

# The Association Between Periodontal Disease and Periosteal Lesions in the St. Mary Graces Cemetery, London, England A.D. 1350–1538

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**ABSTRACT** Numerous studies have demonstrated significant associations between periodontal disease and many other diseases in living populations, and some studies have shown that individuals with periodontal disease are at elevated risks of mortality. Recent analysis of a medieval skeletal sample from London has also shown that periodontal disease was associated with increased risks of mortality in the past. This study examines whether periodontal disease is associated with periosteal lesions in a skeletal sample from the urban St. Mary Graces cemetery ( $n = 265$ ) from medieval London. The results reveal a significant association between

periodontal disease and periosteal lesions in the St. Mary Graces sample (i.e., individuals with periodontal disease were also likely to have periosteal lesions), and the association between the two is independent of age. The association between the two pathological conditions might reflect underlying reduced immune competence and thus heightened susceptibility to pathogens that cause periodontal disease or periosteal lesions, exposure to an environmental factor, or underlying heightened inflammatory responses. *Am J Phys Anthropol* 146:609–618, 2011. © 2011 Wiley Periodicals, Inc.

Periodontal disease is an infection that causes inflammation and destruction of gum tissue (gingiva), the periodontal ligament, root cementum, and alveolar bone, and can be caused by a variety of pathogenic infectious agents that are found in oral biofilms (dental plaque), including the bacteria *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Treponema denticola* and various herpes viruses (van Winkelhoff and Slots, 1999; Li et al., 2000; Slots, 2004). Periodontal disease is one of the most common chronic diseases in living populations (Abdellatif and Burt, 1987), with severe forms affecting an estimated 10–15% of people worldwide and mild forms of the disease affecting as much as 90% of people in some populations (Beck et al., 1996; Pihlstrom et al., 2005). Numerous bioarchaeological investigations have also identified periodontal disease at varying frequencies in skeletal samples from past populations (e.g., Clarke et al., 1986; Kerr, 1994; Chazel et al., 2005; Eshed et al., 2006; Oztunc et al., 2006; Palubeckaite et al., 2006; Lieverse et al., 2007).

Periodontal disease has repeatedly been found to be a risk factor for other diseases and is associated with increased risks of mortality. One study found that among adults in the United States, periodontal disease is associated with a 46% increased risk of all-cause mortality (DeStefano et al., 1993), and Garcia et al. (1998) found that severe periodontal disease is associated with a 1.85-fold increase in mortality. Many studies within living populations have shown significant associations between periodontal disease and other diseases, such as cardiovascular diseases, respiratory infections, cancer (e.g., lung, kidney, pancreatic, oral, esophageal, upper gastrointestinal, gastric, and kidney cancers), Alzheimer's disease, obesity, diabetes, renal disease, osteoporosis, and

rheumatoid arthritis (for example, see the following reviews: Hollister and Weintraub, 1993; Li et al., 2000; Kowolik et al., 2001; Slots, 2004; Pihlstrom et al., 2005; Johnson et al., 2006; Irwin et al., 2008; Williams et al., 2008). Periodontal disease is also associated with increased risks of spontaneous preterm birth, preeclampsia, low birth weight, and stillbirth (Holmstrup et al., 2003; Goepfert et al., 2004; Boggess, 2005; Boggess et al., 2006; Mobeen et al., 2008; Ruma et al., 2008; Polyzos et al., 2009).

The consistent significant association between periodontal disease and general health and mortality in living populations raises questions about how the two were associated in past populations. We recently addressed this issue by examining the relationship between periodontal disease and the risk of mortality in a medieval skeletal sample from the cemetery of St. Mary Graces in London (DeWitte and Bekvalac, 2010). The results of that previous study suggest that periodontal disease was associated with an elevated risk of mortality in the medi-

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TABLE 1. Frequencies of pathological conditions by age group

Age	Periodontal disease			Periosteal lesions		
	<i>n</i>	# with lesions	% with lesions	<i>n</i>	# with lesions	% with lesions
0–9.99	37	0	0	45	18	0.4
10–19.99	16	1	0.06	21	6	0.29
20–29.99	28	4	0.14	23	10	0.43
30–39.99	41	16	0.39	35	19	0.54
40–49.99	40	26	0.65	49	28	0.57
50+	25	9	0.36	31	14	0.45
Total	187	56	0.30	204	95	0.47

