



Dental developmental defects due to mercurial treatment in a child from sixteenth-century Alghero (Sardinia, Italy)

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Abstract

A child aged 3.5 to 4.5 years, exhumed from the cemetery of Alghero that is referable to the plague outbreak of 1582–83, showed remarkable dental anomalies in the permanent dentition. In particular, the central incisors exhibited large hypoplastic pits, and the first molars were characterized by a honeycomb appearance with large areas of missing enamel. Microtomographic analysis revealed very low values of enamel volume, while the dentin volumes of the crowns were mainly preserved; chemical analysis showed very high levels of mercury in the hard tissues. The enamel disturbances observed in the child from Alghero are highly suggestive of the administration of mercurial treatment to the individual during early childhood. Despite the absence of the typical signs of congenital syphilis, such as Hutchinson's incisors, it cannot be excluded that the child was affected by the disease. After the appearance of venereal syphilis in Europe at the end of the fifteenth century, mercury was employed to treat its severe skin manifestations, remaining in use until the nineteenth century despite its well-known negative side effects. However, mercury was also used in the treatment of a number of dermatological conditions and to eliminate head lice and fleas. Regardless of the disease the child was treated for, the case presented provides evidence of some of the highest levels of mercury recorded in osteoarcheological remains so far, making the individual the youngest patient documented in the paleopathological literature to exhibit signs of mercurial treatment.

Keywords Mercury treatment · Hypoplastic enamel defect · Chemical analysis · X-ray Microtomography · SEM analysis

Introduction

Mercury has been used commercially and medically for centuries. In the past, mercury was a common constituent of many medications; it was one of the most popular treatments for skin diseases, but it was also used as a purgative or an antiparasitic medicine (Norn et al. 2008; Beers and Mousavi 2013). Nevertheless, exposure to mercury is associated with a variety of adverse health effects, including neurological, renal, respiratory, dermatological, reproductive, and developmental sequelae (Risher and Amler 2005).

The use of mercury in medicine goes back to 2000 years ago, when the substance was first integrated into the Chinese, Egyptian, Greek, and Arabian medical practices (Buret 1891; Norn et al. 2008). The Arabs employed it to treat several dermatological conditions, such as ulcers, pediculosis, herpes, and scabies. For example, Albucasis (940–1013) practiced frictions with a combination of mercury and laurel oil, a very toxic mixture that frequently caused ulcerations in the mouth of the patient (Busacca 1923). In 1393, Guy de

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Chauliac (ca. 1300–1368) recommended an ointment for the treatment of scabies in his volume *Grande Chirurgie*. The ointment, named “Unguentum Saracenicum” because of its Arabian origin, was composed of gum resin, wild delphinium, mercury, and pig’s grease (Abraham 1948). Later on, mercury-based ointments and solutions began to be extensively employed to treat the severe skin manifestations of venereal syphilis (Claiborne 1911), a disease that seems to have appeared for the first time at the end of the fifteenth century in Naples.

Various theories have been formulated to explain the appearance of venereal syphilis in Europe. According to the Colombian theory, the disease was imported from the New World with the discovery of Columbus (Crosby 1972). Conversely, the pre-Columbian theory suggests that syphilis was already present in Europe but was indistinguishable from other conditions grouped under the name of “leprosy” (Holcomb 1934, 1935). The existence of syphilis in America before the arrival of Columbus is clearly attested (Cook and Powell 2005); however, the increasingly rich body of evidence concerning syphilis in the Old Continent seems to support the pre-Columbian theory (Baker et al. 2020).

Regarding the origins of syphilis, two theories have been proposed. According to the unitary theory, the different forms of treponematoses (pinta, yaws, bejel, and venereal syphilis) are nothing more than adaptations of the same microorganism to different environmental conditions; the pathogen would have accompanied humankind out of Africa and would have therefore been present globally before the end of the fifteenth century (Hudson 1958, 1965). Instead, the evolutionary theory ascribes the various treponematoses to different bacteria that would give rise to different syndromes. It has been hypothesized that a primitive African *Treponema* could have reached the American continent through the Bering Strait with the migrations of late Pleistocene hunter groups. Subsequent mutations of pinta, the form of the disease closest to the original, primitive treponematoses, would have then triggered the manifestation of other treponemal diseases (Hackett 1963).

Recent phylogenetic analyses led researchers to dismiss the evolutionary theory in favor of the unitary theory (Baker et al. 2020). Accordingly, yaws, bejel, and venereal syphilis would be caused by a single pathogen, *Treponema pallidum*, representing the same disease from the pathophysiological point of view. Clinical differences should therefore be related to the mode of transmission, the age at the time of infection, and the host’s immune response, rather than to clear genetic differences between etiological agents (Baker et al. 2020).

