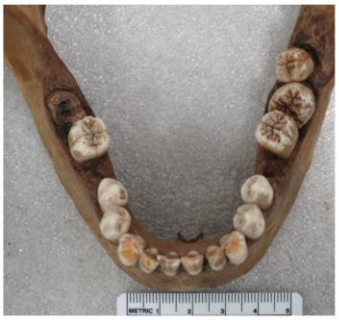


Figure 4. Occlusal surface of the mandible. The first permanent molars were lost ante-mortem. Both second molars, the left third molar and left fourth molar are present. The right third molar is represented by its root only. The fourth molar displays normal molar morphology

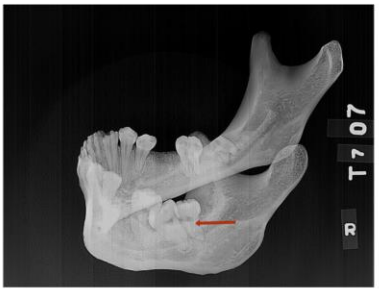


Figure 5. Oblique X-ray image of the mandible shows that the distomolar has only one root and that there is no antimeric distomolar. Note the large extent of the pulp cavity in the distomolar, suggesting it is a taurodont molar.

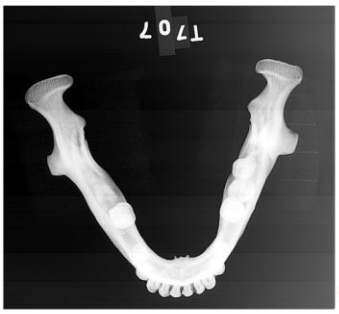
In  the

Figure 6. X-ray of the occlusal view of the mandible does not show any evidence of a right fourth molar

post cranial skeleton, limited areas of nodular periosteal reaction were observed on the long bones including the right tibia, fibula, humeri, radius, ulnae, and femora, as well as the lateral surface of the left ilium. The left femur had lytic destruction along the lateral border of the head in the anterior aspect, "classic" striated periosteal reaction is not noticeable.

DISCUSSION

Here we present a case of congenital syphilis with a supernumerary distomolar in an African American woman. Although this condition is very rare during this time, it is probable, as one other case has been documented (Jacobi et al., 1992). However, in this case, the dental abnormalities in P000707 indicate that she was treated with mercury soon after birth. Changes in the morphology of the central maxillary incisors and left canine have enamel malformations that are compatible with dental abnormalities observed by Hutchinson in patients with congenital syphilis administered treatment containing mercury (Figure 7). Crown formation of the central permanent incisors begins at approximately three to four months postnatally and is complete at approximately 4 to 5 years of age (Nelson and Ash Jr, 2010). The specific changes in enamel caused by mercury are seen in one third of the crown, therefore, treatment would have started in the middle of the first year of life and ceased at approximately 2 years of age. Similarly, severe enamel malformations are observed on the lateral incisors and canines that start forming later than the central incisors.

Figure 7. (A) Anterior teeth of P000707 (B) Patient treated with mercury as presented by Hutchinson in 1878 (16 year old boy). Both (A) and (B) display similarities in enamel abnormalities that occur as a result of treatments containing mercury. Mercury would have been administered at a somewhat older age in P000707 than in Hutchinson's patient. Hutchinson, (1878) p. 53, Plate VI, Items I (A)

The morphology of the maxillary first permanent molars demonstrates a normal groove pattern towards the mesial end of the crown, while the rest of crowns' occlusal surfaces are reduced in size and hypoplastic. As the incisal third of the central incisors and a portion of the occlusal surface of the first permanent molars appears to be normal, the rest of the crown is affected, which may be an indication that the onset of the infection was late in relation to tooth development.

Congenital syphilis is known to produce specific dental abnormalities characteristic of the disease. However, it has been noted that in some cases of congenital syphilis, the classic dental changes that are usually observed such as Hutchinson incisors, Moon's molar and Fournier's molars do not occur (Švejda, 1952). Hutchinson also observed and described certain dental abnormalities that occurred as an effect of treatments containing mercury (Hutchinson, 1878). The dental abnormalities produced by the disease itself and treatments containing mercury were so distinct that Hutchinson deemed it worthy to document and illustrate both as separate entities. It is worth noting that the crescentic notch that occurs in the maxillary central incisors of congenital syphilis patients is not observable if they were treated with mercury (Hutchinson, 1878). The features observed in this P000707 are typical signs of teeth treated with mercury in patients with congenital syphilis (Hutchinson, 1878; Ioannou et al., 2016).

