

The Oral and Systemic Impact of Third Molar Periodontal Pathology

Kevin L. Moss,* Adam D. Serlo, DMD, MD,†
Steven Offenbacher, DDS, PhD,‡ James D. Beck, PhD,§
Sally M. Mauriello, MEd, PhD,|| and
Raymond P. White, Jr, DDS, PhD¶

Purpose: Analyze in pregnant subjects the relationship between third molar periodontal pathology, and subjects' overall periodontal status. Assess also, the associations between postpartum periodontal status by jaw and a systemic impact, preterm birth, or elevated serum C-reactive protein (CRP).

Patients and Methods: Data were from an IRB-approved study, Oral Conditions and Pregnancy. In this clinical study, full-mouth periodontal examinations including third molars were conducted at greater than 24 weeks of pregnancy and again within 72 hours of delivery. For our analyses, mean periodontal probing depth (PD) by visible tooth and by jaw were calculated at enrollment and postpartum. Subjects were categorized by 3 broad levels of periodontal health, considered the primary outcome variable. The primary predictor variable for levels of periodontal health was the presence or absence of visible third molars. Mean periodontal probing depth in the mandible or maxilla at term was considered an indicator of a possible risk of systemic exposure, increasing the odds of preterm birth, less than 37 weeks gestation, or elevated serum CRP levels. Chi-square and *t* tests were used to determine statistical significance, .05. Significant predictor variables were included in multivariable models. Unconditional logistic multivariate models were used to derive odds ratios (OR) and 95% confidence intervals (CI).

Results: Data from examinations at enrollment and postpartum were available for 1,020 and 891 subjects, respectively. Visible third molars were detected in 405 subjects at enrollment and in 360 subjects at term. No subjects had third molars removed during the study. At enrollment and postpartum, subjects with visible third molars were significantly more likely to have moderate/severe periodontal disease, 23.5% versus 8.5%, and 18.3 versus 9.4%, respectively. Mean PD was significantly greater for maxillary and mandibular molars than for more anterior teeth, $P < .01$. In both jaws, mean PD tended to be progressively greater from first to third molars. No differences were found in mean PD by jaw. In subjects with visible third molars, adjusting for the severity of mandibular periodontal disease, the level of maxillary periodontal disease was significantly associated with preterm birth, $P < .01$, OR 2.6 (95% CI 1.1-6.8), or the upper quartile of serum CRP at term, at least 23.0 mg/L postpartum, $P = .05$, OR 2.5 (95% CI 1.2-5.1).

Conclusions: Subjects' detected levels of periodontal disease were greater at enrollment and postpartum if visible third molars were detected.

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Blakey et al have suggested that periodontal pathology in asymptomatic, young adult subjects originated in the third molar region.¹ If subjects had at least one periodontal probing depth (PD) greater than 4 mm in the third molar region, a higher proportion of sub-

jects were likely to have at least 1 PD greater than 4 mm in nonthird molars as compared with subjects with no periodontal involvement in the third molar region.² Periodontal progression in the third molar region, an increase in PD at least 2 mm over time, was

Received from the School of Dentistry, University of North Carolina, Chapel Hill, NC.

*Research Applications Specialist, Department of Dental Ecology.

†Senior Resident, Oral and Maxillofacial Surgery.

‡OraPharma Distinguished Professor, Department of Periodontology.

§Distinguished Kenan Professor, Department of Dental Ecology.

||Associate Professor, Department of Dental Ecology.

¶Dalton L. McMichael Distinguished Professor, Department of Oral and Maxillofacial Surgery.

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Address correspondence and reprint requests to Dr White: Department of Oral and Maxillofacial Surgery, School of Dentistry, University of North Carolina, CB 7450, Chapel Hill, NC 27599-7450; e-mail: ray_white@dentistry.unc.edu

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significantly more likely for these subjects if at least 1 third molar region PD greater than 4 mm was detected at baseline, or subject level "orange" and "red" cluster periodontal pathogens were detected at greater than 10^5 at enrollment.³

In an analysis of the incidence and progression of periodontal disease in subjects over the course of pregnancy in the Oral Conditions and Pregnancy Study (OCAP), Moss et al found that increased PD was more likely at the interproximal probing sites of molar teeth.⁴ For these same subjects, third molar periodontal pathology detected at enrollment, a PD greater than 4 mm, or the upper tertile of subjects with bleeding on probing around third molars increased the odds of periodontal disease progression throughout the mouth, at least 4 probing sites with increased PD greater than 2 mm with resulting PD greater than 4 mm.⁵

This study was designed to analyze the relationship over the course of pregnancy of periodontal pathology with visible third molars and subjects' overall periodontal status. In addition, we investigated the association between postpartum periodontal status by jaw in subjects with visible third molars as an indicator of a possible risk of systemic exposure, increasing the odds of preterm birth less than 37 weeks gestation or elevated serum C-reactive protein (CRP) levels at least 8 mg/L.

