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Preterm low birth weight and periodontal disease among African Americans

Ananda P. Dasanayake, BDS, MPH, PhD[a,*], Shirley Russell, PhD[b], Doryck Boyd, DDS, MS[c], Phoebus N. Madianos, DDS, PhD[d], Teri Forster, DDS[c], Ed Hill, MD[c]

[a]*Department of Epidemiology and Health Promotion, New York University College of Dentistry, 345 East 24th Street, New York, NY 10010, USA*
[b]*Department of Microbiology, Meharry Medical College, 1005 DB Todd Boulevard, Nashville, TN 37208, USA*
[c]*Department of Stomatology, Meharry Medical College School of Dentistry, 1005 DB Todd Boulevard, Nashville, TN 37208, USA*
[d]*University of North Carolina in Chapel Hill School of Dentistry, CB# 7455, Research Building, Chapel Hill, NC 27514, USA*

Preterm delivery (PTD) and low birth weight (LBW), defined as delivery before 37 weeks of gestation and birth weight less than 2500 g, are major public health problems in the world. Infant mortality and morbidity sharply increases as birth weight decreases [1]. LBW babies are about 20 times, and very LBW babies (< 1500 g) are about 80 times more likely to die before their first birthday, and yet the incidence of LBW has been increasing in the United States [2]. The infant mortality rate among non-Hispanic blacks is two times higher than that of non-Hispanic whites [3]. Nearly two thirds of this racial disparity is attributable to a higher rate of PTD among blacks [4], which is two times higher compared with whites [5]. Similarly, the incidence of LBW is 2.4 times higher, and the incidence of very LBW is three times higher among blacks compared to whites [6].

Because there is evidence that LBW, PTD, and infant mortality are higher among blacks, risk factors for preterm LBW (PLBW) among black women that are amenable to prevention must be sought. Oral health of the

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* Corresponding author.
E-mail address: AD75@nyu.edu. (A.P. Dasanayake).

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pregnant woman is one such factor. Offenbacher et al [7] argued that about 25% of PLBW deliveries occur without any suspected risk factors, and bacterial endotoxins related to periodontal infections and maternally produced inflammatory mediators might be related to this unexplained portion of PLBW. Using 93 PLBW cases and 31 controls, they demonstrated that women with extensive and severe periodontal disease were seven to eight times more likely to give birth to PLBW infants. These authors concluded that about 18% of PLBW cases might be attributable to periodontal disease.

In a subsequent matched case-control study, Dasanayake [8] confirmed this finding by showing that healthy periodontal status of the pregnant woman reduces her risk for giving birth to an LBW infant. Offenbacher and colleagues [9] further demonstrated that there is a dose–response relationship between increasing gingival crevicular fluid (GCF)—prostaglandin E_2 (PGE_2) levels (as a marker of current periodontal disease activity) and decreasing birth weight. Levels of four periodontal organisms found in mature plaque (*Bacteroides forsythus, Porphyromonas gingivalis, Actinobacillus actinomycetecomitans, and Treponema denticola*) also were found to be higher among women who delivered PLBW infants. They failed, however, to observe a statistically significant difference in the clinical measurement of periodontal disease between cases and controls, perhaps due to the small sample size (N = 48). In a subsequent prospective study of 814 participants, Offenbacher et al [10] provided further evidence to show that antepartum maternal periodontal disease and disease progression during pregnancy are significant determinants of PTD, low birth weight, and low weight for gestational age.

Jeffcoat and co-workers [11] showed that pregnant women with severe or generalized periodontal disease at 21 to 24 weeks of gestation had higher odds for PTD (odds ratio [OR] = 4.45; 95% confidence interval [CI] = 2.16–9.18). These odds increased in a dose–response fashion as the length of gestation decreased; OR = 5.28 (95% CI = 2.05–13.60) before 35 weeks of gestation and OR = 7.07 (95% CI = 1.70–27.4) before 32 weeks of gestation. In a randomized clinical trial performed in Santiago, Chile, Lopez and co-workers [12] showed that women who were treated for marginal periodontitis before the 28th week of pregnancy (N = 163) had a lower rate of PLBW (1.84%) compared with a group of women who were treated after delivery (N = 188; PLBW rate = 10.11%; $P = 0.002$).