From the Renaissance onward, venereal syphilis became endemic and widespread in Europe. Phillipus Von Hohenheim (1493–1541), also known as Paracelsus, was amongst the earliest proponents of mercurial chemotherapy for

syphilis; Berengario da Carpi (1457–1530), Konrad Schellig (1448–1508), Joseph Grunpeck (1470–1531), Pedro Pintor (1423–1503), and Giovanni da Vigo (1450–1525) were other early supporters of the use of mercurial therapies to treat this condition (O’Shea 1990).

Mercury was administered in four ways, usually beginning at a high dosage for 4 to 6 weeks (O’Shea 1990):

- 1) Mercurial ointment rubbed on different parts of the body (frictions).
- 2) Mercurial plasters applied every 2 or 3 days.
- 3) Fumigations in a hot cabinet with cinnabar (crude mercury sulfide) (Abraham 1948). Patients were placed in an overheated room or barrel and were forced to inhale vapors from heated cinnabar and metallic mercury; treatments could last from weeks to months (Keça et al. 2012).
- 4) Oral administration, for example, in the form of the so-called Barbarossa pills. These pills, containing a mixture of mercury, perfume essence, and fruit flavorings, were named after the Turk admiral who gave them to his soldiers affected by venereal syphilis in the fifteenth century (Forrai 2011).

In sixteenth-century Italy, Nicola Massa (1489–1569) recommended to practice frictions even during pregnancy and early childhood (Busacca 1923), although he acknowledged several negative side effects, such as excessive salivation, stomatitis, and diarrhea.

In fact, all these methods of administration of mercurial treatment could cause adverse effects due to mercury poisoning, including personality changes, oral inflammation, tooth loss, gastroenteritis, and weight loss (Dracoby 2004; Powell and Cook 2005). Most of these symptoms were recognized by early modern physicians, among which Ulrich Von Hutten (1488–1523), the most influential “anti-mercurialist” (Zuckerman 2016), who described tooth loos, hatter’s shakes, and excessive salivation in syphilitic patients treated with mercury.

Nevertheless, mercury remained widely recommended as the main treatment for syphilis and was commonly used until the nineteenth century, even though side effects could include death (Weatherill 1833).

Jonathan Hutchinson (1828–1913), Henry Moon (1845–1892), and Alfred Fournier (1832–1914) were among the most famous syphilis specialists during the nineteenth century. They studied many patients suffering from congenital syphilis when mercury treatment was widespread.

The mechanism whereby mercury accumulates in the body has not been fully understood yet (Garcia et al. 2001; Saber-Tehrani et al. 2007; Brigato et al. 2009). However, it is supposed that the element may bond with the carbonates in the bones or may be incorporated into hydroxyapatite

by replacing calcium ions. Furthermore, dimethyl mercury compounds, Hg (CH₃)₂, can accumulate in the organic matter of the bone (Harris et al. 2008). Mercury was even prescribed to pregnant women and children at a dose of 10 grains or 648.0 mg (Hutchinson 1878, 1887; Sheill 1910), with deleterious effects on the health of the patients. The stigmata of mercurial treatment can be detected in ancient skeletal remains belonging to non-adult individuals, in particular in teeth.

This paper presents a case of mercurial developmental dental defects in a child from the sixteenth-century cemetery of Alghero (Sardinia, Italy).

Material and methods

Archeological context and skeleton 2234

The skeletal remains of 183 probable plague victims were discovered in the courtyard of the former Jesuits' College in San Michele, Lo Quarter (Alghero, Sardinia, 40° 33' 28.6272" N and 8° 19' 9.462" E) (Milanese 2010). The burial ground dates back to the plague epidemic that devastated the city of Alghero in 1582–1583. Sixteen trenches, each containing the remains of 10 to 30 skeletons, and 10 multiple graves with an average number of 6 individuals were identified by the archaeologists (Milanese 2010, 2013). Trenches were usually dug to host collective burials related to catastrophic events, in particular epidemics that made it necessary to bury a large number of corpses in a short period of time. This type of mass grave is rarely attested in the Mediterranean area, where the only other evidence of its use was brought to light in southern France and is more recent than that documented at Alghero (Tzortzis and Signoli 2009). An anthropological and paleopathological study was carried out on the sixteenth-century population from Alghero, which included 181 individuals, of whom 51 were females, 36 males, 5 indeterminates, and 86 non-adults (Giuffra 2022). Several diseases were identified, the most common being dental pathologies and congenital disorders; except for two possible cases of brucellosis, there was no other macroscopic evidence of infectious diseases (Giuffra 2022).

