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Rickets in a High Social Class of Renaissance Italy: The Medici Children

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ABSTRACT Exploration of the Medici Chapels in the Basilica of San Lorenzo in Florence revealed the burials of nine juvenile members of the Medici family (16th–17th centuries). The estimated children's skeletal ages ranged from newborns to 5-year-olds, showing a series of bone abnormalities, in particular diffuse periosteal new bone and bowing of long bones. The comparable pathological lesions, including porosity evident on the skull, orbital roofs, costocondral ribs and growth plates between metaphyses and epiphyses, enlargement of metaphyses and sternal rib ends, and long bone bending, are interpreted as the skeletal manifestation of rickets. The diagnosis of a metabolic disease linked to vitamin D deficiency would appear to be unexpected for children brought up at the court of a Renaissance elite class family like the Medici of Florence. Analysis of the historical and social background is particularly helpful to understand the causes of the onset of the disease in this aristocratic group. Documentary sources, supported by ^{13}C and ^{15}N bone collagen analysis, attest that weaning of these children took place when they were around 2 years old. With a prolonged breast-feeding and a delay in introducing solid food in the diet, vitamin D deficiency is expected to rise considerably, in particular if the other main risk factor, namely inadequate sunlight exposition, is associated with this human milk-based diet. Copyright © 2013 John Wiley & Sons, Ltd.

Key words: vitamin D deficiency; periosteal new bone; paleonutrition; juvenile; Medici children; Florence; Renaissance

Introduction

Rickets is a disease of infancy and childhood caused by vitamin D deficiency. Vitamin D is essential for the metabolism of calcium and phosphorus, which enables bone mineralisation. A deficit in vitamin D absorption prevents normal calcification of the bones and results in soft and possibly deformed bones (Porth, 1994). Because vitamin D is a pro-hormone and not by design a nutrient, it does not occur naturally in any dietary sources in sufficient amount; in fact, only 10% of vitamin D is derived from food, whereas the remaining 90% is synthesised in the skin after exposure to ultraviolet radiations. Therefore, the main causes of deficiency in vitamin D absorption consist in prolonged lack of exposure to sunlight and/or nutritional deficit, even if other rarer hereditary conditions may also play a role in the onset of the disease (Resnick & Niwayama, 1988).

Juvenile rickets in archaeological bone is characterised by abnormal diffuse pitting, in particular on the skull, orbital roofs, costocodral ribs, growth plates between metaphyses and epiphyses, and epiphyseal plates of the long bones, where unmineralised osteoid, not preserved in dry bones, was present during life; the presence of cranial and post-cranial periosteal new bone, although can be caused by numerous conditions, indicates active cases in rickets, whereas in healed individuals the defects are filled in with bone and are therefore obliterated (Ortner & Mays, 1998; Mays *et al.*, 2006). A typical feature of rickets is the widening of the metaphyses, the regions of more rapid growth, and of sternal rib ends, a feature known as rachitic rosary in living people. In prolonged rickets, the characteristic bending of the long bone develops as a consequence of weight-bearing; if rickets occurs in the crawling phase, deformations

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involve both the upper and lower extremities, but if the onset of the disease occurs after walking, only the legs show evidence of deformation. The lack of mineralisation can produce other deformations, such as medial posterior bending of the mandible, as a result of muscular tensions, and superior flattening of femoral metaphyses and coxa vara (a deformity of the hip, by which the angle between head and shaft of the femur is reduced to less than 120 degrees), as a consequence of weight-bearing (Ortner & Mays, 1998; Mays *et al.*, 2006). At the X-ray, demineralisation leads to coarsening of the cortical bone, loss of cortico-medullary distinction and cortical tunnelling (Adams, 1997).

Convincing paleopathological cases of rickets are limited in number (Brickley & Ives, 2008), partly because this condition was relatively rare before the Industrial Revolution and partly because its manifestations in dry bones are difficult to identify, except for severe cases. Bending of the long bones is one of the most recognisable features of rickets in paleopathology, whereas other characteristics are common with other conditions and can be misinterpreted. However, recent research has established the macroscopic and radiological criteria designed to recognise the active disease in juvenile remains (Ortner & Mays, 1998; Mays *et al.*, 2006). None of these features by themselves can be considered sufficient for the identification of rickets but, in combination, they enable diagnosis of the disease in osteoarchaeological remains.

A reason for the paucity of reports on rickets consists in the poor state of preservation of children remains in archaeological contexts and in the limited attention paid to juvenile subjects in anthropological studies. It is only recently that population analyses with a wider perspective than the study of single cases have been carried out to understand which cultural factors may have intervened in the occurrence of the disease (Littleton, 1998; Palkovich, 2008; Ellis, 2010; Stodder & Palkovich, 2012).

The excellent state of preservation of the Medici children's skeletal remains offered a unique opportunity to study this high-social class sample of the Renaissance period.

In this study, all the macroscopic and radiological features listed by Mays *et al*. (2006) were used as diagnostic criteria, with the exception of the ilium concavity, because this aspect is hardly appreciable in juvenile remains.

Materials and methods

The Medici were one of the most powerful families of the Italian Renaissance. Starting from the 14th century, their careful management of banking ventures and skillful political actions brought them to the forefront of social and political power in Tuscany and in Florence, the intellectual centre of the Western world. Lovers of art and science, the Medici were patrons of Michelangelo, Leonardo da Vinci, Botticelli, Galileo and Benvenuto Cellini.

The members of the Medici family were buried under the floor of the crypt of the Basilica of San Lorenzo in Florence. During the 'Medici Project', started in 2004, the remains of the family members belonging to the branch of the Grand Dukes of Tuscany, which began with John of the Black Bands (1498–1526) and ended with Giangastone (1671–1737), were investigated from both an anthropological and paleopathological point of view (Fornaciari *et al.*, 2006, 2007).

Some burials had already been explored during the Second World War (Genna, 1948), and for this reason, we decided to begin our study with the tomb of Giangastone, the last Medici Grand Duke (1671–1737), which was intact.

The removal of a marble disc in the floor of the chapel, initially considered only a simple floor decoration, displayed a secret opening with a small stone stair leading to a hidden crypt. This small funerary crypt revealed a low raised plank supporting a large sarcophagus, which contained the intact funerary deposition of the last Grand Duke. Other small coffins, which stored the remains of children, were not in their original position, but were distributed irregularly on the floor and on the plank of the crypt, as a consequence of the Arno flooding of 1966 (Figure 1). The presence of water in the crypt had also caused large bone movements, so that the remains of many individuals had come out of their coffins and were scattered in different places, in some cases resulting in comingling of bones (Fornaciari, 2008a). A layer of dry mould was still covering the floor and the plank, as well as the bones outside the coffins. The water had caused some superficial damage to the bones, easily recognisable as post-mortem changes. Unfortunately, there were no elements either outside or inside the crypt, for example plates or inscriptions associated with the coffins, which could help identify the children's remains.

In addition to the children buried in the crypt of Giangastone, another juvenile member of the family (Med 9) was found in the lateral chapel of the Grand Duke Francesco I (1541–1587) together with Giovanna of Austria (1547–1578) and Anna (1569–1584); the skeletal remains were contained in a zinc box with an inscription reporting the name of Filippo (1598–1602), sixth child of Ferdinando and Cristina of Lorena (1565–1636).