Other reports on this association are not always consistent with the findings of the above studies. In a smaller cohort study, Mitchell-Lewis and colleagues [13] failed to observe any differences in clinical periodontal status between PLBW cases and women with normal birth outcomes. PLBW women had significantly higher levels of *B forsythus* and *Campylobacter rectus*, however, and consistently elevated counts of the other periodontal pathogens. In this study, PLBW occurred in 18.9% of the women who did not receive periodontal intervention compared with 13.5% of those who received such therapy [13]. The East London study of Davenport et al [14,15]

also failed to show a significant independent association between LBW and periodontal disease in an urban London population of Bangladeshi origin.

Interestingly, there are more review articles [16–38] on this association than original study reports that include a position paper [39]. According to these reviews, intra-amniotic levels of PGE_2 and tumor necrosis factor (TNF)-α rise steadily throughout pregnancy until a critical threshold is reached to induce labor, cervical dilation, and delivery. These molecules are also produced within the diseased periodontium and can escape into the general circulation together with other lipopolysaccharides, peptidoglycan fragments, and hydrolytic enzymes. One argument is that if the latter factors cross the placental barrier, they can augment the physiologic levels of PGE_2 and TNF-α in the amniotic fluid and induce premature labor [26]. Kornman and Loesche [40] have shown that the ratio of anaerobic Gram-negative bacterial species to aerobic species increases in the dental plaque during the second trimester of pregnancy. If lipopolysaccharides derived from these organisms gain access to the placenta, they could stimulate interleukin-1β and PGE_2 production in the chorioamniotic and trophoblastic cells, a process that is associated with preterm labor. Hence, it is conceivable that the inflamed periodontium can act as an endocrinelike source of potentially deleterious cytokines and lipid mediators. More recently, as alternative hypotheses of seeding of placental tissues with orally derived bacteria, and an acute-phase response secondary to severe periodontal disease have been proposed by some investigators [41,42].

Although the observed association between maternal periodontal disease and PLBW is biologically plausible as discussed earlier, there are considerable limitations within the previous studies. These include the small sample sizes, retrospective assessment of the periodontal status, and insufficient control for key confounding variables such as the socioeconomic status (SES). We conducted a prospective follow-up study among a group of predominantly African–American individuals while taking the potential confounding factors into account. This study [43] is described below with the written permission from the *Journal of Periodontology*.

Materials and methods

The study methods are described in detail in the previously published article [43]. Study participants were 448 women recruited during the second trimester of their first pregnancy from two study centers, University of Alabama at Birmingham (UAB) and Meharry Medical College (MMC) in Nashville, Tennessee. Initial oral examination data; questionnaire data on behavioral risk factors such as smoking, alcohol, and drug use; and blood and saliva samples were obtained at the second trimester prenatal clinic visit. Pregnancy outcome data were gathered using medical records.

The MMC School of Dentistry study participants were recruited from the OB/GYN clinic. Data comparable with the UAB cohort were collected from

these participants. Periodontal Screening and Recording (PSR) was used to reflect the clinical periodontal status of the participants. The MMC examiner who performed the oral examinations was trained and calibrated against the UAB examiner prior to data collection.

From the 39 LBW cases that emerged from the follow-up study, we excluded full-term deliveries, those with missing second trimester serum samples, and those who had elective preterm deliveries. The resulting 17 spontaneous PLBW cases were compared with 63 controls that were randomly selected from women who delivered normal birth weight (NBW) infants and who also had a second trimester serum sample (nested case–control approach) using logistic regression analyses.

The primary exposure variable was the periodontal pathogen specific IgG levels measured in the second trimester maternal serum samples. Serum samples were shipped to the University of North Carolina in Chapel Hill laboratory to be analyzed using the checkerboard immunoblotting assay [44]. The IgG levels were measured against *P gingivalis, Prevotella intermedia, Prevotella nigrescens, Prevotella melaninogenica, B forsythus, T denticola, A actinomycetemcomitans, Fusobacterium nucleatum, C rectus, Eikenella corrodens, Peptostreptococcus micros, Capnocytophaga ochracea, Eubacterium nodatum, Selenomonas noxia, Streptococcus intermedius, Streptococcus oralis, Streptococcus sanguis,* and *Veillonella parvula.*

UAB and MMC Institutional Review Boards for human participants approved the study protocol, and the study was in accordance with the Helsinki declaration of 1975, as revised in 1983.