For each pathological condition, *n* = the number of individuals with a scoreable, relevant skeletal element.

eval population, as individuals with periodontal disease were at higher risks of mortality compared to their peers without it. No determination was made in that previous study of the systemic diseases or other physiological stressors with which the oral lesions were associated in the medieval population. To further our general understanding of how oral health and systemic health were associated in past populations, this study builds upon previous research by examining whether periodontal disease is significantly associated with periosteal lesions (i.e., periosteal new bone formation) in the St. Mary Graces cemetery from medieval London, England. To examine possible reasons for a relationship between the two pathological conditions, we also determine whether the two conditions were associated with physiological stress during development or with social status.

## MATERIALS AND METHODS

### Skeletal sample

**St. Mary Graces Cemetery.** The Cistercian Abbey of St. Mary Graces was established in London shortly after the first outbreak of the Black Death ended in London in 1350 and was in use until the Reformation in 1538 (Grainger and Hawkins, 1988; Grainger et al., 2008). While the Abbey of St. Mary Graces was active, members of the general population were interred in a cemetery associated with the Abbey, and monks and important lay people were buried within the Abbey's church and chapels; it is likely that lower status people were buried farther from the Abbey, and burials closer to the Abbey were for higher status individuals; those buried in the church and chapels were certainly high status, (Grainger and Hawkins, 1988; Rogers and Waldron, 2001; Grainger and Phillipotts, 2011). Excavation of St. Mary Graces in the 1980s by the Museum of London Archaeology Service revealed several hundred skeletons from within the Abbey church and chapels and from the larger lay cemetery (Grainger and Hawkins, 1988; Grainger and Phillipotts, 2011). The St. Mary Graces cemetery contains individuals of all ages, both sexes, and both higher and lower socioeconomic statuses and thus provides a good sample of the late medieval population of London.

This study uses a sample of 265 individuals from the St. Mary Graces cemetery. This sample includes all the excavated individuals from the cemetery who were preserved well enough to be scored for skeletal indicators of age and the presence of skeletal lesions, as described below.

TABLE 2. Contingency table for periodontal disease and periosteal lesions

Age		Periodontal disease	No periodontal disease
0–19.99	Periosteal lesions	0	8
	No periosteal lesions	1	26
20–39.99	Periosteal lesions	8	11
	No periosteal lesions	5	19
40+	Periosteal lesions	15	8
	No periosteal lesions	11	14

### Age estimation

Age estimates for subadults (i.e., individuals <18-years-old) were based on the diaphyseal lengths of major long bones (for fetal and neonatal remains between ages 10 and 50 gestational weeks), epiphyseal fusion, and dental development and eruption (Moorrees et al., 1969; Gustafson and Koch, 1974; Scheuer et al., 1980; Smith, 1991; Scheuer and Black, 2000). Estimates of adult ages (i.e., individuals 18 years or older) were based on tooth wear (Brothwell, 1981), and age-related changes of the pubic symphysis (Brooks and Suchey, 1990), iliac auricular surface (Lovejoy et al., 1985; Buckberry and Chamberlain, 2002), and sternal rib ends (Iscan et al., 1984, 1985). The age estimation methods used for this study yielded age-interval estimates. We only included in our analysis individuals for whom we could estimate age using one or more of the methods listed above. Given that not all individuals in the St. Mary Graces cemetery were equally well preserved, it was not possible to apply all aging methods to determine age for some individuals. Because of this, we used relatively broad age intervals for our analyses, as shown in Tables 1 and 2.

### Pathological conditions

**Periodontal disease.** As mentioned above, periodontal disease can result in the gradual destruction of periodontal tissues and alveolar bone (Irfan et al., 2001). Periodontal disease is often identified in skeletal material by the loss of alveolar bone that exposes the underlying trabecular bone and thereby produces porosity (Clarke and Hirsch, 1991; Larsen, 1997) or causes the alveolar crest (AC) to recede relative to the cemento-enamel junction (CEJ) of the associated dentition (Larsen, 1997). For this study, periodontal disease was scored as present if the alveolar bone displayed porosity (Ogden, 2008) or if the distance between the CEJ and AC was greater than 2 mm. An example of periodontal disease is shown in Figure 1. Only alveolar bone that had no postmortem damage and also lacked signs of periodontal disease was given a score of “no lesion,” alveolar bone that had no observable periodontal disease but which had surface area obliterated by postmortem damage was scored as “unobservable” with respect to periodontal disease. Although the alveolar bone surrounding each tooth was scored individually during data collection, the analyses presented here use pooled data for the left mandible to assess periodontal disease at a broader scale.

