

# A possible association between preterm birth and early periodontitis

## Pilot study

Márta Radnai<sup>1</sup>, István Gorzó<sup>1</sup>,  
Erzsébet Nagy<sup>2</sup>, Edit Urbán<sup>2</sup>,  
Tibor Novák<sup>3</sup> and Attila Pál<sup>3</sup>

<sup>1</sup>Department of Dentistry and Oral Surgery,

<sup>2</sup>Institute of Clinical Microbiology and

<sup>3</sup>Department of Obstetrics and Gynaecology,  
Faculty of Medicine, University of Szeged,  
Szeged, Hungary

Radnai M, Gorzó I, Nagy E, Urbán E, Novák T, Pál A: A possible association between preterm birth and early periodontitis. Pilot study. J Clin Periodontol 2004; 31: 736–741. doi: 10.1111/j.1600-051X.2004.00564.x. © Blackwell Munksgaard, 2004.

### Abstract

According to many studies, generalised periodontitis can be a risk factor for preterm birth (PB). A case-control study was carried out to examine if early localised periodontitis could be a risk factor for adverse pregnancy outcome.

**Material and Methods:** Postpartum women without any systemic disease were included into the study. Similar numbers of patients belonged to the case (41) and to the control (44) groups. A PB case was defined if a patient had a threatening premature labour during pregnancy, preterm premature rupture of membranes, or spontaneous preterm labour, and/or the weight of the newborn was  $\leq 2499$  g. Control women had delivery after the 37th gestational week and the newborn's weight was  $\geq 2500$  g. Known risk factors like smoking, alcohol, drug consumption, socio-economic status and the periodontal status were recorded.

**Results:** A significant association was found between PB and early localised periodontitis of the patient with the following criterion having bleeding at  $\geq 50\%$  of the examined sites (6 at each tooth) and having at least at one site  $\geq 4$  mm probing depth ( $p = 0.001$ ). The odds ratio was 5.46 at the 95% confidence interval. The average weight of the newborns in the periodontitis group was less than in the control group, the difference is significant ( $p = 0.047$ ).

**Conclusion:** The results indicate that early localised periodontitis of the patient during pregnancy can be regarded as an important risk factor for PB.

Key words: adverse effects; newborn; periodontal disease; pregnancy; preterm birth; risk factors

Accepted for publication 14 November 2003

In Hungary, the number of live births per year is around 95,000, of which about 7500 (8.2%) are preterm deliveries. Preterm birth (PB) implies that delivery occurs before the 37th gestational week and is generally accompanied with a birth weight  $< 2500$  g. Prematurity is a great health problem even in economically developed countries. According to current knowledge, there are several risk factors for preterm low birth weight (PB), e.g. maternal age of  $< 17$  year, or  $> 35$  years, low socio-economic status, alcohol/drug abuse, smoking, multiple pregnancies, or the poor general health of the pregnant woman. These factors can be called “tra-

ditional risk factors” (Cohen et al. 2000) but, in about 25% of PB cases, these risk factors are absent (Gibbs et al. 1992).

The health problems of PB newborns can result in early death (Shapiro et al. 1980), or different illnesses such as asthma, upper and lower respiratory infections (Hack et al. 1983, McCormick et al. 1993) or congenital anomalies (Christianson et al. 1981). These children can have different degrees of neuromotor abnormality, cerebral palsy, behavioural problems (McCormick et al. 1990), or difficulties in learning, reading, spelling and mathematics (Ross et al. 1991). PB children become ill more readily than others and their

treatment can be more difficult. They also need special care, both from their family and society in general. Whilst every effort is made to decrease the number of PB newborns by diminishing the effects of all traditional risk factors and by clearing up new ones, until now many PB cases could be explained by known risk factors.