Sample size and power

A study with 17 LBW cases and 63 NBW controls has a power of 93% to yield statistically significant results at 5% level of significance if we assume that the mean difference in *P gingivalis*-specific serum IgG levels is 44.0 μg/mL (corresponding to means of 58.0 versus 14.0) and the common within-group standard deviation is 46.3 (based on standard deviation estimates of 82.0 and 31.0, respectively).

Statistical analyses

Data were analyzed using the *t* test, Wilcoxon Rank Sum test, Fisher's exact test, and linear and logistic regression analysis (treating birth weight as a continuous or a discrete variable). The selected measure of the association was the OR. This measure indicates the odds of giving birth to PLBW infants among participants who are exposed (ie, high serum immunoglobulin) compared who those who are not exposed. The cutoff point for the determination of the exposure status was based on the median (0 μg/mL) or the 75th percentile value (10.25 μg/mL) of the distribution of the IgG levels in the control group. The fit of the multivariable model was tested

using the "lack fit" option in SAS based on the Hosmer and Lemeshow technique [45]. For all statistical tests, two-sided type 1 error probability less than or equal to 5% was considered as the level of significance.

Results

The overall rate of PLBW in this cohort was 87 cases per 10^3 live births. When the level of IgG against *P gingivalis* above the median value was considered as the exposure, the rate of PLBW among exposed IgG above median was significantly higher (three times) than that of the unexposed IgG below median (rate of PLBW among exposed = 342 per 10^3 live births; unexposed = 111 per 10^3 live births).

Table 1 indicates the distribution of the key variables between the two groups. As expected, the PLBW group had significantly lower birth weight and gestational age. Although the other variables showed no statistically significant differences, perhaps due to the small study size, women in the PLBW group were slightly older. The PSR values, a crude measure of clinical periodontal status, failed to demonstrate differences in the clinical disease between PLBW and NBW women. Although both groups were predominantly African American, the PLBW group had about 15% more African-Americans compared with the NBW group.

Fig. 1 indicates the mean IgG levels against four periodontal pathogens that are associated with mature and undisturbed plaque and progressing periodontal disease. The PLBW group had significantly higher IgG levels against *P gingivalis* Although not statistically significant, IgG against *B forsythus* and *T denticola* was in the same direction and was approaching statistical significance (Wilcoxon Rank Sum test). Of the 18 species tested, higher IgG levels in the PLBW group were also observed against *C ochracea, P intermedia, P nigrescens, S noxia, F nucleatum,* and *V parvula,* but the differences failed to demonstrate statistical significance (data not shown).

Table 1
Characteristics of the study subjects

Variable mean (SD)	Normal birth weight (n = 63)	Low birth rate (n = 17)	*P*
Birth weight: g	3179 (441)	2157 (356)	<0.0001
Gestational age: weeks	39.1 (1.9)	36.2 (3.3)	<0.0003
Age: years	21.3 (4.3)	22.0 (6.4)	NS
Height: cm	160.8 (7.4)	163.2 (8.3)	NS
Periodontal Screening and Recording	1.6 (0.8)	1.6 (0.5)	NS
Race: % black	73	88	NS
Smoking: % yes	6.3	14.5	NS
Alcohol: % yes	1.6	0	NS

Adapted from Dasanayake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. J Periodontol 2001;72:1493.