The use of the distance between the CEJ and the AC as a criterion for the presence of periodontal disease is potentially problematic, given that non-pathological processes associated with aging can increase the distance beyond 2 mm (Costa, 1982; Clarke et al., 1986; Clarke, 1990; Clarke and Hirsch, 1991; Hildebolt and Molnar,



**Fig. 1.** Example of periodontal disease on the right mandible. Destruction of cortical bone has exposed the underlying trabecular bone along the alveolar margin, producing a porous appearance (From DeWitte and Bekvalac, *Am J Phys Anthropol*, 2010, 142, 341-354, © Museum of London).

1991; Varrela et al., 1995; Hillson, 1996; Ogden, 2008). For example, the distance between the CEJ and AC can increase because the teeth continue to erupt throughout adulthood (i.e., super-eruption) without simultaneous growth of the alveolar crest (Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991). This super-eruption of teeth compensates for normal dental attrition that occurs with age and the effects of diet, and it maintains lower facial height and the occlusal level of teeth (Whitaker et al., 1990; Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991; Varrela et al., 1995; Ogden, 2008). Another nonpathological process that can increase the distance between the CEJ and AC is the continued growth of the facial skeleton in adulthood, which also results in continued eruption of the teeth to maintain dental occlusion (Clarke and Hirsch, 1991; Hildebolt and Molnar, 1991).

Because the distance between the CEJ and AC can occur without any pathological destruction of the alveolar bone, use of the "greater than 2 mm" criterion alone to diagnose periodontal disease can lead to the overestimation of the prevalence of periodontal disease in past populations. The inclusion of individuals who are false positives for periodontal disease is potentially problematic for this study, as it might result in a spurious association between the oral lesion and periosteal lesions. That is, some of the individuals in the samples used for these analyses scored as having both periosteal lesions and periodontal disease might not actually have had periodontal disease, and the estimated association between the two pathological conditions might therefore be stronger than is actually the case. Because the distance between the CEJ and AC can occur because of nonpathological processes that are primarily associated with aging, the individuals who are incorrectly diagnosed with periodontal disease on the basis of the CEJ-AC distance are most likely to be older adults. Therefore, age must be included in the analysis of the association between the two pathological conditions. If a significant association exists between periodontal disease and periosteal lesions, and that association is consistent across age groups (i.e., the association is not restricted to older

adults), we can be confident that the observed relationship is not simply the result of including false positives for periodontal disease in the sample.

Because the early stage of periodontal disease is not detectable in dry skulls (Strohm and Alt, 1998), it is possible that our sample includes false negatives for the oral pathological condition. The possible effect of the presence of such false negatives on the results of this study is described in the Discussion section.

**Periosteal lesions.** To investigate the association between periodontal disease and systemic health in the medieval population of London, we focus on periosteal lesions, which, like periodontal disease, frequently have an inflammatory or infectious etiology. An additional benefit of including periosteal lesions in this analysis is that such pathological conditions are common in bioarchaeological samples (Larsen, 1997), and we were able to obtain sample sizes of individuals with periosteal lesions that were large enough to test the association between the two pathological conditions.

Periosteal new bone formation occurs in response to stimuli that tear, stretch, or otherwise traumatize the periosteum and because of local or systemic infection or inflammation associated with a variety of factors (Walton and Rothwell, 1983; Larsen, 1997; Ortner, 2003; Weston, 2008). Periosteal lesions are often used by bioarchaeologists as nonspecific indicators of physiological stress (Larsen, 1997; Weston, 2008). Although it is possible, in some cases, to attribute periosteal lesions to specific diseases through careful differential diagnosis, we have not used that approach for this study. Our objective here is to establish whether periodontal disease was significantly associated with an extra-oral marker of health, rather than to evaluate the association between periodontal disease and any one particular cause of periosteal lesions in the medieval population of London.