Galloway (cited by Offenbacher et al. 1996) was the first to suggest in 1931, that infection of the periodontium by Gram-negative anaerobic bacteria may “...provide sufficient infectious microbial challenge” to have “potentially harmful effects on the pregnant patient and developing fetus”. Since the 1990s,

several studies have found a relationship between preterm birth and periodontal disease, with many publications showing that the severe, generalised infection of the periodontium is a possible risk factor for PB (Hillier et al. 1993, Offenbacher et al. 1996, Hill 1998, Offenbacher et al. 1998b, Jeffcoat et al. 2001, Gibbs 2001, López et al. 2002a, b, Romero et al. 2002). However, others have not found such evidence (Mitchell-Lewis et al. 2001, Davenport et al. 2002, McGaw 2002). Because of the controversies raised, more case-control studies, or other types of examination, are necessary to find evidence for the hypothesis that periodontal infection during pregnancy can be an independent risk factor for PB.

The aim of the present study was to investigate if there was indeed an association between the periodontal status of pregnant women and PB in the southeast region of Hungary. The authors also wished to attempt to determine the most important signs of periodontitis, which might have the greatest influence, on both fetal development and time of delivery.

## Material and Methods

In total, 85 women were included in the cross-sectional study. All took part in the prenatal care programme provided by the Hungarian National Health Service, which generally begins before the 12th gestational week. The patients participating in the study were volunteers who had delivery in the University of Szeged, Department of Obstetrics and Gynecology. They were informed about the aim of the study and a detailed Ethics Committee approved Consent Form for dental, obstetrical and microbiological investigation was signed by them. Only systematically healthy women without any sign of inflammation were enrolled into the case-control study. For example patients with diabetes, asthma, cardiac problems, glomerulonephritis, hypothyroidism, ulcers, chronic infectious disease or multiple pregnancies were excluded. Patients who would require prophylactic antibiotics for dental treatment, and patients receiving antibiotics at the time of the dental examination were not included. However, those taking antibiotics for any reason, more than four weeks prior to examination, could participate. The examination was performed within 3 days post partum (Offenbacher et al.

1996) by the dentist member of the team, blind to case-control status.

All subjects had a record detailing personal data, marital status, medical and obstetrical history, as well as prenatal care. Before the dental examination, a questionnaire which included queries regarding the socio-economic status of both the patient and the father was completed by each subject. Adverse habits, e.g. smoking, alcohol/drug abuse, were also sought. Regarding smoking, alcohol/drug consumption, there was a choice between *Yes* or *No* answers; however, details regarding the quantities consumed (or their frequencies) were not pursued. The socio-economic status was assessed by the education level attained by both parents, i.e. primary school (8 years), technical school (3 years after primary school) grammar school (4 years after primary school), higher education (university or college), as well as the occupation of the patient and father (categorised as manual worker, intellectuals/professionals or 'other occupation').

The dental examinations were performed following WHO guidelines (Oral Health Surveys 1987) at the Department of Obstetrics and Gynecology, where the subjects were seated in a comfortable chair with a head support, and a dental light source was used. Third molar teeth were not included in the examination. A full periodontal status was taken, which included plaque index according to the criteria of Silness & Loe (1964) plaque index, recorded on a 0–3 scale on Ramfjord teeth, at four surfaces per tooth; the presence or absence of calculus (dichotomously); recession of buccal marginal gingivae (recorded in mm); tooth mobility using the Miller scale (Lindhe 1995); probing depth, and bleeding on probing (BOP) recorded dichotomously (Mitchell-Lewis et al. 2001). BOP was recorded positive if it occurred at any site of the tooth within 15 s after measuring the probing depth. To measure probing depth, a disposable periodontal probe was used with a tip diameter of 0.5 mm. The probing depths were not recorded at the third molars nor at retained roots, and were measured at six sites per tooth, i.e. mesiobuccal, mid-buccal, distobuccal, mesiolingual, mid-lingual and distolingual.

## Case definition

According to the WHO, premature delivery means that labour begins be-

fore gestational week 37. A patient was regarded as such a case if the newborn's weight was  $\leq 2499$  g, or she had spontaneous preterm labour, preterm premature rupture of membranes before the 37th gestational week. Patients, who had threatening preterm labour received special obstetric treatment to maintain their pregnancy as long as possible. As a result, labour could then be delayed until after week 37. In spite of this, women with a threatening premature labour during pregnancy were entered into the case group. Patients, who had delivery after week 37 without any problem, and had a newborn with a weight  $\geq 2500$  g, were allocated to the control group.