The skeletal remains of the Medici children were submitted to anthropological examination. The single burials were rearranged, and the bones scattered in

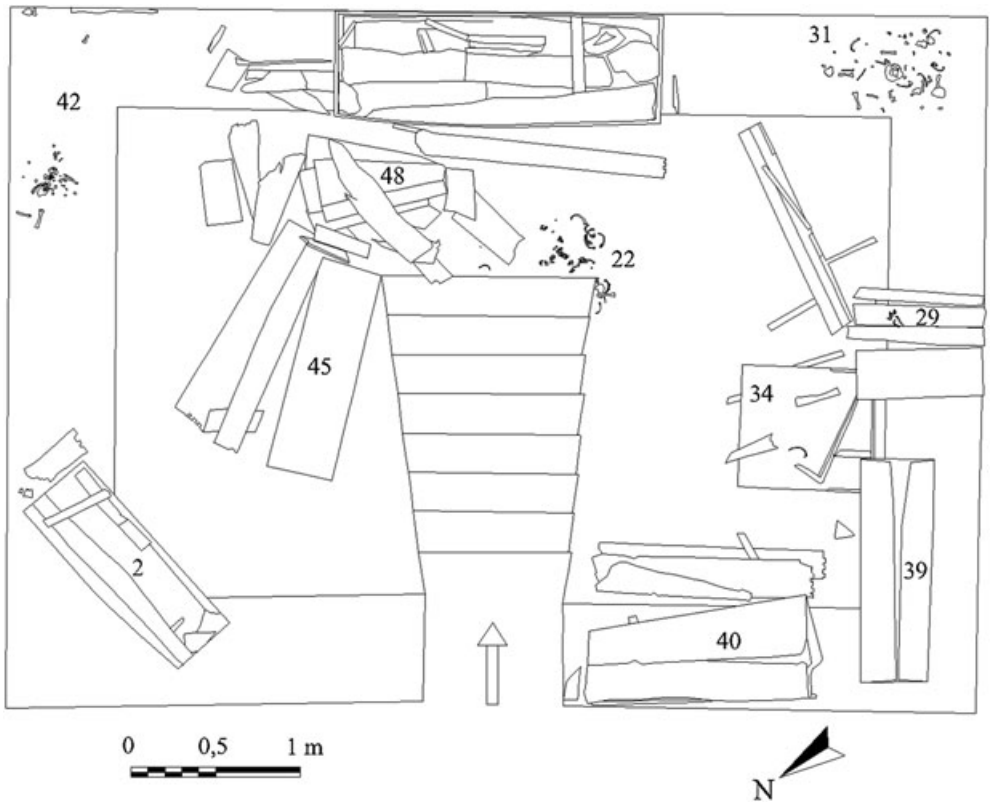

Figure 1. Plan of the crypt of Giangastone, with the small coffins, collapsed to the floor or randomly distributed on the raised plank and containing the children's remains.

the crypt were assigned to the children, on the basis of length and size. All in all, there were eight children buried in the crypt of Giangastone and one in the chapel of Francesco, making a total of nine for the basis of the study. The age at death for each child was determined on the basis of tooth development (AlQahtani *et al.*, 2010) and long bone measurements (Scheuer & Black, 2000).

Sex estimation for foetal and juvenile individuals is a highly contested subject (Scheuer & Black, 2000). Morphognostic analyses of infant mandibles performed by Loth & Henneberg (2001) were successful in determining sex based on the shape of male and female mandibles, although the reliability of this method was criticised (Scheuer, 2002). Mandibles of the Medici children were examined, but attempts to determine sex were successful for only one child, Med 40.2, that showed reasonable sexual dimorphism (Schutkowski, 1993).

The results of the anthropological study were compared with the information provided by archival and documentary sources consisting of letters, court physicians' reports and ambassadors' accounts of the family children who died in juvenile age (Pieraccini, 1986), and an identification of the children was proposed (Vitiello *et al.*, in press).

A paleopathological study by macroscopic examination was performed, and when possible, some bone samples were submitted to radiological study. A paleonutritional analysis of stable isotopes ratios was also carried out, in order to investigate the diet of this juvenile sample belonging to the Renaissance aristocracy.

Results

Macroscopic features

The skeletal ages were those of newborns to 5-year-old children, the majority of whom showed a series of bone abnormalities, in particular diffused periosteal new bone. No dental changes nor dental pathologies were observed. A detailed description of the macroscopic abnormalities observed in each child is provided later, and the results are summarised in Table 1. With respect to the skeletal remains, the term infant is used to refer

Table 1. Macroscopic features of rickets in the nine Medici children

	Med 40.2	Med 40.22/42	Med 40.29/31	Med 40.34	Med 40.39	Med 40.40	Med 40.45	Med 40.48	Med 9
Age at death	4–5 years	12–18 months	6–9 months	Newborn	5 years	1.5–2 years	Newborn	6–12 months	6–12 months
Cranial vault porosity	A	–	**P**	**P**	A	**P**	**P**	**P**	**P**
Orbital roof porosity	–	–	A	A	A	**P**	A	**P**	**P**
Deformed mandibular ramus	A	–	A	A	A	**P**	A	**P**	**P**
Rib deformity	A	A	A	A	–	–	A	–	A
Costochondral rib flaring	A	**P**	**P**	**P**	–	–	**P**	–	A
Costochondral rib periosteal new bone	A	**P**	**P**	A	–	–	**P**	–	A
Deformed leg bones	A	–	**P**	A	**P**	**P**	A	A	**P**
Deformed arm bones	A	**P**	**P**	A	A	A	A	**P**	**P**
Long-bone metaphyseal flaring	A	A	**P**	A	–	**P**	A	A	**P**
Long-bone general thickening	A	A	**P**	A	A	A	A	A	A
Long-bone metaphyseal periosteal new bone	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**
Superior flattening of femoral metaphysis	A	–	**P**	A	–	**P**	A	**P**	A
Coxa vara	A	–	**P**	A	A	**P**	A	**P**	A
Porosis/roughening of bone underlying long-bone growth plates	A	**P**	**P**	A	–	**P**	A	**P**	**P**
Long-bone concave curvature periosteal new bone	A	**P**	**P**	A	**P**	**P**	A	A	**P**

P, present; A, absent; –, not scored (bone missing or damaged).

to an individual of 1 to 12 months and the term child to refer to individuals older than 1 year of age.

Med 40.2

The mandible morphology, especially the chin shape and gonial eversion, suggested a male sex (Schutkowski, 1993). This child with dental age of 4 years ± 9 months and diaphyseal age of 5–6 years could be identified with Filippo (9 April 1598–3 April 1602), seventh child of Ferdinando I and Cristina of Lorena, who died at nearly 4 years of age. The remains of this child presented periosteal new bone in the metaphyseal region of the long bones.

Med 40.22/42

This child with an anthropological age slightly older than 1 year was identified with Anna (10 March 1552–6 August 1553), who died at nearly 18 months of age, and was the 11th child of Cosimo I (1519–1574) and Eleonora from Toledo (1522–1562). The skeleton was largely incomplete, as the skull and lower extremities were completely missing, except for a few feet bones, and only the ribs and arm long bones were available for examination of diagnostic criteria of rickets.

Both humeri showed slight bending and diffused periosteal new bone, more marked in the metaphyseal and epiphyseal regions, and in correspondence to the concave curvature; roughening of the bone underlying the growth plates of the proximal humeri was evident. Marked periosteal new bone also affected the left ulna, left ilium and left scapula. Alterations were observed in the costochondral ends of the ribs, especially flaring and periosteal new bone.