For this study, periosteal lesions were scored on the tibia, because studies have demonstrated that the tibia is commonly affected by such lesions (Eisenberg, 1991; Milner, 1991; Larsen, 1997; Roberts and Manchester, 2005) and, because it is robust, the tibia is often well preserved in skeletal samples (Galloway et al., 1997; Waldron, 1997; Willey et al., 1997; Stojanowski et al., 2002). Only the anterior surface of the tibial diaphysis was assessed for periosteal lesions; neither the metaphyses nor the posterior diaphysis were scored as these surfaces have muscle markings that can interfere with the identification of lesions, particularly smaller, resorbed periosteal lesions. Periosteal lesions were identified macroscopically and scored as present if there was at least one distinct patch, of any size, of woven or sclerotic bone (or a combination of the two) laid down on the surface of the diaphysis. Examples of periosteal lesions are shown in Figures 2 and 3. Only tibiae with anterior diaphyseal surfaces that were free of both periosteal new bone growth and postmortem damage were scored as lacking periosteal lesions; tibiae with no visible lesions but with postmortem damage that prevented visual assessment of the anterior surface were given a score of "unobservable" with respect to periosteal lesions and thus excluded from our analyses. Both right and left tibiae, if present, were scored for periosteal lesions during data collection; however, only data from the left tibia were used in the analyses described here, as this maximized our sample size for analysis.



**Fig. 2.** Example of mild periosteal lesion on an adult tibia.



**Fig. 3.** Example of more severe periosteal lesions on an adult tibia.

**Indicators of childhood physiological stress.** To potentially explain any observable relationship between periodontal disease and periosteal lesions, we assessed how each of these conditions is associated with two indicators of childhood and adolescent exposure to physiological stress: enamel hypoplasia and adult femur length. Linear enamel hypoplasia is a tooth enamel defect caused by the disruption of enamel formation during childhood because of infection or malnutrition (Huss-Ashmore et al., 1982; Dahlberg, 1991; Roberts and Manchester, 2005). Linear enamel hypoplasias appear as horizontal lines of varying width on the surface of the affected tooth. For this study, linear enamel hypoplasias were identified macroscopically on the buccal surface of the mandibular canines, which have relatively long developmental time-spans (~ 10 years) and are highly sensitive to physiological stress (Goodman et al., 1980; Huss-Ashmore et al., 1982; Santos and Coimbra, 1999). Linear enamel hypoplasias were scored as “present” if one or more lesions on the surface of the tooth were palpable and were visible to the naked eye under good lighting.

Adult stature reflects, among other things, exposure to chronic stress during development (Haviland, 1967; Powell, 1988; Steckel, 1995; Roberts and Manchester, 2005). Children who are malnourished or fighting infection and disease must expend energy resources toward basic tissue maintenance and the immune response, diverting energy from growth and development to these essential metabolic functions. Therefore, short adult stature, relative to other individuals within the population, likely indicates poor health or poor nutrition during the developmental years. For our analyses, we used adult femur length as a proxy for stature. The maximum length of the femur was measured in centimeters using an osteometric board (Buikstra and Ubelaker, 1994).

### Statistical analyses

**Hierarchical log linear analysis.** The associations among periodontal disease, periosteal lesions, and age were evaluated using hierarchical log linear analysis with SPSS version 19. This approach was used because the data include both categorical (i.e., age-interval) and binary (i.e., presence/absence of pathological conditions) variables. Hierarchical log-linear analysis was used to test the significance of the three-way interaction among age, periodontal disease, and periosteal lesions, as well

as all other lower order interactions (e.g., the interaction between age and periodontal disease, and between age and periosteal lesions). Backwards elimination was used to remove nonsignificant interactions among variables with a statistical significance criterion of 0.05. Because hierarchical log-linear analysis allows for the evaluation of interactions between more than two variables, it is possible to determine whether a significant association between periodontal disease and periosteal lesions exists in the absence of age. In the event that a significant association is observed between the two conditions, this approach is informative about whether the relationship is consistent across all age groups or if it is dependent on age (Green, 1988).

Because of a lack of young children and adolescents with signs of periodontal disease in our sample, we collapsed age categories, as shown in Table 2, to minimize the number of cells with counts of less than five in our analysis.

**Binary logistic regression.** To assess the possible influence of childhood or adolescent physiological stress (i.e., malnutrition or disease) on the development of periodontal disease or periosteal lesions, we analyzed the relationship between adult femur length and each pathological condition, separately, using binary logistic regression with SPSS version 19. To avoid the potential confounder of sexual dimorphism, we analyzed the relationship between femur length and lesions separately for men and for women.