A skeleton (code number, 2234) exhumed from Trench 4 (Fig. 1) showed remarkable dental anomalies. The skeletal remains were partially preserved; the cranial bones were highly fragmented, and several teeth were missing due to *post-mortem* loss. These included the permanent right maxillary second incisor and second molar, permanent right maxillary canine, deciduous left maxillary second incisor, permanent left mandibular first incisor and canine, permanent right mandibular second molar, and both permanent mandibular second incisors. Age at death was estimated based on



Fig. 1 Trench 4 of the cemetery of Alghero with skeleton 2234

the measurement of long bone diaphyseal lengths (Scheuer and Black 2000) and tooth development (AlQahtani et al. 2010). Periosteal reaction was evaluated according to the method of Stothers and Metress (1975).

Among the preserved permanent teeth, the maxillary central incisors, left canine, and first molars, and the mandibular left second incisor, left canine, and first molars showed dental anomalies.

Microtomography and scanning electron microscopy

The teeth were imaged on a high-resolution Micro-CT Skyscan 1172 (Bruker Skyscan®, Kontich, Belgium). The parameters used for acquisition were pixel size = 9.93 μm, source voltage = 100 kV, source current = 100 μA, binning = 2 K × 1 K, filter = aluminum and copper, rotation step = 0.5°, exposition time = 1825 ms.

Raw data were reconstructed with NRecon®. Dental tissues were virtually isolated using the Avizo 9® software. The crowns were separated from the roots with a curved plane along the cervical line, following the protocol of Benazzi et al. (2014). The enamel volume (V_e, mm³) and the dentin volume of the crowns (V_d, mm³) were recorded.

Overall enamel thickness distribution was then computed as the minimum distance between the outer enamel surface and the underlying surface area of the enamel–dentin junction (EDJ), and the results were displayed using spectral colors (from red to violet to represent thickest to thinnest enamel, respectively) of fixed range (from 0 to 1.23 mm with reference to the enamel thickness values observed in the sample).

A scanning electron microscope (FEI Quanta 200, high-vacuum, low-vacuum, and ESEM mode) was used for the microscopic analysis of tooth surfaces.

Chemical analysis

The chemical analysis of total mercury was carried out on seven bone samples obtained from two long bone fragments and on three dentin samples obtained from the first permanent molars. The use of a semi-automatic analytical system employing atomic absorption spectroscopy, AMA-254 (Automatic Mercury Analyzer) from ALTEC (Prague, Czech Republic), allowed direct measurement of the total mercury present in the solid samples without any chemical treatment (such as dissolution in a concentrated acid medium). Through volatilization at high temperature (+550° C), elemental mercury is entrained by a stream of oxygen and amalgamated on a gold trap. After heating the trap to dissociate the amalgam, mercury vapor is quantified by atomic absorption spectrometry. The solid samples were finely ground in a mini Agathe mortar before analysis to obtain a homogeneous powder. Certified reference materials, IAEA-405 and IAEA-433 (IAEA, Vienna, Austria), were used to check the accuracy of the method for total mercury determination. Precision (expressed as relative standard deviation of four replicate samples) was found to be better than 5%.

Results

Skeleton 2234 belongs to a child of 3.5–4.5 years of age. The deciduous teeth showed no evidence of abnormal enamel formation. The permanent dentition displayed pathological alterations.

Macroscopic analysis

Examination of the teeth of individual 2234 revealed extensive lesions. All permanent teeth demonstrated developmental anomalies manifesting as wide hypoplastic bands interrupted by oval pits of various sizes.

The buccal surface of both maxillary central incisors displayed three wide linear furrows (Fig. 2a). The surface was notched, with large hypoplastic pits nearly spanning the whole width of the teeth. Both incisors displayed a discontinuous hypoplastic band on the lingual side and three small mamelons on the incisal edge. The right mandibular first incisor also showed a disturbed enamel surface on the buccal side (Fig. 2b).

The left maxillary and mandibular canines had a fang-like shape, with tapering tips and thin enamel. The vestibular and lingual surfaces were marked by a circumferential groove at mid-crown. The surface of the canines was dotted with small depressions exposing the underlying dentin (Fig. 2c). Enamel defects did not affect the entire tooth crown; indeed, the cervical aspect appeared normal.