While the results of the chemical analysis detected no levels of mercury, this neither confirms nor disproves that mercury was administered to this individual. Various explanations could be considered. It is possible that the low levels of mercury in the enamel could not be detected by the equipment. Another possible explanation for the lack of mercury detected could be due to the quick turnover rate of mercury in the body. The half-life of mercury ranges from 58 days for elemental mercury, 1-2 months for mercuric mercury (e.g. $HgCl_2$), to 70-80 days for methylmercury (National Research Council (US) 2000). Taking into account that this individual was treated with mercury for congenital syphilis in the early stages of life and died at 26 years of age, it is not abnormal to find extremely low levels of mercury. As indicated by Hutchinson, if 648 mg (10 grains) of mercury were introduced in a body of a young individual, after 20 years only a minute quantity of mercury would remain ($2.13*10^{-25}$mg). Thus, it is more likely that a majority of the mercury would be cleared out, making it undetectable.

Other elements considered in the differential diagnosis include lead, zinc, copper and cadmium. High levels of lead can cause a decrease in microhardness of enamel (Gerlach et al, 2002) but cannot cause malformations of the enamel (Gerlach et al, 2002; Youravong et al, 2005). Fosse and Berg-Justesen (1977, 1978, 1978) and Tvinnereim et al. (1999) examined concentrations of zinc, copper, and cadmium in teeth and bone in humans and mice and recorded the difference in concentration of these elements between enamel, dentin, and bone, but did not record any changes or malformations in enamel development.
In relation to changes on the post cranial skeleton of P000707, since the individual died of tuberculosis, it is difficult to say which of those described pathological changes could be due to treponemal infection.

The crown morphology of the distomolar is normal, unaffected by the disease, nor by treatments containing mercury. The smaller size of the distomolar is unlikely to be caused by congenital syphilis. Clinical studies have shown that distomolars can demonstrate normal molar morphology, have as many as three to seven cusps and be reduced in size, in comparison to the other permanent molars (Asrani et al., 2006; Ceperuelo et al., 2015; Kumar and Gopal, 2013; Ohata et al., 2013; Shahzad and Roth, 2012). The normal crown morphology in this case may be due to the time at which the development of the fourth molar began. It is the early stage of the disease that affects dental development. It occurs soon after birth and becomes the tertiary stage after several weeks. Tertiary syphilis does not affect tooth development. The development of the third permanent molar begins at approximately 7 to 10 years of age and the tooth is fully erupted between the ages of 17 and early 20s (Liversidge, 2015). It is possible that the fourth distomolar could have developed at the same age or even later. If the fourth molar had developed soon after the third molar, P000707 would have been in the tertiary stage of the disease; therefore, the disease could be asymptomatic and would not have affected amelogenesis or odontogenesis of the supernumerary fourth molar. However, it is possible that the fourth molar developed sooner. Studies have shown that fourth molars can appear between the ages of 11 and 16 years (Delgado et al., 2014; Menardía-Pejuan et al., 2000; Orhana et al., 2006; Vlaykov et al., 2015).

It also appears common that distomolars demonstrate a single root, unlike the multiple roots observed in the other permanent molars (Ceperuelo et al., 2015; Ohata et al., 2013; Rahnama et al., 2014). However, root formation can vary among individuals (complete with closed apex or incomplete) (Ceperuelo et al., 2015; Kokten et al., 2003; Ohata et al., 2013). Since the distomolar in this case is taurodontic, it is not possible to determine whether it had fused multiple roots or a single root because no separate root canals can be seen. At least formally, the root is a single unit. The cause of taurodontism is unclear. It has been associated with various syndromes (Andersson et al., 2013; Keeler, 1973; Rajić and Mestrović, 1998) and multiple theories have been suggested in the literature (Alvesalo and Varrela, 1991; Witkop Jr et al., 1988). In this case, it should be considered that the proportions of the root to crown size and pulp cavity to root canal volumes may have developed abnormally in the supernumerary, thus not normal, tooth without any special causes.

The development of extra teeth is not fully understood, although multiple theories have been suggested such as hyperactivity within the dental lamina, and dichotomy of the tooth germ and these may be linked to genetic factors (Kokten et al., 2003; Kumar and Gopal, 2013). For instance, Martínez-González et al. (2012) found them in 0.96%, Shahzad and Roth (2012) in 2.2% and Kara et al. (2012) in 0.33%. It has been found that supernumerary molars were also more prevalent in African Americans (6.4%), than in European Americans (0.9%) (Shahzad and Roth, 2012). It has been suggested that African Americans exhibit extra teeth more often than European Americans (Harris and Clark, 2008), which may be related to African Americans having larger dental arches and greater crown and root dimensions. This would increase a probability of the appearance of the distomolar in an African American suffering from congenital syphilis.

CONCLUSION

A systemic infection such as congenital syphilis and its treatment with mercury may not influence the development of supernumerary teeth due to: (1) the age at which the development of the fourth molar takes place, (2) the stage of the infection at the time of development and (3) the age at which treatments containing mercury are administered to patients with congenital syphilis.

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