**Chi-square tests.** The effect of childhood/adolescent physiological stress on the development of periodontal disease or periosteal lesions was also assessed using a Chi-square test of the relationship between each of these pathological conditions and enamel hypoplasia.

Chi-square tests were also used to examine the relationship between social status and periodontal disease and periosteal lesions, as an association between these two pathological conditions might have resulted from an environmental factor, such as unsanitary conditions, exposure to which was mediated by socioeconomic status. For the Chi-square tests, we used burial location as a proxy for social status. Because the burials within the St. Mary Graces site generally lack grave goods and other artifacts that might be useful markers of status (as is typically true of many medieval Christian burials), the best information available about social status is bur-

TABLE 3. Results of the hierarchical log linear analysis of the interaction of age, periodontal disease, and periosteal lesions in St. Mary Graces

Interaction	Chi-square	P value
Age × Periodontal disease × Periosteal lesions	1.12 (df = 2)	0.572
Age × Periodontal disease	29.49 (df = 2)	<0.000
Age × Periosteal lesions	2.334 (df = 2)	0.311
Periodontal disease × Periosteal lesions	7.70 (df = 1)	0.006

TABLE 4. Results of binary logistic regression on femur length

	No Lesion	Lesion	OR (95% CI)	P	
Periodontal disease	Female	16 (76%)	5 (24%)	0.998 (0.952–1.046)	0.92
	Male	13 (43%)	17 (57%)	1.011 (0.978–1.046)	0.52
Periosteal lesions	Female	13 (43%)	17 (57%)	1.029 (0.983–1.077)	0.22
	Male	11 (32%)	23 (68%)	0.99 (0.958–1.024)	0.57

ial location within the site. As described above, people buried in the church and chapels were certainly high status, and burials close to the Abbey were likely also for higher status individuals; lower status people were buried farther from the Abbey. Therefore, for our Chi-square tests, we considered burials in and near the Abbey as “high status,” and burials located farthest from the Abbey as “lower status.” All Chi-square tests were performed using SPSS version 19.

**RESULTS**

**Periodontal disease and periosteal lesions**

The frequencies of periosteal lesions and periodontal disease, by age, in the St. Mary Graces sample are shown in Table 1, and Table 2 is the three-way contingency table for age group and the two pathological conditions. The results of the hierarchical log linear analysis are shown in Table 3. In the St. Mary Graces sample, the three-way interaction between age, periodontal disease, and periosteal lesions is not significant. However, significant associations exist between periodontal disease and periosteal lesions and between periodontal disease and age; assessment of the direction of the relationship based on binary logistic regression (results not shown) confirms that in each case the relationship is a significantly positive association. No significant relationships exist among any other combination of the three variables within the St. Mary Graces sample. These results indicate that the frequency of periodontal disease increased with age, and that independent of age, individuals in the St. Mary Graces population with periodontal disease were likely to also have periosteal lesions. Given the lack of a significant three-way interaction among age and the two pathological conditions, and the lack of a significant association between age and periosteal lesions, the positive association between periodontal disease and periosteal lesions is likely not an artifact of both pathological conditions being associated with age. These results also indicate that the association between periodontal disease and periosteal lesions is not likely the result simply of the inclusion of false positives for periodontal disease, most of which, if they are included in the sample, are likely to be contributed by older adults.

TABLE 5. Results of Chi-square analysis of the relationship between enamel hypoplasia (EH) and periodontal disease and periosteal lesions

	No EH	EH	Chi-Square results
No periodontal disease	68	26	$X^2 = 8.1$ ; df = 1; $P = 0.004$
Periodontal disease	27	28	
No periosteal lesions	40	17	$X^2 = 0.72$ ; df = 1; $P = 0.398$
Periosteal lesions	28	17	

TABLE 6. Results of Chi-square analysis of the relationship between burial location and periodontal disease and periosteal lesions

	High Status	Low Status	Chi-Square results
No periodontal disease	51	77	$X^2 = 1.12$ ; df = 1; $P = 0.29$
Periodontal disease	27	29	
No periosteal lesions	43	65	$X^2 = 1.17$ ; df = 1; $P = 0.28$
Periosteal lesions	45	50	

**Childhood physiological stress**

The results of binary logistic regression of each pathological condition on femur length are shown in Table 4. The results indicate that for both sexes there is no significant association between femur length and either of the two pathological conditions. The results of the Chi-square tests of the association between enamel hypoplasia (the frequency of which was 35.9%) and periodontal disease and periosteal lesions are shown in Table 5. The results indicate that enamel hypoplasia is significantly associated with periodontal disease but not with periosteal lesions in the St. Mary Graces sample.