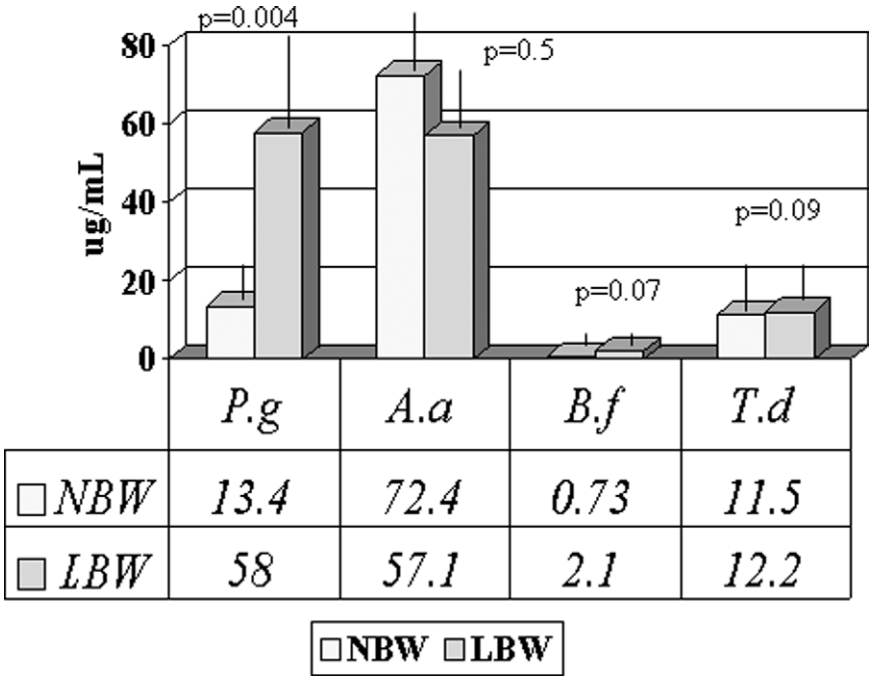

Fig 1. Mean maternal serum IgG levels against selected periodontal pathogens participants. *P.g*, *Porphyromonas gingivalis*; *A.a*, *Actinobacillus actinomycetemcomitans*; *B.f, Bacteroides forsythus*; *T.d*, *Treponema denticola*; NBW, normal birth weight; LBW, low birth weight. *P* values are based on the Wilcoxon Rank Sum Test. (*Adapted from* Dasanayake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. J Periodontol 2001;72:1493.)

Table 2 shows the strength of the association between the IgG levels against *P gingivalis* and PLBW. When the IgG levels were dichotomized by using either the median value of the distribution or the 75th percentile value, those women who had higher levels of IgG against *P gingivalis* had nearly four times higher odds of giving birth to a PLBW infant at the $P < 0.05$ level. It should be noted, however, that a more conservative *P* value of 0.0125 (0.05/4) could be considered, to adjust for the comparisons of the four hypothesized pathogens.

The results of the multiple logistic regression analyses are shown in Table 3. The full model that included the IgG levels against the four organisms, age, race, and smoking yielded a Hosmer and Lemeshow Goodness-of-Fit chi-square value with 8 *df* of 4.8, indicating that the model fit the data well ($P = 0.78$). In this model, IgG levels against *P gingivalis* yielded a unit OR (increasing odds per one-unit increase of IgG against *P gingivalis*) of 1.02 (95% CI = 1.01–1.04). When the stepwise procedure was used with 0.3 significance level as the criterion for entry and staying in the model, *P gingivalis, B forsythus*, age, and race remained in the final model, while the

Table 2
Strength of the association between *Porphyromonas gingivalis*, specific IgG levels and low birth weight

IgG (against *P gingivalis*)	Low birth weight	Normal birth weight	Odds ratio	95% Confidence interval
Median				
Above	12	23	4.1	1.3–12.8
Below	5	40		
75th percentile				
Above	8	12	3.8	1.2–11.6
Below	9	51		

Adapted from Dasanyake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. J Periodontol 2001;72:1494.

IgG levels against *P gingivalis* still showed statistical significance at the ≤ 0.05 level.

When birthweight was treated as a continuous variable rather than a binary outcome variable, there was a 3.7-gm decrease in birthweight for one-unit increase in IgG levels against *P gingivalis* when controlling for the same covariates.

Discussion

In our study, the incidence of LBW was 87.1 per 1000 live births. This is lower than what is reported in the literature [6]. This discrepancy is due to our selection of only first-time pregnancies.

Women with higher second trimester levels of serum IgG against *P gingivalis* (above the median) had four times higher odds of giving birth to

Table 3
Predictors of low birth weight multiple logistic regression: full model[a]

Variable	Odds ratio[b]	95% Confidence interval
Porphyromonas gingivalis[c]	1.02	1.01–1.04
Bacteroides forsythus[c]	1.15	0.96–1.38
Actinobacillus actinomycetemcomitans	1.0	0.99–1.01
Treponema denticola	0.99	0.95–1.02
Age[c]	1.12	0.97–1.29
Race: (black versus others)[c]	2.85	0.34–20.99
Smoking: (yes versus no)	1.81	0.19–17.67

[a] Hosmer and Lemeshow Goodness-of-Fit χ^2 (8) = 4.8; $P = 0.78$.
[b] Unit odds ratio for continuous variables.
[c] Final model.