## Criteria of early localised periodontitis

A subject with periodontal disease (Armitage 1999, 2002) was categorised if she had  $\geq 4$  mm probing depth, 'critical probing depth' (Lindhe et al. 1982), at least at one site and bleeding on probing at  $\geq 50\%$  of the teeth. Subjects without these criteria were regarded as periodontally healthy.

## Statistical analysis

For the comparison of mean values, the *t*-test and one-way analysis of variance were used, as well as the Mann-Whitney and Kruskal-Wallis tests in case of non-normality. The normal distribution of samples was tested using the Kolmogorov-Smirnov test. The Spearman correlation coefficient was employed to assess correlations between continuous and ordinal variables. Categorical data were analysed using the chi-square and Fisher's Exact test. The multivariable dependence of the target variable on both categorical and continuous data were analysed using logistic regression with stepwise (forward) model selection based, on the likelihood ratio criterion ( $p_{in} = 0.05$ ,  $p_{out} = 0.10$ ).

## Results

Data for 85 subjects were analysed statistically, the cases numbering 41 (mean age 28.3 years, range 16.7–42.2 years), while there were 44 controls (mean age 27.6 years, range 18.3–39.2 years), with few differences between the groups. The age of the patients followed normal distribution and there was no significant difference between the mean ages ( $p = 0.589$ ).

Table 1. Education level and occupation of patients and fathers

|                                                            | Case<br>N = 41 | Control<br>N = 44 | All<br>N = 85 | $\chi^2$ test<br>p-value |
|------------------------------------------------------------|----------------|-------------------|---------------|--------------------------|
| Education level of patients                                |                |                   |               |                          |
| primary school (6–14 years of age)                         | 9 (64.3%)      | 5 (35.7%)         | 14            | 0.42                     |
| technical school (14–17 years of age)                      | 12 (54.5%)     | 10 (45.5%)        | 22            |                          |
| grammar school (14–18 years of age)                        | 12 (40.0%)     | 18 (60.0%)        | 30            |                          |
| higher education (university, college, tertiary education) | 8 (42.1%)      | 11 (57.9%)        | 19            |                          |
| Occupation of patients                                     |                |                   |               |                          |
| manual worker                                              | 14 (53.8%)     | 12 (46.2%)        | 26            | 0.68                     |
| intellectual                                               | 13 (41.9%)     | 18 (58.1%)        | 31            |                          |
| other                                                      | 14 (50.0%)     | 14 (50.0%)        | 28            |                          |
| Education level of fathers                                 |                |                   |               |                          |
| primary school                                             | 7 (87.5%)      | 1 (12.5%)         | 8             | 0.19                     |
| technical school                                           | 18 (48.6%)     | 19 (51.4%)        | 37            |                          |
| grammar school                                             | 9 (39.1%)      | 14 (60.9%)        | 23            |                          |
| higher education                                           | 6 (42.9%)      | 8 (57.1%)         | 14            |                          |
| no data                                                    | 1 (33.3%)      | 2 (66.7%)         | 3             |                          |
| Occupation of fathers                                      |                |                   |               |                          |
| manual worker                                              | 20 (46.5%)     | 23 (53.5%)        | 43            | 0.87                     |
| intellectual                                               | 10 (47.6%)     | 11 (52.4%)        | 21            |                          |
| other                                                      | 10 (55.6%)     | 8 (44.4%)         | 18            |                          |

Table 2. Incidence of smoking and alcohol consumption in the case and control groups

|         | Case<br>N = 41 | Control<br>N = 44 | All<br>N = 85 | Fisher's exact test<br>p-value |
|---------|----------------|-------------------|---------------|--------------------------------|
| Smoking |                |                   |               |                                |
| yes     | 7              | 0                 | 7             | 0.004**                        |
| no      | 34             | 44                | 78            |                                |
| Alcohol |                |                   |               |                                |
| yes     | 6              | 9                 | 15            | 0.575                          |
| no      | 35             | 35                | 70            |                                |

\*\*Significance level:  $p \leq 0.01$ .