**Burial location**

The results of the Chi-square tests of the associations between burial location (high status vs. lower status) and periodontal disease and periosteal lesions are shown in Table 6. The results indicate that there is no significant difference between burial locations in the frequency of either pathological condition.

**DISCUSSION**

The results of these analyses reveal that in the St. Mary Graces cemetery, periodontal disease is positively associated with age, which is not surprising given that in living populations, the prevalence of periodontal disease increases with age (Abdellatif and Burt, 1987). Several bioarchaeological investigations have also revealed increases in the frequency of periodontal disease with age in past populations (e.g., Costa, 1982; Kerr, 1991, 1994; Hillson, 1996; Oztunc et al., 2006). In some cases, the relationship between age and periodontal disease in modern populations is at least partly explained by behavioral factors, such as changes in oral hygiene or the increased use of medications that reduce salivary flow (Abdellatif and Burt, 1987; Sjögren and Nordström, 2000; Leal et al., 2010). However, some researchers have found that the significant relationship between age and periodontal disease persists when other factors, such as oral hygiene, are controlled for (Streckfus et al., 1999). Studies have yielded evidence that the increase in the prevalence of periodontal disease with age is related to age-related changes in inflammatory status (Benatti

et al., 2009; Liang et al., 2010). According to Benatti et al. (2009), periodontal disease and other age-associated diseases increase with age because of an underlying chronic inflammatory status; as people age, the accumulated effects of years of exposure to oral pathogens and their byproducts lead to elevated levels of proinflammatory cytokines, which are associated with periodontal tissue destruction, and the reduced production of anti-inflammatory cytokines in periodontal tissues. Regardless of the underlying reason, individuals in the St. Mary Graces population were more likely to suffer from periodontal disease as they aged.

The results of this study also indicate that in the St. Mary Graces sample, periodontal disease and periosteal lesions are significantly positively associated, and that the association between the two pathological conditions is not explained by age. As mentioned above, early stages of periodontal disease are not detectable in skeletal material (Strohm and Alt, 1998), so it is possible that our sample includes people who truly had periodontal disease but whom we failed to score as such. The possible presence of such false negatives for periodontal disease in our sample means that we might have underestimated the strength of the association between periodontal disease and periosteal lesions in medieval London. However, the possibility that the relationship between the two pathological conditions is stronger than indicated by the results in Table 1 does not affect the conclusions that we have drawn.

#### **Mechanisms linking periodontal disease to systemic health in living populations**

There are several mechanisms by which periodontal disease in living populations is thought to be associated with disease elsewhere in the body. The relationship between periodontal disease and several other diseases is explained by the direct spread of the infectious pathogens or components of pathogens (e.g., endotoxins and outer membrane proteins) from the oral cavity to other parts of the body where they cause infection or exacerbate disease processes (Li et al., 2000; Loos, 2005; Amabile et al., 2008). For example, oral pathogens can be aspirated from the mouth into the lungs and thereby cause respiratory infections (Scannapieco et al., 2003; Pan et al., 2009). Oral pathogens can also disseminate from the oral cavity and invade arterial walls and initiate or exacerbate the inflammatory response of atherosclerosis (Dorn et al., 2000; Demmer and Desvarieux, 2006). Periodontal pathogens have been found in coronary artery atherosclerotic plaques, which suggest that these pathogens, after disseminating from the mouth, played a direct role in the formation of such plaques (Pucar et al., 2007).

The association between periodontal disease and certain diseases might also reflect an underlying impaired immune system. In the case of periodontal disease and certain associated cancers, for example, such an impaired immune system can neither efficiently fight infection nor monitor and control tumor growth (Michaud et al., 2008).