Adapted from Dasanayake AP, Boyd D, Madiaons PN, Offenbacher S, Hills E. The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. J Periodontol 2001;72:1494.

a PLBW infant compared with those women who had lower IgG levels. The strength of the association observed was lower than what was reported by Offenbacher et al [7] for extensive and severe periodontal disease and LBW (OR = 7–8), but closer to what was reported in the Lopez et al [12] study (OR for marginal periodontitis compared with treated periodontitis = 4.7, 95% CI = 1.7–18.2). Our ability to demonstrate a significant difference in serum IgG levels against at least one periodontal pathogen (*P gingivalis*) is consistent with the concept that PLBW women have had a considerable exposure to periodontal pathogens and is consistent with the earlier findings of higher levels of "red cluster" organisms in PLBW women [9]. This notion is also consistent with the results of the Mitchell-Lewis et al [13] study, which indicated a significantly higher level of *C rectus* among PLBW women.

In a larger cohort study, however, Madianos et al [46] demonstrated that the postpartum prevalence of selected periodontal pathogens is similar among women who delivered term and preterm infants. Furthermore, in contrast to what we observed, lack of maternal IgG aganst "red cluster" organisms (that include *P gingivalis*) in their study was associated with an increased rate of prematurity (OR = 2.2; 95% CI = 1.48–3.79). They argue that this is consistent with the concept that maternal antibodies protect the fetus from exposure and resultant prematurity. They also observed a high prevalence of elevated fetal IgM to *C rectus* among premature infants and argue that *C rectus* may serve as a primary fetal infectious agent in eliciting prematurity [46]. In our study, however, there were no differences in *C rectus*-specific IgG in maternal serum between PLBW and NBW groups. These contrasting results among studies warrant further investigation on this association.

The finding that serum antibody levels against periodontal pathogens during the second trimester of pregnancy are related to the birth weight of the infant also lends credibility to the temporal sequence of this association. Unlike the previous case–control studies in which the putative "exposure" (perio status) was measured after the occurrence of the outcome (postpartum), in this longitudinal study we were able to show that mid-trimester maternal IgG against *P gingivalis* can increase the risk for LBW. Although we did not find differences in periodontal status using the PSR score, the elevated maternal serum IgG is consistent with a higher maternal exposure to periodontal pathogens. Craig et al [47] have shown that the mean serum IgG antibody to *P gingivalis* was higher in African Americans, and they also had greater mean probing depth, attachment loss, and number of missing teeth. Colombo and colleagues [48] have also shown that the participants with periodontal disease exhibit higher levels of serum antibodies against a wide range of subgingival bacterial species than do successfully treated or periodontally healthy participants. Ebersole [49] has reviewed the utility of higher serum IgG levels against *P gingivalis(B gingivalis)* as related to periodontal disease status.

Among the strengths of this study are the measurement of the exposure variable prior to the onset of the "disease" or PLBW, thus allowing for evaluation of the temporal sequence between exposure and disease of interest. The use of predominantly African American low-income inner-city women, who can be viewed as a socioeconomically homogenous group, minimizes the possible confounding of this association due to SES. Exclusion of women with previous pregnancies and those who had elective PTD due to maternal or fetal complications allowed for the evaluation of the hypothesis that periodontal infection may be related to spontaneous PTD among those who were not subjected to previous pregnancy-related risk factors. Finally, the evaluation of the exposure variable by an independent laboratory that was blind to the birth-weight status of the participant further minimized the potential information bias.

Small study size, the lack of a good clinical measurement of the periodontal disease status and other related measures such as cellular mediators and bacteriologic profiles, and the use of self-reported data on smoking and alcohol and drug use are among the limitations of the study. Although these data are preliminary at best and require cautious interpretation, they lend further credibility to the hypothesized association between periodontal disease and LBW.

In conclusion, in a prospective follow-up study among predominantly African American women who were pregnant for the first time, we were able to demonstrate that the second-trimester level of serum antibody against *P gingivalis* is related to PLBW. Before causal inferences can be made regarding the role of periodontal health of the pregnant woman in the incidence of PLBW, however, there is a continued need for further molecular epidemiological studies and randomized clinical trials.