Patients and Methods

The Oral Conditions and Pregnancy Study (OCAP) was an Institutional Review Board-approved, longitudinal study of maternal oral health, with a focus on periodontal pathology as it related to a negative pregnancy outcome, preterm birth. Eligible patients had to be enrolled prior to 26 weeks gestation as confirmed by ultrasound. Patients with systemic illness that predisposed to periodontal disease, such as diabetes mellitus, or to preterm birth, such as chronic hypertension, were excluded. Patients who required antibiotic prophylaxis for periodontal examinations also were excluded.

Research dental hygienists were trained and calibrated annually for this trial. They conducted the periodontal examinations for OCAP at enrollment and postpartum within 72 hours of delivery. Data from full-mouth periodontal examinations, 6 probing sites for each tooth visible in the mouth including third molars, were used to determine periodontal status. Each PD detected with a UNC-15 probe was rounded to the lower whole mm.

For our analyses, subjects were categorized by 3 broad levels of periodontal health: health/disease absence, mild disease, and moderate/severe disease. Periodontal health was defined as no PD greater than

4 mm and no sites of PD 3 mm with bleeding on probing (BOP), mild disease at least 1 PD greater than 4 mm or at least 1 PD greater than 3 with BOP up to a maximum of 15 PD sites greater than 4 mm, and moderate/severe disease 15 or more PD sites greater than 4 mm.^{6,7}

In addition, mean PD by visible tooth and mean PD by jaw were calculated at enrollment and postpartum as measures of the level or severity of periodontal pathology. The methodology for data collection and management has been reported by Lieff et al and readers are referred to this publication for further details.⁶

The primary outcome variable for this study was subjects' 3-level periodontal status at enrollment and postpartum examinations. In addition, the relationship between the postpartum periodontal disease status in subjects with visible third molars by jaw and preterm birth less than 37 weeks gestational age or the upper quartile of levels of serum CRP at term were assessed.

The primary predictor variable for levels of periodontal health was the presence or absence of visible third molars at enrollment or postpartum examinations. The severity of periodontal disease by jaw in subjects with visible third molars, the mean PD by jaw, was considered as a possible systemic exposure, with increased risk of preterm birth (gestational age at delivery <37 weeks) or the upper quartile of serum CRP at term.

Covariates, other variables evaluated as possible predictors of the risks of more severe periodontal disease or preterm birth based on the findings from Offenbacher et al, were: maternal age, maternal weight, race/ethnicity, marital status, health insurance status, participation in the Women, Infants and Children Program (WIC) or food stamps program, previous preterm delivery, and smoking during the current pregnancy.⁷

Subject level and PD by visible tooth data sets were created. For predictor variables and covariates, χ^2 tests and *t* tests were used to determine statistical significance set at .05. Variables at enrollment and postpartum found to be significant on bivariate analysis were included in multivariable models. Unconditional logistic multivariate models were used to derive odds ratios (OR) and 95% confidence intervals (CI). Data were analyzed using SAS (version 9.1; SAS, Research Triangle Park, NC).

Results

Data from examinations at enrollment and postpartum were available for 1,020 and 891 subjects, respectively. Mean age for subjects at enrollment was 28.2 ± 6.6 years; 46% were African American and 48% Cau-