Med 40.29/31

This infant with an estimated age at death of 9 months ± 3 months, on the basis of dental development, and of 6 months, on the basis of diaphyseal length, could be identified with three possible members of the family: Don Pietro or Pedricco (August 1546–9 June 1547), sixth child of Cosimo I and Eleonora, who died at 10 months of age; Isabella (30 September 1571–8 - August 1572), fourth child of Francesco I (1541–1587) and Giovanna of Austria (1547–1578), who died at 11 months of age; and Antonio (1 July 1548–?), eighth child of Cosimo I and Eleonora of Toledo, whose date of death is unknown.

A marked periosteal new bone widely affected the skull bones, mandible, left clavicle, both scapulae, ilia and ribs; in the left humerus and ulna, the periosteal new bone was visible all over the bone surface, whereas in the radii, left femur and fibula, it was limited to the metaphyseal and epiphyseal regions. The left humerus, radii (Figure 2a) and left ulna (Figure 2b) showed slight diaphyseal bending, more evident in the fibula (Figure 2c), whose laterality could not be determined. Marked flaring could be observed in the costochondral ends of the recovered ribs (Figure 2d). The long bones presented periosteal new bone/roughening of the bone underlying the growth plates. Metaphyseal flaring was particularly evident in the distal radii (Figure 2a).

Med 40.34

From the length of long bones and dental age, this was a newborn of a few weeks of age. This infant could be identified with Romola (20 November 1568–2 December 1568), second child of Francesco I and Giovanna of Austria, who survived only 12 days after birth, or with an unnamed daughter (31 May 1641) of Ferdinando II (1610–1670), fifth Granduke of Tuscany, and of Vittoria della Rovere (1622–1694). In this infant, who died on the same day of her birth, periosteal new bone of the skull bones was observed, as well as of metaphyseal and epiphyseal regions of the long bones; slight periosteal new bone was also diffusely present on the clavicles, scapulae and coxal bones, more marked on the gluteal side of the ilia. The costochondral ends of the ribs showed flaring.

Med 40.39

This child, who revealed a diaphyseal age of 6/7 years and dental age of 5 years ± 16 months, can certainly be identified with Don Filippino (20 May 1577–29 March 1582), seventh child of Francesco I and Giovanna of Austria. According to historical accounts, the young prince underwent autopsy, and the skullcap was cut and removed; as a matter of fact, the skull showed a horizontal craniotomy (Fornaciari *et al.*, 2008). The presence of the clothes allowed only a partial recovery of the skeletal remains, in particular of the skull, right clavicle, cervical vertebrae, first two right ribs, left tibia and both fibulae. The remaining bones were left inside the costume.

The cranium revealed an increase in the biparietal diameter, high frontal bone and frontal bossing, whereas the facial skeleton had a normal conformation, with the exception of a relatively high mandibular symphysis (Figure 3a–b); the coronal suture was widely separated, especially in the *bregma* region. The endocranial surface was heavily marked by falciform impressions, especially in the region of the parietal and occipital lobes; grooves of the branches of the middle meningeal vessels and nerves were abnormally deep and expanded; the parietal theca appeared to be very thin and translucent; these features indicated an intracranial pressure as a consequence of rickets hydrocephalus. As for the post-cranial skeleton, the left tibia and fibulae showed

a marked bending of the diaphysis, with periosteal new bone limited to the metaphyseal and epiphyseal regions (Figure 3c).

Med 40.40

This child, estimated to be 24 months ± 8 months old on the basis of dental maturity levels, and 18 months on the basis of long bone length, could be identified with Lucrezia (7 November 1572–14 August 1574), who died at the age of 22 months, and was the fifth child of Francesco I and Giovanna of Austria.

Porosity affected the skull, more severely the parietal bones around the parieto-temporal sutures (Figure 4a–c) and along the parieto-occipital suture. On the endocranial surface, diffused new bone formation and spongy bone apposition with porosity were visible in correspondence to the parietal eminences, on the frontal and occipital squama. Cribra orbitalia of degree 2 of Hengen (1971) were present on the orbital roofs (Figure 4d). The mandibular ramus showed medial posterior bending (Figure 4e). As for the post-cranial skeleton, periosteal new bone affected the epiphyseal and metaphyseal regions of all the long bones. Periosteal new bone was also

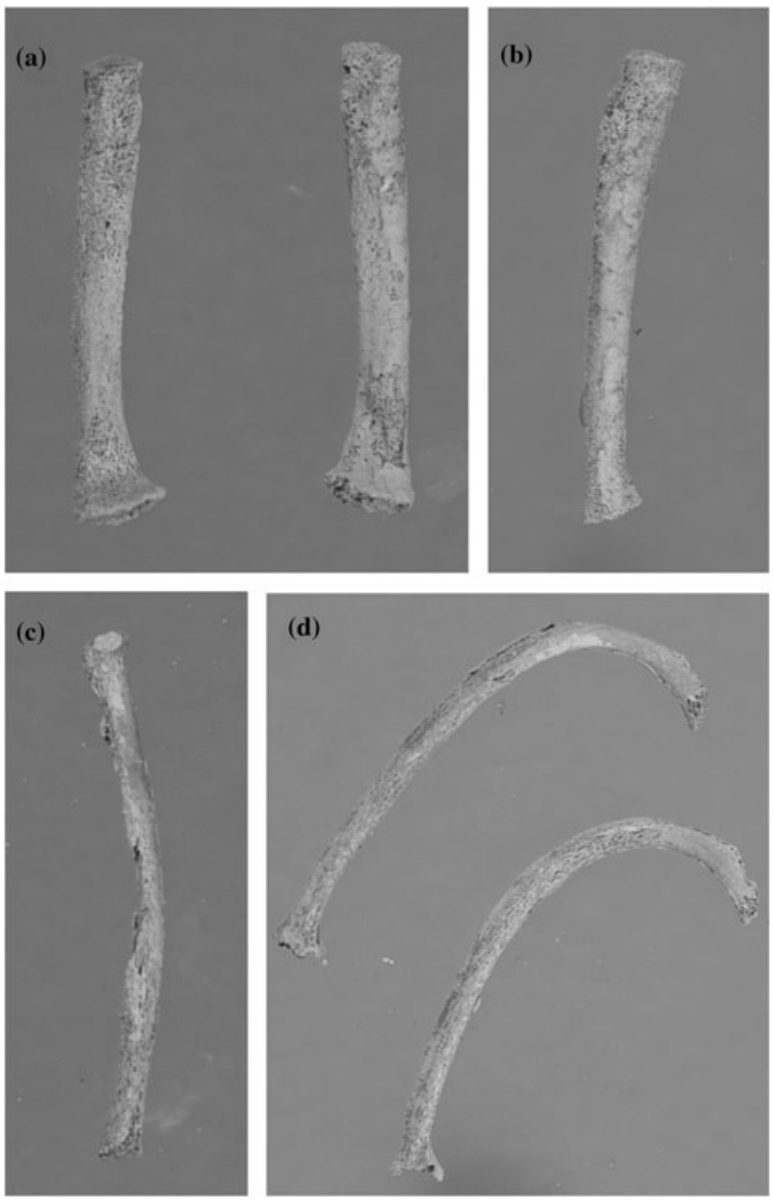

Figure 2. Med 40.29/31: deformed radii (a); posterior view of deformed ulna (b); anterior view of deformed fibula (c); costo-chondral rib flaring (d).