The same type of lesions was observed on the four first molars (Fig. 3a–d). The enamel on the cusps showed crests with hypoplastic defects. There was a sharp circumferential groove around the crown, at the base of the atrophic cusps. A rough occlusal surface was noted between the cusps, with several small grooves and rounded enamel nodules,

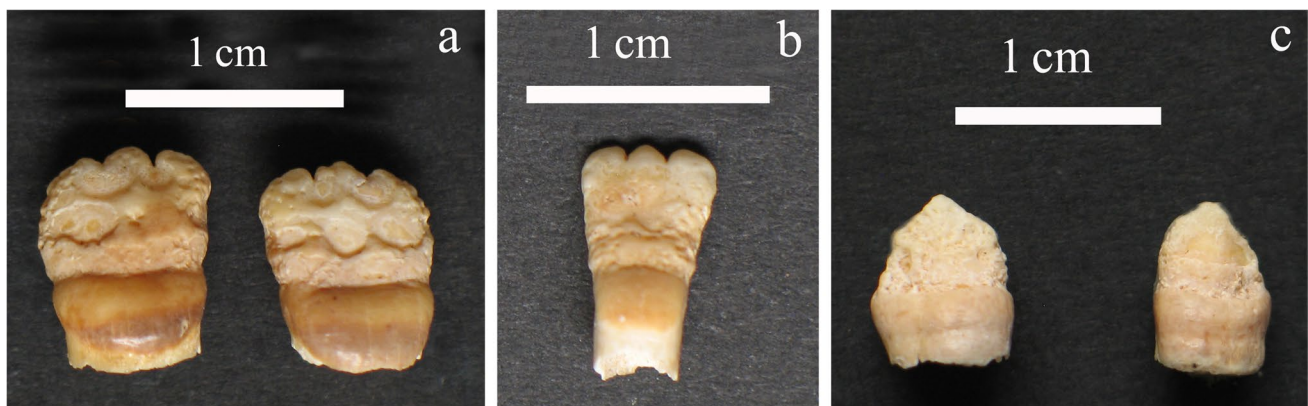
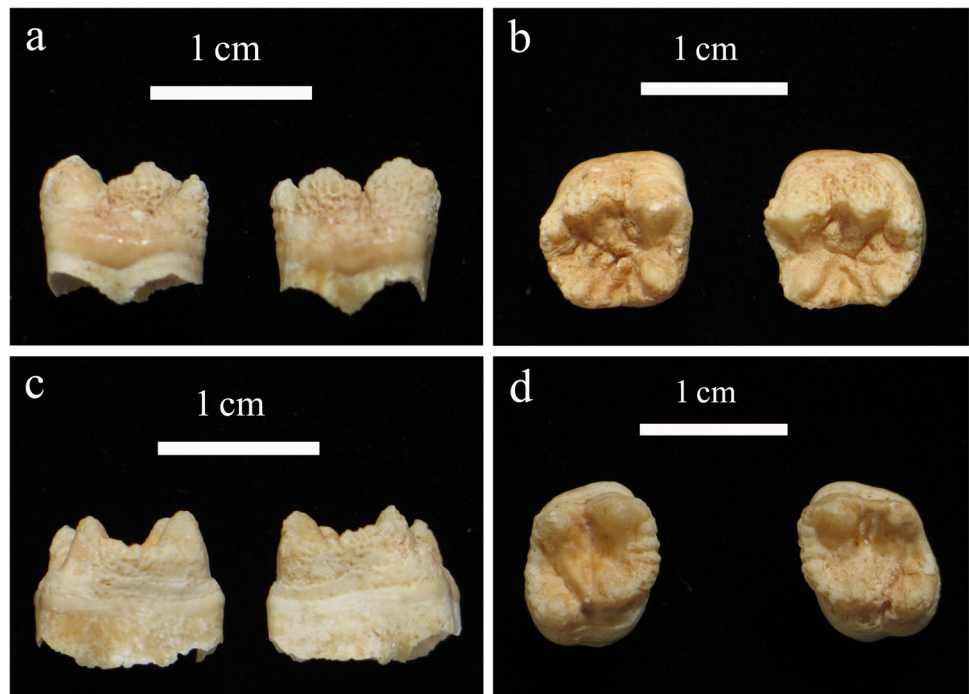


Fig. 2 Anterior teeth of skeleton 2234: maxillary central incisors (a), left mandibular central incisor (b), and left maxillary and mandibular canines (c)

Fig. 3 First molars of skeleton 2234: buccal (a) and occlusal view (b) of the mandibular first molars; buccal (c) and occlusal view (d) of the maxillary first molars



and some areas exhibiting a honeycomb appearance (Fig. 3a and c).

Under the scanning electron microscope (SEM), the buccal surface of the right maxillary central incisor showed several deep hypoplastic grooves (Fig. 4a). SEM images of the permanent molars evidenced the honeycomb appearance of the surface (Fig. 4b and c).

In the postcranial skeleton, the right humerus, radius, and ulna, and the left radius and ulna, demonstrated grade 1 periosteal bone reaction limited to the distal parts of the diaphyses. The posterior surface of the distal diaphyses of both tibiae exhibited grade 1 periosteal reaction as well.