Lastly, associations between periodontal disease and other diseases in living populations can exist because the body responds to the presence of bacteria and bacterial antigens in the oral cavity and in the bloodstream through the production of proinflammatory immune cytokines, such as interleukin-1 (IL-1) and tumor necro-

sis factor- $\alpha$  (TNF- $\alpha$ ), which can have systemic or distant effects (Loos, 2005; Moutsopoulos and Madianos, 2006; Spahr et al., 2006). These effects include causing or accelerating atherogenesis (the formation of plaques within arteries) and thus contributing to cardiovascular disease (Amabile et al., 2008; Kamer et al., 2008; Watts et al., 2008), affecting cell growth control and leading to carcinogenesis (Meyer et al., 2008), or priming microglial cells and other factors associated with Alzheimer's disease pathology (Watts et al., 2008).

Several researchers have hypothesized that both the severity of periodontal disease and the association between the oral disease and other diseases in the body are the result of an underlying hyperinflammatory trait, that is, the excessive production of inflammatory mediators and systemic markers of inflammation in response to stimuli (Beck et al., 1996; Genco et al., 2005; Moutsopoulos and Madianos, 2006; Shaddox et al., 2010; Trombone et al., 2010). Beck et al. (1996), for example, hypothesize that the association between periodontal disease and cardiovascular disease occurs because individuals with a hyperinflammatory trait secrete abnormally high levels of inflammatory cytokines, which elevates their risks of both periodontal and cardiovascular disease. This hyperinflammatory trait might be at least partly the result of polymorphisms in genes for inflammatory cytokines, which result in exaggerated inflammatory responses to infection (Beck et al., 1996; Kornman et al., 1999; Moutsopoulos and Madianos, 2006; Sasaki et al., 2008; Watts et al., 2008; Trombone et al., 2009; Shaddox et al., 2010). The hyperinflammatory trait might also be the result of epi-genetic events, such as hypermethylation and hypomethylation of cytokine genes, which result in over-transcription of those genes (Gomez et al., 2009).

#### **Association between periodontal disease and periosteal lesions in medieval London**

Of the various mechanisms explaining the relationships between periodontal disease and other diseases in living populations, which most likely accounts for the association between periodontal disease and periosteal lesions in medieval London? There is currently no clinical evidence to suggest that the two pathological conditions are significantly associated in the St. Mary Graces cemetery because of the spread of infection from the mouth to the tibia. Numerous cases of oral infections causing, or at least preceding (and therefore strongly suspected of causing), infections elsewhere in the body have been documented in living populations (e.g., Kao and Wang, 1992; Van den Bossche et al., 1993; Caruso et al., 2006; Rallis et al., 2006). However, it is not clear that periodontal pathogens cause periosteal new bone growth elsewhere in the body. In fact, studies of the effect of periodontal pathogens on osteogenesis demonstrate that such pathogens actually inhibit growth of bone and induce osteoclastogenesis (Loomer et al., 1995; Jiang et al., 2002). The destruction of bone in the mouth is part of the inflammatory response to the presence of periodontal pathogens and functions to create additional space to accommodate immune defense cells (Preshaw et al., 2004).

Rather than reflecting direct spread of infection from the mouth, the two pathological conditions might have been significantly associated in the medieval population of London because they both reflect an underlying sus-

ceptibility to infection. As described above, periodontal disease is an infection caused by a variety of pathogens. Some researchers have argued that the risk of developing periodontal disease is higher in individuals with reduced immunocompetence (Tolo, 1991; Boyd and Madden, 2003), and studies have shown that the severity of periodontal disease increases in people with immune systems compromised by such factors as HIV infection or chemotherapy for treatment of cancer (Beck et al., 1996). Though it can be caused by a variety of factors that affect the periosteum, periosteal lesions can, like periodontal disease, have an infectious etiology. For example, infectious diseases such as tuberculosis, treponemal infections, and leprosy can cause periosteal lesions, and such lesions can also occur as a result of the spread of a localized infection of nearby soft tissue to the underlying bone (Larsen, 1997; Weston, 2008). Periodontal disease and periosteal lesions both might have been more likely to occur in people in the medieval population of London who had reduced immunocompetence for a variety of reasons (e.g., malnutrition or genetic factors), and thus heightened susceptibility to pathogens that can cause either periodontal disease or infections sufficient to induce periosteal new bone formation.