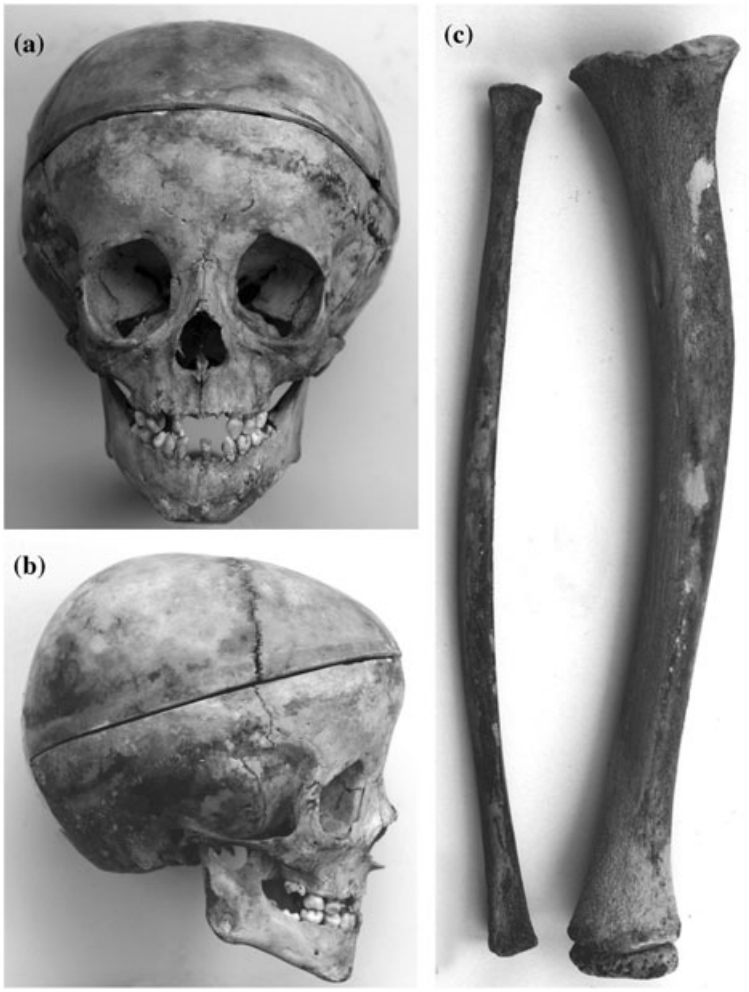

Figure 3. Med 40.39: anterior (a) and lateral view of the skull (b); posterior view of the deformed tibia and fibula (c).

observed diffusely on the mandible, on the external surface of the maxilla and hard palate, clavicles, scapulae, right coxal bone and pubis, both ischia. The femora and fibulae showed evident antero-posterior diaphyseal bending with periosteal new bone in correspondence with the concave curvature. Unfortunately, only the first right and left ribs were recovered so that flaring of the costochondral ends could not be evaluated. Metaphyseal flaring and roughening of the bone underlying the growth plates were evident in the long bones of the legs.

Med 40.45

According to the diaphyseal length and dental age, this was a newborn. This infant had two possible identifications: Romola (20 November 1568–2 December 1568), daughter of Francesco I and Giovanna, or the unnamed daughter (31 May 1641) of Ferdinando II and Vittoria della Rovere.

Porosity affected all the cranial bones, as well as the sphenoid, maxillar bones, left zygomatic bone (the right was missing), the two hemi-mandibles and the zygomatic bones; porosity was also observable on the endocranial surface (Figure 5a). In the post-cranial skeleton, periosteal new bone was evident in the metaphyseal and epiphyseal regions of the long bones (Figure 5c–d), and was widespread in both scapulae, clavicles, ilia (Figure 5b), ischia and pubis. The costochondral ends of the ribs showed flaring and periosteal new bone.

Med 40.48

This infant had a dental age estimate of 9 ± 3 months and a diaphyseal age of 6–12 months, similarly to Med 40.29/31, and could therefore be identified with Don Pedricco (August 1546–9 June 1547), son of Cosimo I and Eleonora, or with Isabella (30 September

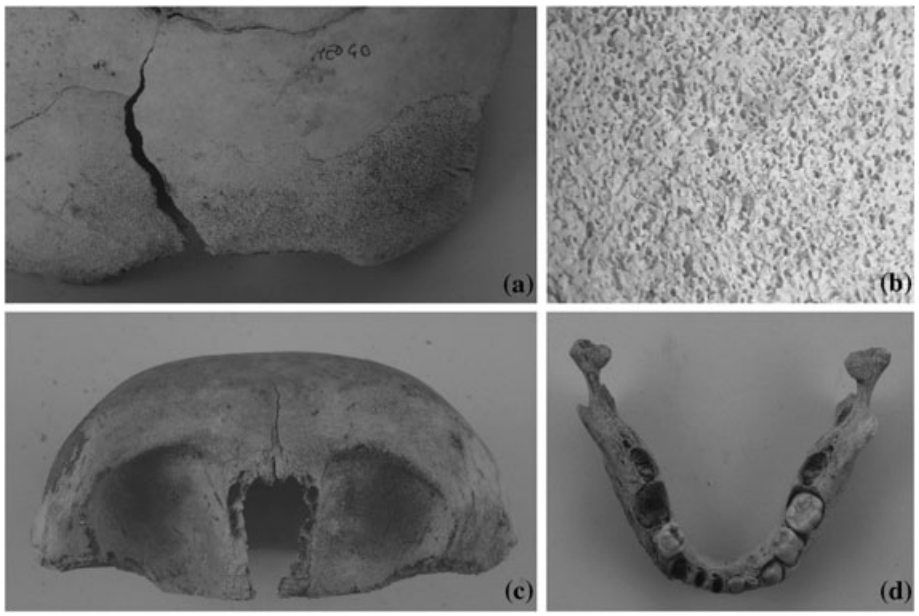

Figure 4. Med 40.40: porosity on the external surface of the parietal bone (a); porosity on the parietal bone viewed under the stereomicroscope (magnification ×10) (b); orbital roof porosity (c); deformed mandibular ramus (d).

1571–8 August 1572), daughter of Francesco I and Giovanna, or with Don Antonio (1 July 1548–?), son of Cosimo I and Eleonora.

Cribra orbitalia of degree 2 of Hengen were visible on both orbital roofs (Figure 6a). Porosity affected the skull bones (Figure 6b), as well as the endocranial surface of the temporal bones. The mandibular rami showed medial posterior bending. Periosteal new bone was also evident on the metaphyseal and diaphyseal regions of the long bones (Figure 6c). The arm bones showed slight diaphyseal bending. Periosteal new bone/roughening of the bone underlying the long-bone growth plates was also present.

Med 9

The anthropological study revealed that the bones of this infant did not belong to Filippo, son of Ferdinando and Cristina, who died at 4 years of age, as reported by the inscription, because the age at death was considerably younger. Filippo was identified with Med 40.2, whose remains showed in fact an age at death of 4–5 years. It is likely that the zinc box with the epigraph reporting the name of Filippo had been erroneously used for another child, but it is not possible to establish when this mistake was made.