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References

[1] Shapiro S, McCormick MC, Starfield BH, Krischer JP, Bross D. Relevance of correlates on infant deaths for significant morbidity at 1 year of age. Am J Obstet Gynecol 1980;136: 363–73.

[2] Centers for Disease Control. Increasing incidence of LBW—United States, 1981–1991. Morb Mortal Wkly Rep CDC Surveill Sum 1994;43(18):335–9.
[3] MacDorman MF, Atkinson JO. Infant mortality statistics from the period 1997 linked birth/infant death data set. Natl Vital Stat Rep 1999;47(23):1–23.
[4] Iyasu S, Becerra JE, Rowley DL, Hogue CJ. Impact of very LBW on the black–white infant mortality gap. Am J Prev Med 1992;8:271–7.
[5] Taylor D. State-specific changes in singleton pre-term births among black and white women—United States, 1990 and 1997. MMWR Morb Mortal Wkly Rep 2000;49(37): 837–40.
[6] Kleinman JC, Kessel SS. Racial differences in LBW. Trends and risk factors. N Engl J Med 1987;317(12):749–53.
[7] Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, et al. Periodontal infection as a possible risk factor for pre-term LBW. J Periodontol 1996;67:1103–13.
[8] Dasanayake AP. Poor periodontal health of the pregnant woman as a risk factor for LBW. Ann Periodontol 1998;3:206–12.
[9] Offenbacher S, Jared HL, O'Reilly PG, Wells SR, Salvi GE, Lawrence HP, et al. Potential pathogenic mechanisms of periodontitis-associated pregnancy complications. Ann Periodontol 1998;3:233–50.
[10] Offenbacher S, Lieff S, Boggeess KA, Murtha AP, Madianos PN, Champagne CM, et al. Maternal periodontistis and prematurity. Part I: obstetric outcome of prematurity and growth restriction. Ann Periodontol 2001;6(1):164–74.
[11] Jeffcoat MK, Geurs NC, Reddy MS, Cliver SP, Goldenerg RL, Hauth JC. Periodontal infection and preterm birth: results of a prospective study. J Am Dent Assoc 2001; 132(7):875–80.
[12] Lopez NJ, Smith P, Gutierrez J. Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized control trial. J Periodont 2002;73(8):911–24.
[13] Mitchell-Lewis D, Engebretson SP, Chen J, Lamster IB, Papapanou PN. Periodontal infections and pre-term birth: early findings from a cohort of young minority women in New York. Eur J Oral Sci 2001;109(1):34–9.
[14] Davenport ES, Williams CE, Sterne JA, Murad S, Sivapathasundram V, Curtis MA. Maternal periodontal disease and preterm low birth weight: case-control study. J Dent Res 2002;81(5):313–8.
[15] Davenport ES, Williams CECS, Sterne JAC, Sivapathasundaram V, Fearne JM, Curtis MA. The East London study of maternal chronic periodontal disease and pre-term LBW infants: study design and prevalence data. Ann Periodontol 1998;3:213–21.
[16] Bankey TA. Entering a new era: periodontics today and tomorrow. Ont Dent 1998;75(1):13–6.
[17] Baer PN. Caution is prudent when interpreting preliminary reports. Periodont Clin Invest 1997;19(2):4.
[18] Chen I. The Surgeon General's report on oral health: implications for research and education. N Y State Dent J 2000 Nov;(66):38–42.
[19] Cohen DW, Rose LF, Minsk L. Potential effects of oral infections on systemic health. Alpha Omegan 2001;94(1):24–31.
[20] Damare SM, Wells S, Offenbacher S. Eicosanoids in periodontal diseases: potential for systemic involvement. Adv Exp Med Biol 1997;433:23–35.
[21] DeBowes LJ. The effects of dental disease on systemic disease. Vet Clin North Am Small Anim Pract 1998;28(5):1057–62.
[22] Engebretson SP, Lalla E, Lamster IB. Periodontitis and systemic disease. N Y State Dent J 1999;65(8):30–2.
[23] Fowler EB, Breault LG, Cuenin MF. Periodontal disease and its association with systemic disease. Mil Med 2001;166(1):85–9.
[24] Hill GB. Preterm birth: associations with genital and possibly oral microflora. Ann Periodontol 1998;3(1):222–32.