The relationship between PB and socio-economic status was evaluated statistically, and in this some differences are evident. For example, PB is more frequent amongst women who were less educated and had lower social status, but the difference was insignificant. A similar conclusion can be drawn between the education level and occupation of fathers (Table 1). Logistic regression was conducted involving all the recorded risk factors for PB and periodontal status factors. None of the control group women smoked during pregnancy and only seven smoked in the case group (Table 2). The difference in the incidence of smokers and non-smokers between case and control group was significant ( $p = 0.004$ ). No subject admitted to consuming alcohol regularly (nor in excess), and there was no connection between PB and alcohol consumption ( $p = 0.575$ ). Also, no patient admitted to drug taking, either before or during pregnancy.

Oral-health-related factors were the presence of plaque, calculus, gingival recession, tooth mobility, periodontal pockets and bleeding on probing. The presence and amount of plaque is an indicator of the oral hygiene status, teeth without plaque being found in 34.3% in the study and 41.1% in the control group. The mean plaque index in the study group was 0.79 and 0.67 in the control group, the difference was not significant ( $p = 0.141$ ). Teeth with calculus occurred at 17.4% of study group and at 14.2% of control group. The difference was insignificant ( $p = 0.495$ ). Gingival recession and tooth mobility was found only in very few cases, and it was not possible to find a statistically significant difference between the groups.

Preliminary univariate analysis of the periodontal, and other risk factors, was undertaken using Fisher's Exact test. Data in Table 3 show the association between (a) the (PB) probing depth

$\geq 4$  mm at one site (4 mm) and (b) BOP at  $\geq 50\%$  of the teeth, both one by one and (c) their pairwise interactions. The Fisher's Exact test showed that bleeding on probing was the most important factor associated with preterm birth ( $p = 0.007$ ). When interactions between the signs of periodontitis pairwise were considered, the BOP and existence of at least one site with  $\geq 4$  mm probing depth had the strongest significance with adverse pregnancy outcome ( $p = 0.001$ ). Almost half of the women in the study group had early localised periodontitis, while only 11.4% of the control group suffered from it.

Because of the correlation between the periodontal risk factors, a multivariate analysis using logistic regression with stepwise model building procedure, based on the likelihood ratio selection criterion, was performed. The outcome of this method was a univariate model: only the interaction factor PB  $\geq 4$  mm and BOP contributed significantly to the prediction of preterm birth, the rest of the considered periodontal and other risk factors could not significantly improve the prediction rate. Smoking as a risk factor was not included in the logistic regression procedure, because of the absence of controls who smoked. The smoker cases (7) were left out from the calculation of the odds ratio (Table 4). Subjects with periodontitis had odds ratio of 5.460, taking BOP and the  $\geq 4$  mm probing depth as important signs of periodontitis. These women had  $5.46 \times$  greater odds of preterm delivery or low birth weight, than did periodontally healthy women.

In Table 5, details relating to the average weight of the neonates in the group of women with periodontal infection (i.e. with  $> 50\%$  bleeding, and one  $\geq 4$  mm probing depth) and in the group of periodontally healthy women are given. The minimum weight in the periodontitis group was only 1.050 g, but was significantly greater at 1.620 g in the group of periodontally healthy women ( $p = 0.047$ ), i.e. there was no birth weight under 1500 g in women with a healthy periodontium. A significant difference was found between the mean birth weight in the case and the control groups ( $p = 0.047$ ).

## Discussion

In agreement with other studies (Offenbacher et al. 1996, 1998b, Jeffcoat et al.