Microtomography and scanning electron microscopy

The surface of the teeth appeared eroded, rough, and notched. The enamel and dentin volumes of the crowns are summarized in Table 1. Very low values of enamel volume were noted, while dentin volumes were mainly preserved (Fig. 5).

No disturbance of dentin formation was emerged from the μ CT data: dentin horns were of normal height and shape and the EDJ was well demarcated. Below the circumferential groove, enamel displayed a normal aspect and thickness.

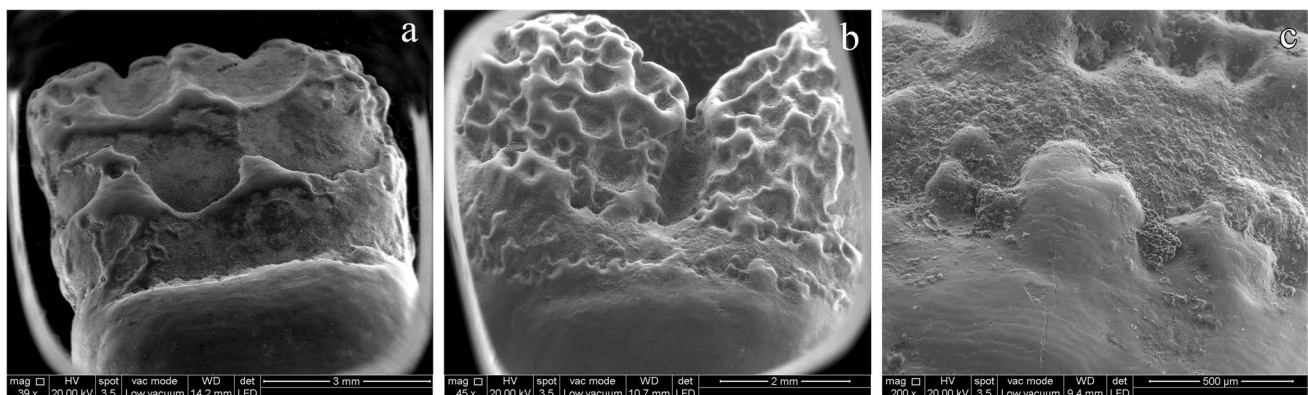
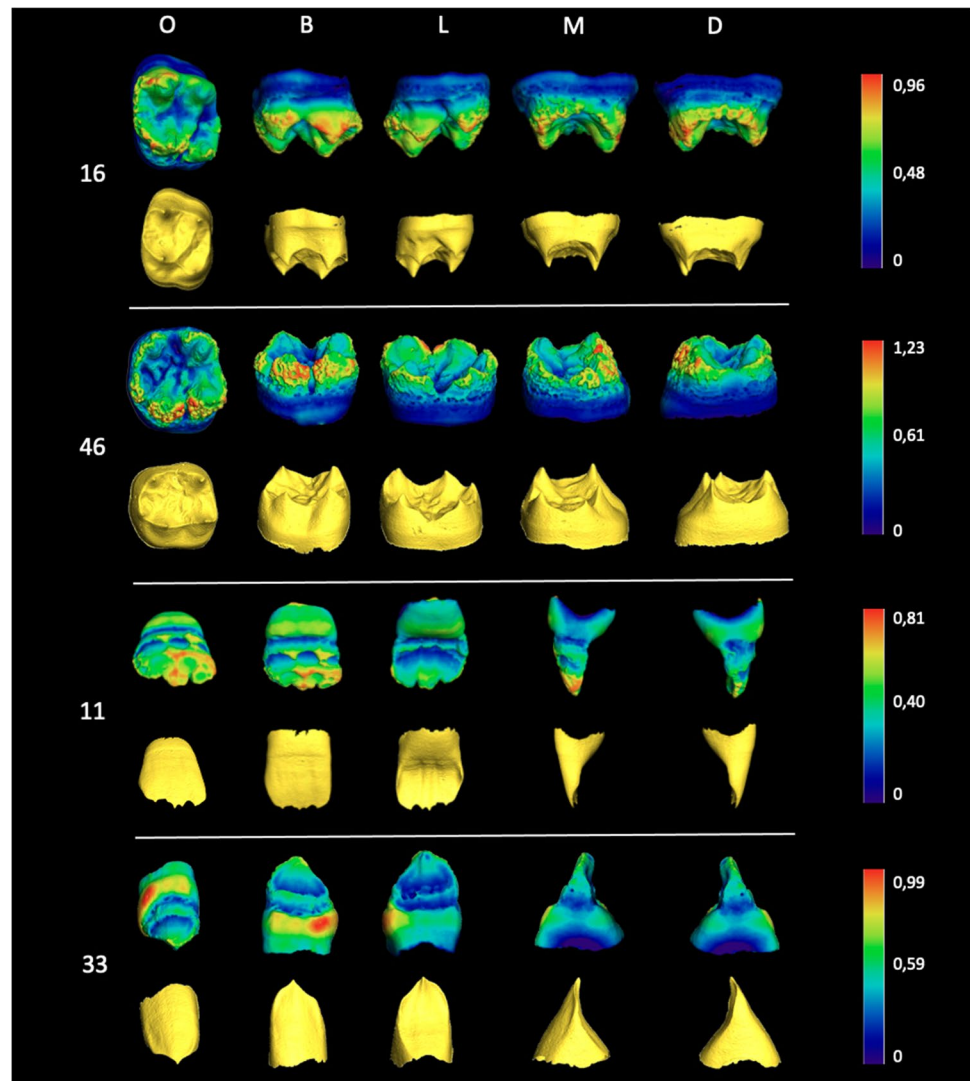