Table 1. DESCRIPTIVE ANALYSIS BY PERIODONTAL STATUS AT ENROLLMENT*

Variable	Antepartum Periodontal Status			P Value
	Healthy 285 (27.9%)	Mild 588 (57.7%)	Mod/Severe 147 (14.4%)	
African American	59 (12.5%)	305 (64.8%)	107 (22.7%)	<.0001
Caucasian	211 (43.3%)	247 (50.7%)	29 (6.0%)	
Other race	15 (24.2%)	36 (58.1%)	11 (17.7%)	
Maternal age (years, mean ± SD)	30.4 (6.3)	27.4 (6.5)	27.3 (6.3)	<.0001
Maternal weight (pounds, mean ± SD)	154.7 (40.7)	163.8 (45.1)	165.5 (41.4)	.005
Smoke at enrollment	19 (11.7%)	103 (63.6%)	40 (24.7%)	<.0001
Did not smoke	266 (31.0%)	485 (56.5%)	107 (12.5%)	
No alcohol	63 (37.1%)	84 (49.4%)	23 (13.5%)	
Alcohol	222 (26.1%)	504 (59.3%)	124 (14.6%)	.01
Married	209 (40.0%)	276 (52.8%)	38 (7.3%)	
Not married	76 (15.3%)	312 (62.8%)	109 (21.9%)	<.0001
WIC or food stamp eligibility	20 (10.9%)	108 (58.7%)	56 (30.4%)	<.0001
No WIC or food stamp eligibility	265 (31.7%)	480 (57.4%)	81 (10.9%)	
No medical insurance	76 (14.2%)	340 (63.4%)	120 (22.4%)	<.0001
Medical insurance	209 (43.2%)	248 (51.2%)	27 (5.6%)	
Previous preterm delivery	33 (19.8%)	100 (59.9%)	34 (20.4%)	.007
No previous preterm delivery	252 (29.5%)	488 (57.2%)	113 (13.3%)	
Have visible third molars	48 (11.9%)	262 (64.7%)	95 (23.5%)	<.0001
No third molars visible	237 (38.5%)	326 (53.0%)	52 (8.5%)	

*n = 1020 subjects; with visible third molars, n = 405.

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casian. Visible third molars were detected in 405 subjects at enrollment and in 360 subjects at term. No subjects had third molars removed during pregnancy. At enrollment, most subjects (57.7%) had mild periodontal disease (Table 1). Twice as many subjects (27.9%) were considered periodontally healthy as had moderate/severe periodontal disease (14.4%).

Subjects with visible third molars were significantly more likely to have moderate/severe periodontal disease at enrollment, 23.5% versus 8.5%, and less likely to be periodontally healthy, 11.9% versus 38.5%, *P* less than .0001 (Table 1). Being African American, smoking at enrollment, not married, WIC or food stamp eligible, not having medical insurance, and a previous preterm delivery also were significantly related to more severe periodontal disease. If third molars were visible, odds for more severe periodontal disease were more than double at enrollment, controlling for covariates that might also impact subjects' periodontal status, OR 2.4 (95% CI 1.8–3.2) (Table 2).

At the postpartum examination, half of the subjects were periodontally healthy, almost twice as many as those at enrollment (Table 3). However, the proportion of subjects with moderate/severe periodontal disease were only minimally lower just after delivery, 14.4% versus 13%. Subjects with visible third molars were significantly more likely to have moderate/severe periodontal disease postpartum, 18.3% versus 9.4%, and less likely to be periodontally healthy, 34.7% versus 60.6%, *P* less than .0001. If third molars were visible, odds for more severe periodontal dis-

ease were almost double at term, OR 1.7 (95% CI 1.3–2.3) (Table 4). Being African American, smoking while pregnant, not married, WIC or food stamp eligible, and not having medical insurance were also significantly related to more severe periodontal disease.

At both the enrollment and postpartum examinations, if third molars were visible, mean PD for non-third molars was significantly greater, *P* less than .001 (Figs 1, 2). At enrollment and postpartum, mean PD was significantly greater for maxillary and mandibular molars than for more anterior teeth, *P* less than .01 (Table 5, Fig 3). In both jaws, mean PD tended to be progressively greater from first to third molars. Differences between jaws in mean PD were minimal and

Table 2. ADJUSTED LOGISTIC REGRESSION MODEL FOR MORE SEVERE 3-LEVEL PERIODONTAL DISEASE AT ENROLLMENT*

Variable	Odds Ratio (95% CI)
Have third molars at enrollment	2.4 (1.8-3.2)
Non-Caucasian	2.2 (1.6-3.1)
Smoke at enrollment	1.7 (1.2-2.5)
WIC/food stamps	1.9 (1.3-2.7)
No insurance	2.3 (1.6-3.4)

Also adjusted for maternal age, maternal weight, marital status, alcohol use, previous preterm delivery in the same model.