Table 3. Association analyses between the different signs of periodontitis and preterm birth one by one and pairwise

|            | Case<br>N = 41 (100%) | Control<br>N = 44 (100%) | Fisher's exact test<br>p-value |
|------------|-----------------------|--------------------------|--------------------------------|
| 4 mm       |                       |                          |                                |
| yes        | 22 (53.6%)            | 18 (4.9%)                | 0.281                          |
| no         | 19 (46.4%)            | 26 (59.1%)               |                                |
| BOP        |                       |                          |                                |
| yes        | 20 (48.8%)            | 9 (20.5%)                | 0.007**                        |
| no         | 21 (51.2%)            | 35 (79.5%)               |                                |
| 4 mm + BOP |                       |                          |                                |
| yes        | 19 (46.3%)            | 5 (11.4%)                | 0.001***                       |
| no         | 22 (53.7%)            | 39 (88.6%)               |                                |

4 mm = probing depth >4 mm at least at one site; BOP = bleeding on probing at >50% of the teeth.

\*\*Significance level:  $p \leq 0.01$ .

\*\*\*Significance level:  $p \leq 0.001$ .

Table 4. Result of the logistic regression analysis of odds ratio between PB and early localised periodontitis

| Variables in the model | Coefficient<br>B | Standard error | Wald-test<br>p | Odds ratio<br>$e^B$ | 95% confidence interval |
|------------------------|------------------|----------------|----------------|---------------------|-------------------------|
| 4 mm + BOP             | 1.6974           | 0.5891         | 0.0040         | 5.4600              | 1.7207 17.3244          |
| constant               | -0.6678          | 0.2750         | 0.0152         |                     | NA                      |

Overall prediction rate: 67.95%. Sensitivity: 41.18%. Specificity: 88.64%. NA = not available.

Table 5. The average weight of newborns of patients with and without periodontitis

| Periodontitis | N  | Mean (g) | SD    | Min  | Max  | t-test<br>p-value |
|---------------|----|----------|-------|------|------|-------------------|
| yes           | 24 | 2975.7   | 666.3 | 1050 | 3820 | 0.047*            |
| no            | 61 | 3274.4   | 579.7 | 1620 | 4370 |                   |

\*Significance level:  $p \leq 0.05$ .

2001) these data confirm an association, not only between moderate or severe chronic periodontitis, but also between early localised periodontitis of the patient during pregnancy, and preterm birth, as well as low birth-weight from the 85 women studied. Here, the numbers in case and control groups were almost equal, as were the average ages of participants. As was stated in the Material and Methods section, all pregnant women who had some known risk for preterm birth were excluded from the study, i.e. those examined were healthy, with no known risk for preterm delivery.

Among criteria used to determine periodontitis, clinical attachment loss (CAL) is often employed (Offenbacher et al. 1996, Jeffcoat et al. 2001), although here the state of the periodontium was characterised by probing depth and BOP. There were several reasons for taking this decision. Firstly, statistical analysis showed that the most important factors associated with preg-

nancy outcome were gingival bleeding and deep probing depth. Secondly, CAL as a criterion only shows that periodontal disease is present, but not necessarily in an active phase. Furthermore, the surface area of the gingiva, where bacteria or their products can invade/diffuse the tissues, is larger if the probing depth is greater, and is independent from CAL as it depends on the inner surface of the pocket. Hormonal changes due to increased level of estrogens and progesterone during pregnancy have a special effect on the periodontium (Löe & Silness 1963, Sooriyamoorthy & Gower 1989, Ojanotko-Harri et al. 1991, Raber-Durlacher et al. 1994, Salomon & Chung 1994), as vascular permeability increases in the gingival tissues and, as a consequence, bacteria and/or their products can diffuse through tissues more readily than normally (Lindhe & Bråne-mark 1967, Lindhe et al. 1968, Hugoson 1970). Thus our findings may be explained by the fact that bleeding on

probing had the strongest association with preterm birth. Such bleeding is present during the active phase of periodontitis, and means that the sulcar/pocket epithelium is no longer intact, being more permeable to LPS (lipopolysaccharide) and other bacterial products. In addition, if the 'wound' surface of the sulcus/pocket is calculated, an area around 50 cm<sup>2</sup> results (Offenbacher et al. 1998a), which permits bacterial product penetration into host tissues. Such bleeding is an important sign of gingival inflammation, and it was for this reason that probing depth and BOP were used to categorise periodontal status. This way a strong association was found between periodontal disease and PB in our study.