Fig. 4 SEM images: right maxillary central incisor (buccal view; 39 \times) (a), mandibular first molar (buccal view; 45 \times) (b), detail of the mandibular first molar (buccal view; 200 \times) (c)

Table 1 Dental tissue volumes in mm³. Ve, enamel volume; Vd, dentin crown volume. Canine enamel volumes are in italic, as the crowns were not complete. Dental notation: R, right; L, left; I, incisor; C, canine; M, molar; superscript, upper; subscript, lower

	RI ¹	LI ¹	RI ₁	LC [*]	LC ₁	RM ¹	LM ¹	LM ₁	RM ₁
Ve	55.52	55.95	50.23	<i>50.23</i>	<i>48.11</i>	74.20	76.08	75.51	79.57
Vd	68.72	73.06	57.70	/	/	328.98	355.04	303.39	256.64

Fig. 5 Micro-CT 3D-rendered volume of the right maxillary central incisor (11), right maxillary and mandibular first molars (16–46), and left mandibular canine (33). Occlusal (O), buccal (B), lingual (L), mesial (M), and distal (D) views. The upper views show the enamel thickness color maps, and the lower views show the enamel–dentin junction (EDJ)



Chemical analysis

The results of the chemical analysis are presented in Table 2. Very high levels of mercury were detected in the hard tissues of skeleton 2234. The two bone fragments had average mercury levels of 8.968 ± 0.401 mg/kg and 9.759 ± 0.221 mg/kg, respectively; the dental samples revealed an average mercury concentration of 3.748 ± 0.317 mg/kg.

Discussion

Several conditions that can cause enamel defects have to be considered in differential diagnosis. In the case of traumatic lesions, the number of teeth affected is usually smaller, and adjacent elements are involved. In congenital diseases, such as amelogenesis or dentinogenesis imperfecta, the entire dentition displays defects, including enamel discoloration, bulbous crowns, obliterated pulp chambers, and soft and

Table 2 Hg concentration in S2234 bone and dental samples

Bones	Mg	Concentration (mg/kg)
Fragment 1a	9.84	9.284
Fragment 1b	6.04	8.482
Fragment 1c	2.61	9.309
Fragment 1d	6.21	8.797
<i>Mean</i>		<i>8.968 ± 0.401</i>
Fragment 2a	6.11	9.689
Fragment 2b	3.28	10.008
Fragment 2c	2.88	9.582
<i>Mean</i>		<i>9.759 ± 0.221</i>
Teeth	Mg	Concentration (mg/kg)
Sample 1	3.62	3.51
Sample 2	3.08	4.11
Sample 3	3.51	3.63
<i>Mean</i>		<i>3.748 ± 0.317</i>

Italic entries correspond to mean concentration values per sample

friable enamel (Barron et al. 2008; Sabandal and Schäfer 2016), which were not observed in the child from Alghero. Vitamin D deficiency and malnourishment can also affect tooth mineralization, resulting in hypoplastic enamel, dentin mineralization defects, large pulp chambers, short roots, malocclusion, and persistent periodontal disease (Foster et al. 2014), all features that are different from those seen in skeleton 2234.

Mercurial treatment can also cause enamel disturbances. The term “mercurial teeth” was first used by Hutchinson, who recognized various morphological differences between the teeth of individuals affected by congenital syphilis, syphilitic-mercurial teeth, and teeth with anomalies ascribable to mercury exposure (Hutchinson 1878, p. 53). As observed by Hutchinson (1878, 1887) and Moon (1884), mercurial treatment caused dental growth defects, resulting in markedly hypoplastic incisors, molars with eroded occlusal surfaces and multiple tubercles, and canines with a reduced occlusal surface and a fang-like shape.