To explore the role of immune competence in the development of both pathological conditions, we examined other skeletal conditions that are often attributed to childhood/adolescent episodes of malnutrition or disease, as malnutrition can result in reduced immune competence and disease can both be the cause of or result from reduced immune competence. To determine whether a history of physiological stress was associated with periodontal disease and periosteal lesions, we assessed the relationship between the two pathological conditions and enamel hypoplasia and adult femur length (as a proxy for stature). The results of binary logistic regression of periodontal disease and periosteal lesions on femur length suggest that the lesions are not significantly associated with adult height for either sex. These results might indicate that periodontal disease and periosteal lesions were not strongly associated with childhood and adolescent nutritional status or disease, as measured by adult stature. However, it is also possible that femur length is an imperfect proxy for adult stature, and thus the relationships between the two pathological conditions and adult stature warrant further investigation using better measures of stature.

Over one third of the individuals in our sample had mandibular enamel hypoplasia, which suggests that physiological stress because of malnutrition or disease during childhood was common in this population. The results of our analyses of the relationship between enamel hypoplasia and the two pathological conditions indicate that enamel hypoplasia is significantly associated with periodontal disease but not with periosteal lesions in the St. Mary Graces sample. These results suggest that physiological stress caused by malnutrition or disease that was sufficient to result in enamel hypoplasia might also have been a contributing factor to, or reflect an underlying risk factor in common with, periodontal disease. However, these results do not support such childhood stressors as a cause of the observed association between periodontal disease and periosteal lesions.

Rather than (or in addition to) reflecting immune competence, the association between periodontal disease and periosteal lesions in St. Mary Graces might reflect

heightened inflammatory responses or a hyperinflammatory trait. Periodontal disease is caused by infectious pathogens, but the destruction of oral tissues that characterizes the disease is the result of a persistent inflammatory response, rather than the infection itself (Moutsopoulos and Madianos, 2006). As mentioned above, the development and severity of periodontal disease, and the association between it and other diseases may be determined by the elevated production of proinflammatory cytokines (Beck et al., 1996; Beck and Offenbacher, 2005; Genco et al., 2005). Proinflammatory cytokines also play a role in the proliferation of bone in response to stimuli such as trauma. For example, IL-1 $\beta$  and TNF- $\alpha$  and  $\beta$  are likely involved in bony callus formation following fracture, as they stimulate human osteoblastic proliferation and the production of mineralized bone matrix (Frost et al., 1997; Lange et al., 2010). Many proinflammatory mediators are potent vasodilators (DeFranco et al., 2007), and damage to tissues can cause an acute inflammatory response, including increased blood flow at the site of trauma that results in periosteal hyperplasia and thus new bone formation, even in the absence of fracture and when the periosteum itself remains intact, (Walton and Rothwell, 1983). Perhaps, compared to people with normal inflammatory responses, individuals with heightened responses in the medieval population of London were more likely to develop both new periosteal bone in response to trauma and periodontal disease when challenged with periodontal pathogens.

It is also possible that the association between the two pathological conditions was the result of an environmental factor, such as unsanitary living conditions, exposure to which increased the chances of developing both lesions and was mediated by social status. Our analysis of the relationship between burial location within St. Mary Graces (as a proxy for social status) and each pathological condition revealed that for both lesions there was no significant difference in lesion frequency between burial locations. This may mean that there really was no significant difference in the frequency of these pathological conditions between high and low status individuals and thus no significant difference between the two groups in exposure to a contributing factor. However, it is also possible that burial location is not an ideal proxy for social status. Furthermore, social status is not the only thing that could have affected an individual's exposure to environmental factors that might have affected risks of developing periodontal disease and periosteal lesions. Therefore, the results of our analysis of burial location are not sufficient to support or to rule out an environmental factor as contributing to both pathological conditions.

## CONCLUSION

The results of this study demonstrate the existence of a significant positive association between periodontal disease and periosteal new bone formation in the St. Mary Graces sample from medieval London. The association between the two pathological conditions is not explained by age, and might reflect underlying susceptibilities to infection, heightened proinflammatory responses, or some, as yet unidentified environmental factor. As mentioned above, we used periosteal lesions as a general indicator of infection or inflammation, rather than attempting to evaluate the association between periodontal disease and any one particular cause of peri-

osteal lesions in the medieval population of London. However, given the results of this study, it may prove fruitful, with larger sample sizes than those used here, to diagnose specific conditions associated with periosteal lesions and thereby establish the existence of statistically significant relationships between periodontal disease and specific diseases in past populations.

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