In the study of Jeffcoat et al. (2001), their association was examined at the level of generalised periodontitis, where 90 or more sites were found with attachment loss  $\geq 3$  mm in about 40% of all sites. In the current series,  $\geq 3$  mm probing depth maximum was recorded for 41.0% of sites in one case only. Generally this level was not seen at more than 20.0% of sites. A possible reason for the more healthy periodontal status of these Hungarian subjects may be due to the ethnic homogeneity of the sample, albeit different levels of education and socio-economic status were included in the current study groups. By contrast, in several of the above-cited studies, the examined populations were of Afro-American or Hispanic origins, often of low socio-economic status (Offenbacher et al. 1996, Dasayanake et al. 2001, López 2002b), usually having association with poor oral hygiene and periodontal conditions (Machuca et al. 1999, Yalcin et al. 2002).

There was also a significant association between the newborns' weight and the periodontitis. The mean weight of neonates was lower in the case group (2975.7 g) than in the control group (3274.4 g), in spite of the fact that pregnant women received special therapy in order to avoid the threatening preterm births (Table 5). This difference has also been shown elsewhere (Offenbacher et al. 2001).

Regarding smoking as a traditional risk factor for PB, statistical analysis showed a significant association between smoking and preterm labour, but in the present control group, no patient reported a smoking habit. Hence, this zero frequency prevented the inclusion of smoking in the logistic regression

analysis and, as a result, this series will be extended and re-analysed in the future.

The results of the current case-control study support the data of publications dealing with the possible association between periodontitis and PB. A case-control study of 124 pregnant or postpartum women was carried out by Offenbacher et al. (1996). Here, women with preterm or low birth weight newborns had significantly worse periodontal status than those with a healthy periodontium, and multivariate logistic regression modelling showed that periodontal disease was a significant risk factor for PB (odds ratio 7.9) and primiparus PB (odds ratio 7.5). The odds ratio in the present study was close to this value at 5.46 taking the criteria "bleeding on probing at  $\geq 50\%$  of the teeth" and the " $\geq 4$  mm probing depth at least at one site" as the indicators of early periodontitis. In a later paper from the same group dealing with results of a case-control study of 48 subjects, the data suggested a dose-response relationship for increasing GCF-PGE (gingival crevicular fluid-prostaglandin-E) as a marker of current periodontal disease activity and decreasing birth weight (Offenbacher et al. 1998b). A total number of 1313 pregnant women at 21–24 weeks' gestation were examined by Jeffcoat et al. (2001) in Alabama, when women with severe or generalised periodontitis had an adjusted odds ratio of 4.45 for preterm delivery.

More recently, López et al. (2002b) reported that probing depth was associated with both preterm birth and low birth-weight as independent risk factors. After studying the data of 329 delivered women' periodontal health status, López et al. (2002a) drew the conclusion that women with PB ( $N = 22$ ) had poorer periodontal status than women with normal birth weight newborns ( $N = 329$ ), and that periodontal therapy significantly reduced the risk of PB (López et al. 2002a).

## Conclusions

The results reported in this text provide additional evidence regarding the question as to whether periodontal infection, in terms of early localised periodontitis of the women during pregnancy, has an association with PB, given the above findings of poorer pregnancy outcome

and a decrease in foetal weight. However, further investigations are necessary to prove the casual association between prematurity and periodontal infection.

## Acknowledgments

This study was partly supported by project grant ETT (Scientific Research Fund in Hungary) 579/2000. The authors thank Dr. József Eller for his invaluable contribution to the statistical analyses.