[25] Li X, Kolltveit KM, Tronstad L, Olsen I. Systemic diseases caused by oral infection. Clin Microbiol Rev 2000;13(4):547–58.
[26] Loesche WJ. Association of the oral flora with important medical diseases. Curr Opin Periodontol 1997;4:21–8.
[27] MacNeill SR. Update in periodontology. J Ir Dent Assoc 1999;45(1):4–9.
[28] Mealey BL. Influence of periodontal infections on systemic health. Periodontol 2000;21: 197–209.
[29] Newman HN. Periodontal therapeutics–a viable option? Int Dent J 1998;48(3):173–9.
[30] Offenbacher S, Beck JD, Lieff S, Slade G. Role of periodontitis in systemic health: spontaneous preterm birth. J Dent Educ 1998;62(10):852–8.
[31] Offenbacher S. Saving more than smiles: a new frontier for dentistry. Northwest Dent 1998;77(1):21–5.
[32] Offenbacher S. The link between periodontal disease and systemic health: a scientific update. Interview by Phillip Bonner. Dent Today 1999;18(7):88–9.
[33] Ratcliff PA, O'Hehir T. A risk to expectant mothers? Rdh 1997;17(4):24–6.
[34] Rivera-Hidalgo F. Systemic disease and periodontal disease. Tex Dent J 2001;118(10):944–53.
[35] Slavkin HC. First encounters: transmission of infectious oral diseases from mother to child. J Am Dent Assoc 1997;128(6):773–8.
[36] Slots J, Kamma JJ. General health risk of periodontal disease. Int Dent J 2001;51(6):417–27.
[37] Williams CE, Davenport ES, Sterne JA, Sivapathasundaram V, Fearne JM, Curtis MA. Mechanisms of risk in preterm low-birthweight infants. Periodontol 2000;23:142–50.
[38] Zachariasen RD, Dennison DK. Periodontal disease and preterm low birth weight deliveries. J Gt Houst Dent Soc 1998;70(4):16–9.
[39] Scannapieco FA. Periodontal disease as a potential risk factor for systemic diseases. J Periodontol 1998;69:841–50.
[40] Kornman KS, Loesche WJ. The subgingival microbial flora during pregnancy. J Periodontal Res 1980;16:111–22.
[41] Offenbacher S, Lieffi S, Jared H, Madianos P, et al. Fetal exposure to maternal periodontal microbes is associated with fetal inflammatory stress and impaired growth [abstract 2540]. J Dent Res 2002;81(SI-A):A-320.
[42] Offenbacher S, Lieffi S, Jared H, Madianos P, et al. Maternal periodontal health impairs fetal growth [abstract 2541]. J Dent Res 2002;81(SI-A):A-320.
[43] Dasanayake AP, Boyd D, Madianos PN, Offenbacher S, Hills E. The association between *Porphyromonas gingivalis*-specific maternal serum IgG and low birth weight. J Periodontol 2001;72:1491–7.
[44] Sakellari D, Socransky SS, Dibart S, Taubman MA. Estimation of serum antibody to subgingival species using checkerboard immunoblotting. Oral Microbiol Immunol 1997;12:303–10.
[45] Hosmer DW, Lemeshow S. The importance of assessing the fit of logistic regression models: a case study. Am J Public Health 1991;81:1630–5.
[46] Madianos PN, Lieff S, Murtha AP, Boggeess KA, Auten RL, Beck JD, et al. Maternal periodontistis and prematurityPart II: maternal infection and fetal exposure. Ann Periodontol 2001;6(1):75–82.
[47] Craig RG, Boylan R, Yip J, Mijares D, Imam M, Socransky SS, Taubman MA, Haffajee AD. Serum IgG antibody response to periodontal pathogens in minority populations: relationship to periodontal disease status and progression. J Periodontal Res 2002;37(2):132–46.
[48] Colombo AP, Sakellar D, Haffajee AD, Tanner A, Cugini MA, Socransky SS. Serum antibodies reacting with subgingival species in refractory periodontitis participants. J Clin Periodontol 1998;25:596–604.
[49] Ebersole JL. Systemic humoral immune response in periodontal disease. Crit Rev Oral Biol Med 1990;4:283–331.