Proportional odds assumption was not violated.

*n = 1020 subjects, 405 subjects had visible third molars.

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Table 3. DESCRIPTIVE ANALYSIS BY POSTPARTUM PERIODONTAL STATUS*

Variable	Postpartum Periodontal Status			P Value
	Healthy 447 (50.2%)	Mild 328 (36.8%)	Mod/Severe 116 (13.0%)	
African American	134 (32.8%)	191 (46.7%)	84 (20.5%)	<.0001
Caucasian	289 (66.4%)	117 (26.9%)	29 (6.7%)	
Other race	24 (5.1.1%)	20 (42.6%)	3 (6.4%)	
Smoke during pregnancy	47 (32.2%)	73 (50.0%)	26 (17.8%)	<.0001
Did not smoke	400 (53.7%)	255 (34.2%)	90 (12.1%)	
Alcohol	79 (53.4%)	54 (36.5%)	15 (10.1%)	
No alcohol	368 (49.5%)	274 (36.9%)	101 (13.6%)	.5
Not married	170 (39.6%)	184 (42.9%)	75 (17.5%)	<.0001
Married	277 (60.0%)	144 (31.2%)	41 (8.9%)	
WIC or food stamp eligibility	56 (34.6%)	72 (44.4%)	34 (21.0%)	<.0001
No WIC or food stamp eligibility	391 (53.6%)	256 (35.1%)	82 (11.3%)	
No medical insurance	182 (39.4%)	193 (41.8%)	87 (18.8%)	<.0001
Medical insurance	265 (61.8%)	135 (31.5%)	29 (6.8%)	
Previous preterm delivery	66 (44.6%)	57 (38.5%)	25 (16.9%)	.2
No previous preterm delivery	381 (51.3%)	271 (36.5%)	91 (12.3%)	
Have visible third molars	125 (34.7%)	169 (46.9%)	66 (18.3%)	<.0001
No third molars visible	322 (60.6%)	159 (29.9%)	50 (9.4%)	

*n = 891 subjects; with visible third molars, n = 360.

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not significant. At enrollment maxillary mean PD was 1.88 mm (SD 0.60) and mandibular mean PD was 1.82 mm (SD 0.59). Postpartum maxillary mean PD was 1.95 mm (SD 0.59) and mandibular mean PD was 1.91 mm (SD 0.59).

Seventeen percent of the subjects with data collected postpartum delivered prematurely, less than 37 weeks gestation. When the subjects with visible third molars postpartum were considered and the levels of their maxillary and mandibular periodontal disease were combined in the same multivariable model, only the severity of maxillary periodontal disease increased the odds of preterm birth, OR 2.6 (95% CI 1.1-6.8) (Table 6). Being non-Caucasian also increased the odds of preterm birth.

Table 4. ADJUSTED LOGISTIC REGRESSION MODEL FOR MORE SEVERE 3-LEVEL PERIODONTAL DISEASE POSTPARTUM*

Variable	Odds Ratio (95% CI)
Have third molars at postpartum	1.7 (1.3-2.3)
Non-Caucasian	2.6 (1.9-3.6)
Smoke during pregnancy	1.6 (1.1-2.3)
WIC/food stamps	1.2 (0.9-1.8)
No insurance	1.5 (>1.0-1.5)

Data on maternal weight missing on 19 subjects.

Also adjusted for maternal age, maternal weight, alcohol use, marital status, previous preterm delivery in the same model.

Proportional odds assumption was not violated.

*n = 872 subjects, 360 subjects had visible third molars.

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Postpartum, the median serum CRP for all the 891 OCAP subjects was 8.0 mg/L (IQ 2.2-23.0), and the mean serum CRP was higher, 20.8 mg/L (SD 27.1), reflecting a wide range in values. If third molars were visible at term, the mean serum CRP was significantly higher as compared with serum levels in subjects without visible third molars, 20.7 mg/L versus 13.3 mg/L, $P = .0002$. Adjusting for mandibular periodontal disease, only the severity of maxillary periodontal disease in subjects with visible third molars was significantly associated with the upper quartile of serum CRP at term, at least 23.0 mg/L postpartum, $P = .01$, OR 2.5 (95% CI 1.2-5.1) (Table 7). Being non-Caucasian in this model was not associated with elevated serum CRP postpartum, $P = .07$.