The changes produced by mercurial treatment have been primarily described in the permanent dentition, with pairs of teeth affected symmetrically; large portions of enamel can be completely lost, especially on the occlusal surfaces, where “dentine grows through, presenting a number of discolored tubercles or spines” (Hutchinson 1887). Moreover, some alterations to the maxillary and mandibular permanent first molars are considered pathognomonic for mercurial teeth (Hutchinson 1878). Typically, the surface of these teeth presents numerous tubercles and ridges; in some cases, the entire crown is involved (Hutchinson 1878, tab. Fig. III), in others it is only the central part of the tooth that shows enamel defects (Hutchinson 1878, tab. IV, V, VI). As a consequence, the tooth surface can appear furrowed, pitted, or

honeycombed. The molars of individual 2234 looked overall pitted and roughened, with a honeycomb appearance in some areas, although some portions of the crowns, such as the mesio-vestibular cusp of the left maxillary first molar, showed no evident defects. According to Hutchinson, the characteristic presentation of mercurial teeth includes the presence of a hypoplastic line crossing the incisors and the canines around their center; as the author states, “a considerable portion of the crown of each tooth is totally devoid of enamel, and its dentine is also deficient to some extent, so that the teeth are thin, sharp-edged, and of a dirty yellowish colour.” In the case of individual 2234, the incisors and the canines showed visible hypoplastic lines crossing the crowns, with large areas of missing enamel. Therefore, the enamel disturbances observed in the child from Alghero are consistent with the effects of mercurial treatment.

The dental defects exhibited by this child could also be partially interpreted as the result of congenital syphilis. The dental expressions of the disease include Hutchinson’s incisors (permanent maxillary incisors characterized by a central notch at the incisal edge); Moon’s molars (dome-shaped permanent first molars with multiple crowded cusps); Mulberry or Fournier’s molars (permanent first molars with reduced cusps and hypoplastic defects on the occlusal third of the crown); and fang-like permanent canines with a circumferential groove on the occlusal third of the crown (Nystrom 2011). Of these dental anomalies, only Moon’s molars and Hutchinson’s incisors are considered pathognomonic in paleopathology (Hillson et al. 1998).

According to Hutchinson’s descriptions, congenital syphilis and mercury treatment produce changes on the teeth that are easily distinguishable from each other. Indeed, the action of syphilis is less extensive and more localized, while mercury-induced changes are more aggressive and involve large portions of the tooth (Hutchinson 1887), as in the case presented here. Syphilitic-mercurial teeth present a combination of lesions, such as notched, hypoplastic, and discolored maxillary central incisors with extensive enamel loss and first molars with enamel loss and defects including hypoplastic pits, furrows, lines, and a honeycomb appearance (Ioannou et al. 2018). All these features were observed in the child from Alghero.

As reported by Hutchinson (1861), the typical crescent-shaped notch on the incisal edge of the incisors, which is considered pathognomonic of congenital syphilis, cannot be mimicked by treatment with mercury. Moon’s molars and Hutchinson’s incisors were not present in the child from Alghero. However, fang-like canines and hypoplastic defects on the occlusal third of the crown of the first molars, similar to mulberry molars, could be observed. Changes in the incisors and molars similar to those seen in individual 2234 were noted in a child from eighteenth-century Vienna and were ascribed to a probable case of congenital syphilis (Gaul and

Grossschmidt 2014). In the case discussed here, the evidence of mercury treatment can indirectly suggest that the child was affected by congenital syphilis. This diagnosis would also be consistent with the presence of other lesions that can be related to the disease and particularly periosteal new bone formation on the diaphyses of the long bones (Mendonça de Souza et al. 2006; Buikstra 2019).

In conclusion, the diagnosis of syphilitic-mercurial teeth in the child from Alghero remains uncertain: mercury could have been used to treat a range of diseases (i.e., pediculosis, scabies, or other dermatological conditions), but it cannot be excluded that the child was affected by congenital syphilis.

The values of enamel volume observed were very low compared to recent published data (Buti et al. 2017; Becam and Chevalier 2019; García-Campos et al. 2021), confirming the hypoplastic nature of the developmental dental defects affecting the incisors, the canines, and the molars. The two canines of skeleton 2234 were not complete, but most of the crown was formed. Significantly lower values of enamel volume were recorded in the left maxillary canine (23), 50.23 mm³ versus 112.34 to 133.65 mm³ (Becam and Chevalier 2019; Buti et al. 2017; García-Campos et al. 2021), and the left mandibular canine (33), 48.11 mm³ versus 88.7–91.82 mm³ (Becam and Chevalier 2019; Buti et al. 2017). The enamel volume of the first molars was reduced by more than half the average volume of a normal molar. The average thickness of the maxillary first molars was 75.14 mm³, significantly lower than other estimates found in the literature, which range from 206 to 239 mm³ (Martín-Francés et al. 2018; Becam and Chevalier 2019). The same difference was detected in relation to the first mandibular molars, with a mean value of 77.54 mm³ versus 226.89 to 247.31 mm³ (Martín-Francés et al. 2018; Becam and Chevalier 2019).