Med 9 had a dental age estimate of 1 year ± 4 months and a diaphyseal age of 6 months, similar to that of Med 40.29/31 and Med 40.48; therefore, the infant could be identified with Don Pedricco (August 1546–9 June 1547), son of Cosimo I and Eleonora, or with Isabella (30 September 1571–8 August 1572), daughter of Francesco I and Giovanna, or with Don Antonio (1 July 1548–?), son of Cosimo I and Eleonora.

Porosity affected the skull, in particular the parietal bones in correspondence of the sutures; cribra orbitalia of degrees 2–3 of Hengen were visible on the left orbit. Periosteal new bone was present on the mandible, on the metaphyseal and epiphyseal regions of the humeri, right ulna, right radius, right femur and tibiae. Post-mortem damage to the left ulna, radius and femur prevented paleopathological observation.

Radiological features

Alterations of the internal bone architecture not visible at macroscopic examination were radiologically investigated, following the evaluation of the criteria suggested by Mays *et al*. (2006). Permission to move the bones from the Medici chapel to the Department of Radiology for radiological examination was obtained only for a selection of long bones and ribs showing macroscopic alterations. The results are summarised in Table 2. Except for the newborns, all the Medici children showed demineralisation of cortical bone and trabecular coarsening, which led to the loss of cortico-medullary distinction, as well as cortical tunnelling, seen

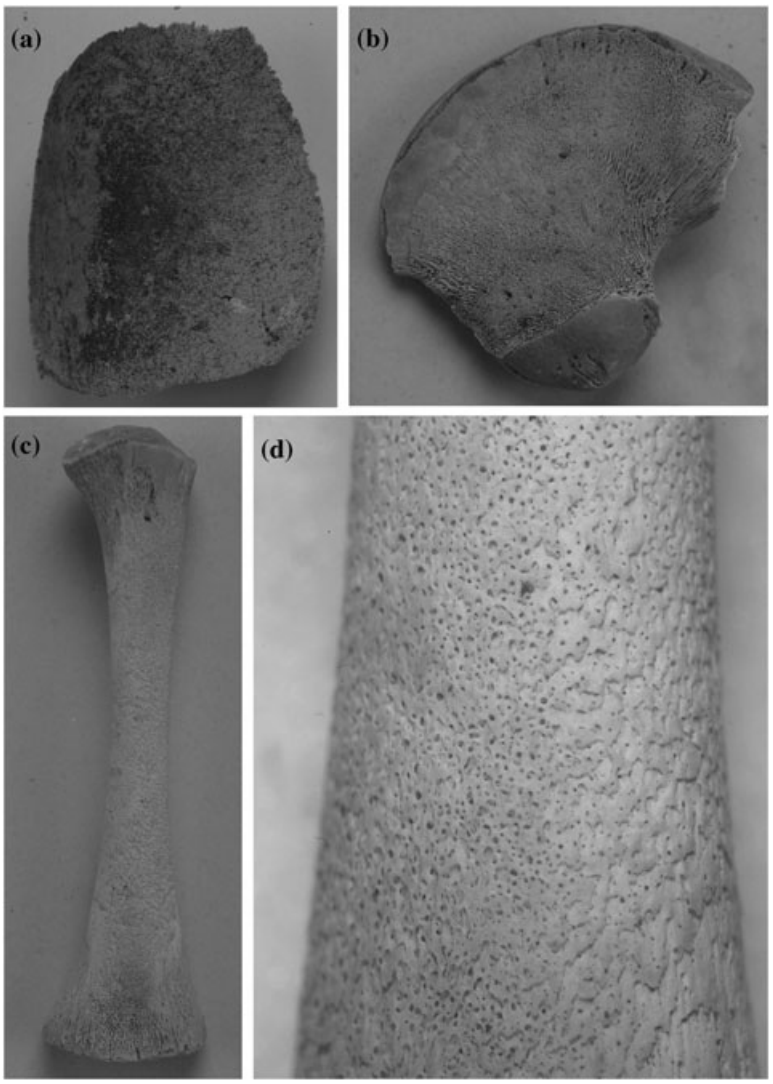

Figure 5. Med 40.45: cranial vault porosity on the endocranial surface of the left parietal bone (a); periosteal new bone on the left ilium (b); periosteal new bone on the anterior view of the left femur (c); periosteal new bone of the femur viewed under the stereomicroscope (magnification ×10) (d).

as linear radiolucencies within the cortex (Figure 7a–d). X-rays confirmed bending of the long bones, as a result of biomechanical alterations.

A particular case is represented by Med 40.39, identified with Filippino, whose skull was submitted both to X-ray and CT; expansion of the neuro-cranium, severe thinning of the cranial theca at the level of the parietal bones, digital impressions and flattening of the cranial base were confirmed (Figure 7e–f). Radiological study of the bones under the costume was carried out *in situ* with a portable apparatus, which revealed an evident curvature also of the right tibia and of both femora. It was more difficult to evaluate the presence of deformities in other skeletal segments.

Paleonutritional study

Stable carbon and nitrogen isotope ratios have been used to detect the timing of the weaning process in past populations (Herring *et al.*, 1998; Schurr, 1998; Fuller *et al.*, 2006). A paleonutritional study was carried out on bone samples of all the members of the Medici family so far exhumed and on other groups of the elite Renaissance class, the Aragonese princes and kings of the Basilica of S. Domenico Maggiore in Naples (Fornaciari, 2008b). Isotope analyses on the two most common stable isotope ratios used for paleodiets, ^{13}C and ^{15}N, were performed by Arthur C. Aufderheide (University of Minnesota) and by Carmine Lubritto

Figure 6. Med 40.48: orbital roof porosity (a); porosity on the temporal bone (b); fraying and increased porosity of the growth plate of the distal femurs (c).

(2nd University of Naples) according to standard methods (Sutton *et al.*, 2010).

Carbon and nitrogen stable isotope analysis of bone collagen showed that the $\delta^{15}N$ values of the Medici children were significantly higher than those of adults, indicating that they were breastfed (Table 3). In particular, $\delta^{15}N$ values were higher at 0.9–2 years of age, during which time children must be gaining all or most of the proteins in their diets from breast milk. Those values decreased in older children after weaning and reached the levels observed in adult subjects. The mean $\delta^{15}N$ value for all individuals less than or equal to 2 years of age was 14.85‰, whereas the mean $\delta^{15}N$ for individuals over 2 years of age was 11.5‰. Overall $\delta^{15}N$ values in the Medici children ranged from 11.45‰ to 16.6‰, with a mean value of 14.7‰.

^{15}N analysis demonstrated that weaning of these high social class children took place around 2 years of age (Schurr, 1998).

The $\delta^{13}C$ values found in the Medici children (Table 3) showed little variation at the different ages and were a little higher or equal to those of adults, reflecting the situation of many other archaeological studies on weaning, which found elevated $\delta^{15}N$ values without increased $\delta^{13}C$ values. The most accepted method for determining the age of weaning is to measure the $\delta^{15}N$ values in bone collagen, which monitor the duration of breast milk consumption. Little significance has been attributed to bone collagen $\delta^{13}C$ values, as they rarely display unique isotopic patterns similar to those of $\delta^{15}N$ results. However, a recent study has shown that $\delta^{13}C$ values can be used as possible indicators for the introduction of solid foods to the diet (Fuller *et al.*, 2006). The values of $\delta^{13}C$ found in the Medici children suggest the possibility that at the moment of death, some infants were still breastfed but were also in the process of consuming solid foods.