## References

- Armitage, G. C. (1999) Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology* **4**, 1–6.
- Armitage, G. C. (2002) Classifying periodontal diseases – a long lasting dilemma. *Periodontology* **2000** **30**, 9–23.
- Christianson, R. E., van den Berg, B. J., Milkovich, L. & Oechsli, F. W. (1981) Incidence of congenital anomalies among white and black live births with long-term follow-up. *American Journal of Public Health* **71**, 1333–1341.
- Cohen, D. W., Friedman, L. & Shapiro, J. (2000) The periodontal-medical risk relationship. *Compendium* **19**, 11–24.
- Dasayanake, A. P., Boyd, D., Madianos, P. N., Offenbacher, S. & Hills, E. (2001) The association between *Porphyromonas gingivalis* – specific maternal serum IgG and low birth weight. *Journal of Periodontology* **72**, 1491–1497.
- Davenport, E. S., Williams, C. E. C. S., Sterne, J. C., Murad, S., Sivapathasundram, V. & Curtis, M. A. (2002) Maternal periodontal disease and preterm low birth weight: case-control study. *Journal of Dental Research* **81**, 313–318.
- Gibbs, R. S. (2001) The relationship between infections and adverse pregnancy outcomes. An overview. *Annals of Periodontology* **6**, 153–163.
- Gibbs, R. S., Romero, R., Hillier, S. L., Eschenbach, D. A. & Sweet, R. L. (1992) A review of premature birth and subclinical infections. *American Journal of Obstetrics and Gynecology* **166**, 1515–1528.
- Hack, M., Caron, B., Rivers, A. & Fanaroff, A. A. (1983) The very low birth weight infant: the broader spectrum of morbidity during infancy and early childhood. *Journal of Developmental and Behavioral Pediatrics* **4**, 243–249.
- Hill, G. B. (1998) Preterm birth: associations with genital and possibly oral microflora. *Annals of Periodontology* **3**, 222–232.
- Hillier, S. L., Witkin, S. S., Krohn, M. A., Watts, D. H., Kiviat, N. B. & Eschenbach, D. A. (1993) The relationship of amniotic fluid cytokines and preterm delivery, amniotic fluid infection, histologic chorioamnionitis, and chorioamnion infection. *Obstetrics and Gynecology* **81**, 941–948.
- Hugoson, A. (1970) Gingival inflammation and female sex hormones: a clinical investigation of women and experimental studies in dogs. *Journal of Periodontal Researches Suppl* **5**, 1–18.
- Jeffcoat, M. K., Geurs, N. C., Reddy, M. S., Cliver, S. P., Goldenberg, R. L. & Hauth, J. C. (2001) Periodontal infection and preterm birth. Results of a prospective study. *Journal of the American Dental Association* **132**, 875–880.
- Lindhe, J. (1995) *Textbook of Clinical Periodontology*, 2nd edition, chapter 12, 317pp. Copenhagen: Munksgaard.
- Lindhe, J., Birch, J. & Brånemark, P.-I. (1968) Vascular proliferation in pseudopregnant rabbits. *Journal of Periodontal Research* **3**, 12–20.
- Lindhe, J. & Brånemark, P.-I. (1967) Changes in vascular permeability after local application of sex hormones. *Journal of Periodontal Research* **2**, 259–265.
- Lindhe, J., Socransky, S. S., Nyman, S., Haffajee, A. & Westfelt, E. (1982) "Critical probing depth" in periodontal therapy. *Journal of Clinical Periodontology* **9**, 323–336.
- López, N. J., Smith, P. C. & Gutierrez, J. (2002a) Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. *Journal of Periodontology* **73**, 911–924.
- López, N. J., Smith, P. C. & Gutierrez, J. (2002b) Higher risk of preterm birth and low birth weight in women with periodontal disease. *Journal of Dental Research* **81**, 58–63.
- Löe, H. & Silness, J. (1963) Periodontal disease in pregnancy I. Prevalence and severity. *Acta Odontologica Scandinavica* **21**, 533–551.
- Machuca, G., Khoshfeiz, O., Lacalle, J. R., Machuca, C. & Bullón, P. (1999) The influence of geneal health and socio-cultural variables on the periodontal condition of women. *Journal of Periodontology* **70**, 779–785.
- McCormick, M. C., Gortmaker, S. L. & Sobol, A. M. (1990) Very low birth weight children: behavior problems and school difficulty in a national sample. *Journal of Pediatrics* **117**, 687–693.
- McCormick, M. C., Workman-Daniels, K., Brooks-Gunn, J. & Peckham, G. J. (1993) Hospitalization of very low birth weight children at school age. *Journal of Pediatrics* **122**, 360–365.
- McGaw, T. (2002) Periodontal disease and preterm delivery of low-birth-weight newborns. *Journal of the Canadian Dental Association* **68**, 165–169.
- Mitchell-Lewis, D., Engebretson, S. P., Chen, J., Lamster, I. B. & Papapanou, P. N. (2001) Periodontal infections and pre-term birth: early findings from a cohort of young minority women in New York. *European Journal of Oral Sciences* **109**, 34–39.
- Offenbacher, S., Beck, J. D., Lieff, S. & Slade, G. (1998a) Role of periodontitis in systemic