According to Hutchinson, mercury treatment principally caused enamel disturbances but could also affect the dentin in severe cases (Ioannou et al. 2016). The micro-CT analysis of the samples from individual 2234 showed exclusive involvement of the enamel, while dentin and the EDJ were preserved. Several factors can influence the presentation of mercurial teeth, including the dosage of mercury administered to the individual, the rate of mercury excretion, and the overall duration of the treatment. Additionally, the variability of dental abnormalities in congenital syphilis, as well as in cases of congenital syphilis treated with mercury, needs to be taken into account. These considerations suggest that the effects of mercurial treatment on the teeth can vary significantly depending on a number of factors.

The biogenic presence of mercury in archeological human bones has been investigated, allowing detection of several sources of high mercury concentrations. Besides being linked to atmospheric mercury pollution (Alvarez-Fernandez et al. 2020; Lopez-Costas et al. 2020), the presence of mercury in ancient bones has been related to mining,

metallurgy practices, and the consumption of contaminated food in prehistoric Spain (Emslie et al. 2019, 2021); to the use of mercury-based cosmetics in Medieval Russia (Alexandrovskaia and Alexandrovskiy 2005); to work in mercury mines in Mesoamerica (Avila et al. 2014); to medical treatment for a variety of conditions in Medieval Denmark and Germany (Rasmussen et al. 2008, 2015); and to the effects of volcanic emissions and medical treatment in postmedieval Iceland (Walser et al. 2019).

The child from Alghero demonstrated a major mercury intoxication, suggesting prolonged exposure to this substance in early childhood, probably for therapeutic reasons. Considering the portions of crown affected and the average time of crown formation according to Reid and Dean (2006), it could be assumed that mercury treatment started shortly after the child's birth and stopped at around 2.7 to 3 years. The Hg concentrations detected are among the highest documented in archeological human remains from Europe (see the review in Alvarez-Fernandez et al. 2020). Compared to the child from Alghero, average Hg values are significantly lower in other samples, corresponding to 0.05–0.1 mg/kg in skeletal remains from six cemeteries in Denmark (Rasmussen et al. 2008); 0.066 mg/kg in the skeleton of an 8-year-old child from medieval north-central Spain (Gómez-González et al. 2020); 2–2.8 mg/kg in two medieval skeletons with evidence of syphilis from north-central Poland (Keřpa et al. 2012); and 0.021–0.054 mg/kg in two samples (Roman and post-Roman, respectively) from Spain (Alvarez-Fernandez et al. 2020).

Therefore, the present study reports one of the most severe paleopathological cases of mercury intoxication; in addition, the child from Alghero is the youngest individual with evidence of mercury treatment to be documented in the literature so far.

Conclusions

Child 2234 from Alghero showed extensive enamel developmental defects typical of mercurial treatment in the permanent dentition; the dental stigmata were associated with high levels of mercury in the bones and teeth.

Mercury was a well-known therapeutic tool in the treatment of a number of dermatological conditions and was also used to eliminate head lice and fleas. From the end of the fifteenth century, when syphilis became endemic in Europe, mercury started to be very popular in treatments against the disease. The absence of dental stigmata pathognomonic for congenital syphilis, such as Hutchinson's incisors and Moon's molars, makes the diagnosis of syphilitic-mercurial teeth in the individual from Alghero uncertain. It cannot be excluded that, having inherited the disease from the mother, the child was treated with mercury in his first years of life,

as some features typical of syphilitic-mercurial teeth and the presence of periosteal reaction on the diaphyses of the long bones seem to suggest.

Regardless of the illness that affected the child from Alghero, the case presented provides evidence of some of the highest levels of mercury ever recorded in osteoarcheological remains. The severe mercury intoxication demonstrated by the skeletal remains of this child aged 3.5 to 4.5 years from sixteenth-century Sardinia makes the individual the youngest patient documented in the paleopathological literature to exhibit signs of mercurial treatment.

Author contribution All the authors contributed to the conception and design of the study. Moreover, they confirm contribution to the paper as follows: material preparation, data collection, and anthropological and paleopathological analyses by Valentina Giuffra and Daniela Lombardo; archeological analysis and chronological contextualization by Marco Milanese; X-Ray microtomography by Thomas Colard; scanning electron microscopy by Pasquale Bandiera; and chemical analysis by Baghdad Ouddane. The first draft of the manuscript was written by Daniela Lombardo and Valentina Giuffra and was then revised by Thomas Colard. All the authors read and approved the final manuscript.

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Declarations

Competing interests The authors declare no competing interests.

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