Discussion

All the Medici children present at least three macroscopic diagnostic criteria for rickets, with the exception of Med 40.02, for which only long-bone metaphyseal periosteal new bone was observed; the presence of only one change makes the diagnosis of rickets highly uncertain. Radiological examination evidenced that the criteria for rickets are detectable in all the children, except for the two newborns.

With regard to differential diagnosis, other conditions can be evaluated to explain the lesions observed

Table 2. Radiological diagnostic features of rickets in the nine Medici children

	Med 40.2	Med 40.22/42	Med 40.29/31	Med 40.34	Med 40.39	Med 40.40	Med 40.45	Med 40.48	Med 9
Age at death	4–5 years	12–18 months	6–9 months	Newborn	5 years	1.5–2 years	Newborn	6–12 months	6–12 months
Trabecular coarsening/thinning	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**
Loss of cortico-medullary distinction	**P**	**P**	**P**	A	**P**	**P**	A	**P**	**P**
Cortical tunnelling	**P**	**P**	**P**	A	A	**P**	A	**P**	**P**
Biomechanical alterations	A	**P**	**P**	A	**P**	**P**	A	**P**	**P**

P, present; A, absent.

in children's skeletal remains. One of the earliest signs of rickets is in the skull; in particular, the deposition of osteoid on the external table mimics porotic hyperostosis. In our sample, cranial porosity was observed in six children and orbital roof porosity in two. It should be reminded that porotic hyperostosis of the skull and cribra orbitalia are not characteristic of a specific disease but represent a morphological feature. However, the diagnosis of anaemia cannot be ruled out in the other samples. Modern clinical studies have in fact demonstrated that infants in developing countries who are exclusively breastfed for more than 6 months may be at increased risk of anaemia (Meinzen-Derr *et al.*, 2006). Therefore, the two conditions may have coexisted in the Medici children.

Another pathology producing lesions similar to those of rickets, such as porosities of the metaphyseal regions and fractures at the costal ends with a 'rosary'-like aspect, is scurvy. Modern clinical studies have demonstrated that exclusively breastfed infants are well protected against vitamin C deficiency, because maternal milk contains sufficient amounts of ascorbic acid (Salmenperä, 1984). Furthermore, even if some superficial abnormal skeletal features of scurvy and rickets overlap, a careful observation of the lesion can help in differential diagnosis. The crucial distinction is that the porosity appearing in scurvy is true porosity with many holes penetrating the cortical bone, as it is caused by a vascular response to local bleeding. Instead, pseudo-porosity in rickets does not usually penetrate the underlying cortex, as it is due to the failure to mineralise the osteoid. In the Medici children, porosity appears as a periosteal new bone, with no involvement of the underlying cortex, and therefore, the lesions are more typical of rickets. However, if the mother is severely malnourished, a very early onset of scurvy can occur (Brickley & Ives, 2008). Congenital scurvy occurring in the first month of life is rare, but it is a candidate for differential diagnosis in the case of MED 40.45 in view of the lesions on the sphenoid and maxilla (Brickley & Ives, 2006). Moreover, stressed out mothers may predispose infants to scurvy at young ages, as a deficient diet is likely to be inadequate in more than one nutritional requirement; the co-occurrence of rickets and scurvy, observed in clinical studies (Follis *et al.*, 1940; Fouron & Chicoine, 1962), cannot be definitively ruled out in some Medici children.

Congenital syphilis can produce periosteal new bone formation as well, with changes to the metaphyseal regions of the long bones in affected infants. Nevertheless, the best-known features of congenital syphilis are Hutchinson's teeth and mulberry molars at the level of teeth and sabre tibia with bowing (Waldron, 2009).

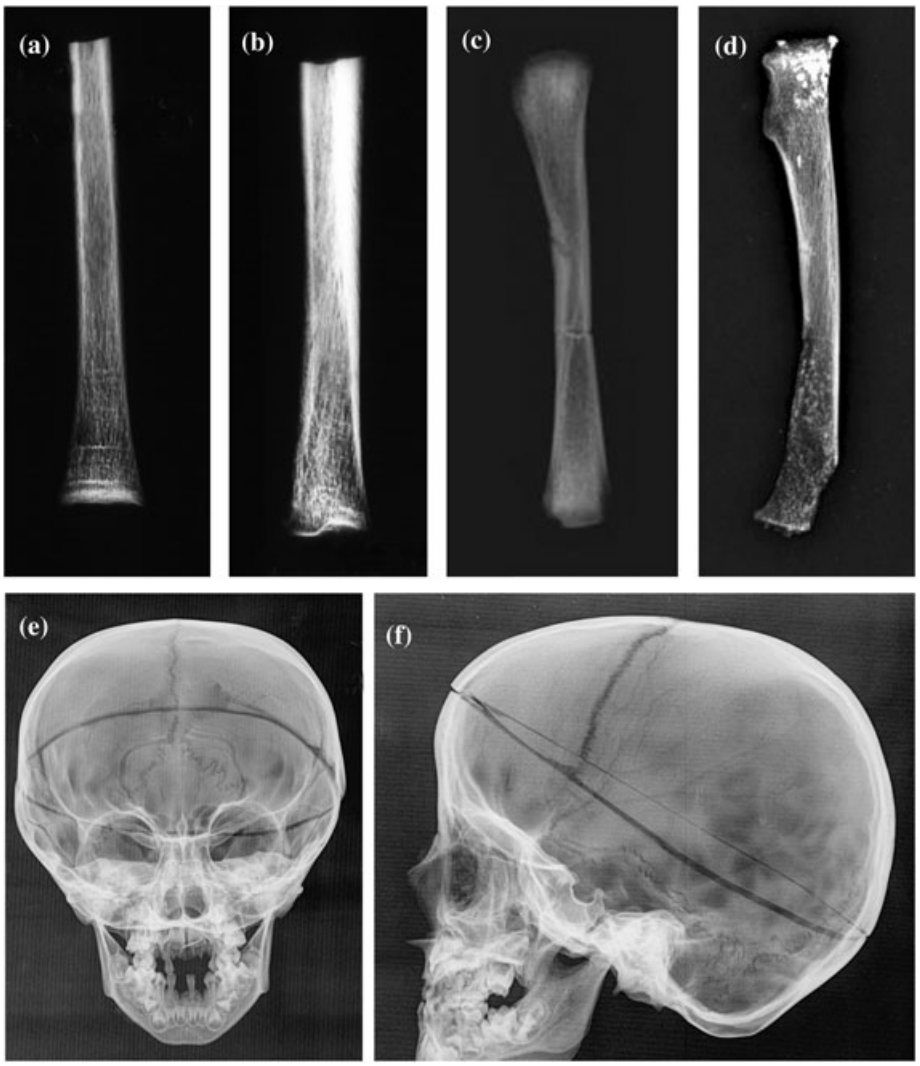

Figure 7. Antero-posterior X-ray projection with mammograph of a portion of right fibula of Med 40.2 (a); AP projection with mammograph of a portion of the left fibula of Med 40.39 (b); AP projection with mammograph of the right tibia of Med 40.45 (c); AP projection with mammograph of the left femur of Med 40.9 (d); Med 40.39: antero-posterior X-ray projection of the skull (e); latero-lateral X-ray projection of the skull (f).

No dental anomalies nor apposition of new bone on anterior surface of tibiae was observed in the Medici children remains. In addition, syphilis was a well-known disease in the 16th and 17th centuries, and no reports are documented on its presence among the women of the family.