- health: spontaneous preterm birth. *Journal of Dental Education* **62**, 852–858.
- Offenbacher, S., Jared, H. L., O'Reilly, P. G., Wells, S. R., Salvi, G. E., Lawrence, H. P., Socransky, S. S. & Beck, J. D. (1998b) Potential pathogenic mechanisms of periodontitis-associated pregnancy complications. *Annals of Periodontology* **3**, 233–250.
- Offenbacher, S., Katz, V., Fertik, G., Collins, J., Boyd, D., Maynor, G., McKaig, R. & Beck, J. (1996) Periodontal infection as a possible risk factor for preterm low birth weight. *Journal of Periodontology* **67**, 1103–1113.
- Offenbacher, S., Lieff, S., Boggess, K. A., Murtha, A. P., Madianos, P. N., Champagne, C. M. E., McKaig, R. G., Jared, H. L., Mauriello, S. M., Auten, R. L. Jr, Herbert, W. N. P. & Beck, J. D. (2001) Maternal periodontitis and prematurity. Part I: Obstetric outcome of prematurity and growth restriction. *Annals of Periodontology* **6**, 164–174.
- Ojanotko-Harri, A. O., Harri, M.-P., Hurttia, H. M. & Sewón, L. A. (1991) Altered tissue metabolism of progesterone in pregnancy gingivitis and granuloma. *Journal of Clinical Periodontology* **18**, 262–266.
- Oral Health Surveys (1987) *Basic Methods*, 3rd edition, pp. 19–21. Geneva: WHO.
- Raber-Durlacher, J. E., van Steenberghe, T. J. M., van der Velden, U., de Graaff, J. & Abraham-Inpijn, L. (1994) Experimental gingivitis during pregnancy and post-partum: clinical, endocrinological, and microbiological aspects. *Journal of Clinical Periodontology* **21**, 549–558.
- Romero, B. C., Chiquito, C. S., Elejalde, L. E. & Bernardoni, C. B. (2002) Relationship between periodontal disease in pregnant women and the nutritional condition of their newborns. *Journal of Periodontology* **73**, 1177–1183.
- Ross, G., Lipper, E. G. & Auld, P. A. (1991) Educational status and school-related abilities of very low birth weight premature children. *Pediatrics* **88**, 1125–1134.
- Salomon, A. & Chung, K. M. (1994) Influence of hormonal variation on the periodontium in women. *Periodontology 2000* **6**, 79–87.
- Shapiro, S., McCormick, M. C., Starfield, B. H., Krischer, J. P. & Bross, D. (1980) Relevance of correlates of infant deaths for significant morbidity at 1 year of age. *American Journal of Obstetrics and Gynecology* **136**, 363–373.
- Silness, J. & Loe, H. (1964) Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavica* **22**, 121–135.
- Sooriyamoorthy, M. & Gower, D. B. (1989) Hormonal influences on gingival tissue: relationship to periodontal disease. *Journal of Clinical Periodontology* **16**, 201–208.
- Yalcin, F., Eskinazi, E., Soyuncu, M., Basgmez, C., Issever, H., Isik, G., Berber, L., Has, R., Sabuncu, H. & Onan, U. (2002) The effect of sociocultural status on periodontal conditions in pregnancy. *Journal of Periodontology* **73**, 178–182.

Address:  
 Dr M. Radnai  
 Department of Dentistry and Oral Surgery  
 Faculty of Medicine  
 University of Szeged  
 Szeged  
 Hungary  
 E-mail: radnai@stoma.szote.u-szeged.hu

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.