As concerns the two newborns, another condition needs to be considered, namely infantile cortical hyperostosis or Caffey's disease (Waldron, 2009). Diffused periosteal new bone formation and cortical thickening are hallmarks of Caffey's disease, but this is a rare self-limiting inflammatory disease, which has a current clinical incidence of 3:1000 infants younger than 6 months of age in the USA and good outcome with spontaneous resolution (Kamoun-Golrat & Le Merrer, 2008). A prenatal form of Caffey's disease is also described; this is a rare disorder with high mortality rate due to prematurity and lung hypoplasia. However, in prenatal Caffey's disease, the periosteal reaction involves the entire length of long bone diaphyses (Hochwald & Osiovich, 2011), whereas in the two Medici newborns, the periosteal new bone affected only the epiphyseal and metaphyseal regions.

As a final consideration, several studies recommend caution in interpreting periosteal new bone production, in particular in infants younger than 2 years of age, because it can be a manifestation of normal bone growth and not the component of a pathological process (Ribot & Roberts, 1996; Weston, 2012); however, as most of the Medici children exhibited long bone

Table 3. $\delta^{15}N$ and $\delta^{13}C$ values in the Medici family

Sample	Age at death	$\delta^{15}N$	$\delta^{13}C$
Med 3	18	11.25	−18.3
Med 4	15	11.56	−18.16
Med 5	40	12.02	−17.9
Med 6	55	11.50	−17.80
Med 8	31	11.75	−18.82
Med 10	15	12.00	−18.2
Med 11	46	12.10	−18.70
Med 12	60	11.85	−18.47
Med 13	20	12.25	−17.85
Med 21	71	12.37	−17.50
Med 29	71	12.22	−18.20
Med 9	1	13.75	−18.19
Med 40.2	4	14.78	−17.95
Med 40.31	0.8	11.45	−19.18
Med 40.34	0	14.3	−17.9
Med 40.39	5	13.9	−17.9
Med 40.40	2	16.5	−17.8
Med 40.42	1	16.6	−17.9
Med 40.45	0	14.8	−17.5
Med 40.48	0.8	16.6	−17.8

bowing, in these cases, periosteal new bone production could not be considered part of the normal growth processes.

As a matter of fact, in the case of the Medici children, periosteal new bone was present in almost all the infants, accompanied by other specific features; these features can be attributed to the same condition, identified with rickets. Brickley and Ives (2008, table 5.5) laid out the 'strongly diagnostic' and 'diagnostic' criteria for the macroscopic features of rickets; adopting these criteria, the evidence for vitamin D deficiency among these elite children is in some cases very strong, as in the case of Med 40.29/31; in other cases, it is relatively convincing, as for Med 22/42, 40.39, 40.40, 40.48 and 9, less convincing for Med 40.34 and 40.45, and inadequate for Med 40.2.

First of all, the children with features suggestive of rickets were affected by the active form of the disease, as the presence of cranial and post-cranial periosteal new bone suggests; the only exception is represented by Med 40.39, in which the absence of porosity on the cranial surface and its presence limited to the growth plates suggested that the disease was not more in the active phase and that therefore the child had recovered from rickets.

The Medici children affected by rickets were distributed in different ages, as reflected in the progression and location of the bone changes: Med 40.34 and Med 40.45 were newborns and showed lesions on the cranial vault, rib extremities and metaphyseal long bones, with no bending; as expected, the children in the age of crawling, such as Med 40.22/42, Med 40.29/31, Med 40.48 and Med 9, showed light bending of the arm bones, whereas the children who should have started walking, such as Med 40.29/31, Med 40.39, Med 40.40 and Med 9, also showed deformed leg bones.

Diagnosis of a metabolic disease linked to vitamin D deficiency would appear unexpected in children brought up at the court of a Renaissance high social class family, like the Medici of Florence; the causes of this pathology need to be investigated.

The presence of the disease in almost all the examined children belonging to the same cultural area leads to hypothesise nutritional and/or environmental factors at the origins of this pathology and rules out rarer conditions, which are present in adults, for example defects in the metabolism, such as longstanding renal failure, chronic acidosis, hepatic or pancreatic disease (Resnick & Niwayama, 1988). Analysis of the historical and social background is particularly helpful to understand the causes for the onset of the disease in this aristocratic group.

Sufficiency of vitamin D is especially critical during pregnancy and lactation (Kovacs, 2008). A mother with adequate vitamin D levels during pregnancy provides her newborn with sufficient vitamin D for 2–3 months after delivery. After that period, vitamin D decreases and has to be synthesised by the skin or introduced with the diet; in fact, the peak incidence of rickets occurs between 3 and 18 months of age. Although human milk is the best source of nutrition for infants, it has been largely demonstrated that maternal milk has low levels of vitamin D, insufficient to reach the recommended intake for children of 200 IU/day (Balasubramanian & Ganesh, 2008). Modern clinical studies prescribe a supplement of vitamin D for exclusively breastfed infants (Balasubramanian, 2011). Considering that these synthetic implementations were impossible in the past, all infants would have been at risk when sunlight exposure was inadequate and before the introduction of solid foods containing vitamin D.

During the Renaissance, a common opinion prescribed that children were not to be weaned before the second year of life; for this reason, among the elite classes, wet nursing was a very widespread practice. Furthermore, in Renaissance royal families, this custom allowed the queens and princesses to obtain new pregnancies and sons for political alliances. The Medici family chose the wet nurses among the servants of the house; the Medici princes were never weaned before the second year, and in most cases, even some months later, although starting from the eighth–ninth month of life, woman's milk was integrated with paps

(Acerboni, 1915–17). The composition of these paps remains unknown, but two centuries earlier, Aldobrandino from Siena suggested to prepare them with the soft parts of bread and apples (Morpugno, 1892); cereal and soup as first solid food are also mentioned (Alberti, 1969).

In a letter of 5 November 1542, Maria Salviati (1499–1543) suggested to Eleonora from Toledo (1522–1562) to wean her niece Maria (1540–1557), who was 2 years and 8 months old, considering that all the child's deciduous teeth had broken out and that it was an appropriate season for weaning. (Acerboni, 1915–17). On 16 May 1578, it was said that Don Filippino (Med 40.39), who was nearly 1 year old, 'sucks very well and is fine for the rest', confirming that the child was still being breastfed (Pieraccini, 1986). As a matter of fact, historical sources support the paleonutritional data, which demonstrated weaning around the second year of age. As suggested by the $\delta^{13}C$ values and by historical sources, the introduction of solid food can be hypothesised for some of these children. However, the introduction of paps made of food such as bread and apple or cereals during breastfeeding could not solve vitamin D deficiency, as plants are extremely poor sources of vitamin D and fruit contains no vitamin D (Zempleni, 2007).

Therefore, with this prolonged breast-feeding, vitamin D deficiency is highly expected to rise, in particular if the other main risk factor, inadequate sunlight exposition, is associated with this diet based on maternal milk. Two hours per week is the required minimum period of exposure to sunlight for infants if only the face is exposed (Specker *et al.*, 1985).

During the spring and summer months, infants were likely to be exposed to sufficient sunlight to prevent vitamin D deficiency, but during the colder winter months, they probably spent less time outdoors and were bundled in several layers of protective clothing, especially when they presented frequent health problems. For example, according to historical sources, Filippo was a weak and unhealthy child, suffering from recurrent illness episodes (Pieraccini, 1986) and likely to have been frequently kept indoors. Furthermore, in the Renaissance period, non-ambulant children were swaddled, leaving very little skin exposed. Finally, the Renaissance Medici residences were large palaces in which the opportunity of sunlight exposure was significantly reduced. In this perspective, the mediaeval cultural practices of swaddling and keeping infants indoors are likely to have been the primary source of vitamin D deficiency.

The presence of rickets was observed not only in the breastfed Medici children but also in the two newborns. Vitamin D status at birth is directly related to maternal vitamin D status. The only source of vitamin D available to the foetus was derived from the mother through the placenta. Advanced maternal osteomalacia and vitamin D deficiency result in congenital rickets of the newborn (Innes *et al.*, 2002; Anatoliotaki *et al.*, 2003). Congenital rickets caused by maternal D deficiency is similar to the vitamin D-deficient rickets observed in older children. Rickets may have been the cause of death for these children or, alternatively, may have contributed to complicating other problems present at birth.

Some considerations can also be made concerning vitamin D deficiency of the mother. Maternal low levels of vitamin D could depend on repeated pregnancies (Okonofua *et al.*, 1986). The women of the Medici family gave birth to several children: Eleonora of Toledo between 18 and 32 years of age had eleven children; Giovanna from Austria had five deliveries between the ages of 19 and 29 years, and died in delivery at 30 years; and Cristina from Lorraine had nine children, besides a miscarriage, between 25 and 39 years of age (Pieraccini, 1986). These multiple and close pregnancies probably depleted the vitamin D levels of these women.

In addition to this, heavy clothes and cosmetics on the face could prevent skin exposure to sunlight. During the Renaissance, wealthy and high social ranking women wore elaborate clothes of fine fabric, such as silk, brocade and velvet, which covered almost all the body. A pale ivory skin was considered a sign of health and elegance, which distinguished noblewomen from peasants engaged in field work. A white skin was highly desired so that women avoided exposure to sunlight and used white powder to achieve it; one of the most popular and well-known lightening creams was Venetian Ceruse, a white powder obtained by mixing vinegar with lead, which remained popular for about 300 years (Angeloglou, 1970; Ames-Lewis & Rogers, 1998). Heavy face make-up was also used to hide disease and illness. The use of powder and avoidance of the sun prevented the exposure of the sole areas of the body free from clothes, strongly limiting the vitamin D synthesis.

Skeletal signs of vitamin D deficiency are difficult to see in the adult skeleton, where bone changes take longer to be manifest than in juvenile subjects. Adult vitamin D deficiency results in a general weakening of the skeleton; bones become thinner and weaker, resulting in vertebral body compression and thoracic kyphosis. A recent study by Brickley *et al.* (2005) evidenced skeletal changes in the scapulae, vertebrae, ribs, sternum, pelvis and femurs. Nevertheless, macroscopic changes

cannot be considered pathognomonic to osteomalacia, and radiological investigation is necessary to help diagnosis (Kozlowski & Witas, 2012).

Eleonora and Cristina died long after their last pregnancy, and only the skeleton of Eleonora, with tibial flattening, witnesses the likelihood of past vitamin D deficiency (Fornaciari *et al.*, 2006, 2007). In any case, macroscopic and radiological examination of the skeletal remains of Eleonora, Giovanna and Cristina showed no signs of osteomalacia, even if these women probably experienced some form of mild rickets during childhood, as suggested by the slight curvature of the tibiae of Eleonora and the scoliosis of Giovanna and Cristina (Fornaciari *et al.*, 2006, 2007).

It is difficult to determine to what extent rickets may have played a role in the short life of the Medici children. Modern clinical studies attest that infants affected by rickets have difficulty in breathing and moving, and are therefore particularly susceptible to gastrointestinal infections, as well as respiratory infections, such as pneumonia (Pettifor, 2003). Although the lives of the members of the Medici family are well known from the extremely rich historical archives, unfortunately the information about some of the children is limited to the dates of birth and death so that it is impossible to ascertain the causes of death from historical sources.

Exceptions are represented by Don Pietro or Pedricco, son of Cosimo and Eleonora, identifiable with Med 40.29/31, Med 40.48 or Med 9, by Filippo, son of Ferdinando and Cristina, identifiable with Med 40.2, and by Don Filippino, identified with Med 40.39. Because Filippo (Med 40.2) was the only child with no significant signs of rickets and that Don Filippino had recovered from rickets, the discussion is limited to the case of Don Pedricco. We know that in March 1547, he experienced a slight fever with some pain, an indisposition that recurred at the beginning of June, when the child died suddenly and unexpectedly. Unfortunately, these symptoms cannot be referred to a specific disease, and therefore, the causes of death remain unknown.

Finally, the correlation between cultural practices and incidence of rickets has been evidenced in other modern and ancient populations. A high incidence of rickets has been observed in modern sunny countries, such as Iran and Israel, where the same cultural practices, that is avoidance of sunlight and prolonged breast-feeding, documented for the Renaissance Medici family, are diffused (Costeff & Breslaw, 1962; Salimpour, 1975).

As for ancient populations, the same epidemiological pattern appeared in ancient cases from Bahrain Island dating from 1000 BC to 250 AD, where there is a long history of cultural practices of this kind (Littleton, 1998). Recent studies carried out on skeletal series from the New World explicitly explored cultural factors linked to the onset of rickets. In the late prehistoric Arroyo Hondo population, the presence of rickets and osteomalacia was attributed to particular social customs in child rearing, such as prolonged exclusive breastfeeding, cloistering children indoors and minimised sun exposure (Palkovich, 2008; Stodder & Palkovich, 2012). In 19th century New York, where over 34% of the subadult tibiae excavated in the Spring Street Presbyterian Church showed signs of rickets, the factors contributing to the high frequency of rickets were identified in the urban industrial environment, likely to have limited exposure to sunlight, in the African ancestry (darkly pigmented skin absorbs low UVB levels) and in a poor diet (Ellis, 2010).

In European archaeological series, extensive studies on the incidence of rickets were reported for a mediaeval rural population from Wharram Percy, England (Ortner & Mays, 1998) and for a 19th century urban population from Birmingham, England (Mays *et al.*, 2006). The frequency of rickets at Wharram Percy is 2% among the 327 juveniles examined, with an age range for active cases of 3 months to 1.5 years and not severe changes. The Authors hypothesise that these infants were sickly and therefore might have led an indoor lifestyle, as in the case of Don Filippino. By contrast, the incidence of rickets was higher in the modern population of Birmingham, in which 13% of the 164 juvenile skeletons examined showed features of vitamin D deficiency, with an age range for active cases of 3 months to 4.5 years and more severe changes. In the crowded cities of the 19th century, sunlight often failed to penetrate the narrow houses, and air pollution by industrial processes lessened insolation, and therefore, a larger number of individuals may have been subject to exclusion from sunlight compared with mediaeval rural populations. In these studies, the contribution of diet to the onset of the diseases was not investigated.

In conclusion, the present study clearly demonstrates how, even in the high social classes, children were at the risk of developing rickets as a result of prolonged breast-feeding and inadequate exposure to sunlight. Integration of osteoarchaeological evidence with historical documentation has provided a relevant support to evaluate health conditions, dietary habits and cultural practices of this aristocratic group.

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Conflict of Interest

All authors declare no conflict of interest.

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