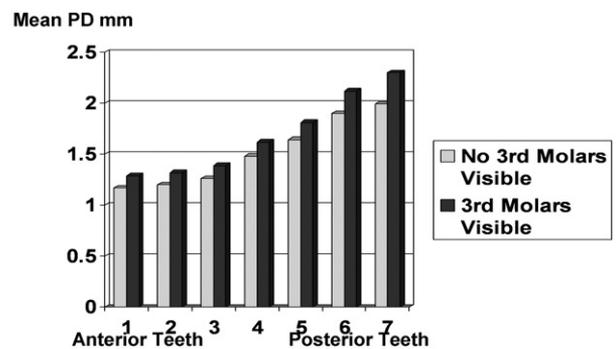


FIGURE 1. Mean periodontal probing depth (PD) at enrollment for each tooth by presence (n = 405) or absence (n = 615) of third molars. Differences are significant by tooth for mean PD, $P < .001$.

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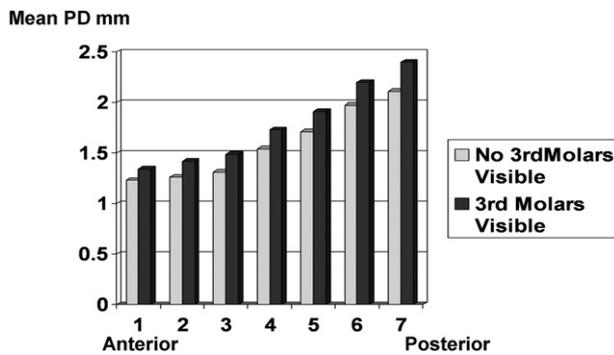


FIGURE 2. Postpartum mean periodontal probing depth (PD) at enrollment for each tooth by presence (n = 360) or absence (n = 512) of third molars. Differences are significant by tooth for mean PD, $P < .0001$.

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Discussion

The data we report suggest that, in these young subjects studied over the course of pregnancy, the molar region harbors significantly more severe periodontal pathology than more anterior regions of the mouth, perhaps the most clinically important finding from our analyses. This was true for either the mandible or maxilla, and third molars were affected more than first or second molars. Periodontal disease severity was greater if third molars were visible.

Until recently, third molars often have been excluded in clinical and population studies of periodontal disease. However, Elter et al did report that the visible presence of third molars in the National Health and Nutrition Estimates Survey (NHANES III) representative of the United States population 18 to 34 years old, more than doubled the risk of finding PD greater than 5 mm on an adjacent second molar.⁸ In Elter et al's analyses of data from subjects enrolled in the Atherosclerosis Risk in Communities (ARIC) study

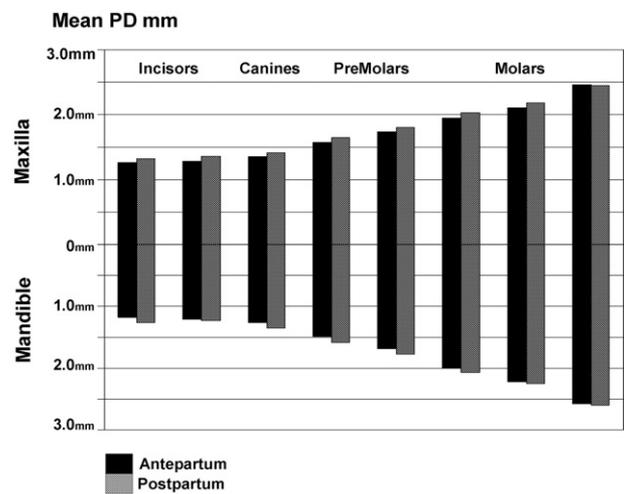


FIGURE 3. Mean periodontal probing depth (PD) by tooth, time point, and jaw. Mean PD significantly greater for molars versus non-molars, $P < .01$.

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targeting those 52 to 74 years old, a visible third molar almost doubled the odds of finding PD greater than 5 mm on an adjacent second molar.⁹

Moss et al have documented that PD around third molars can be assessed as accurately as PD around other teeth, and more recently third molar PD has been included in clinical studies.¹⁰ In the same OCAP subjects we analyzed, at least 1 third molar with PD greater than 4 mm or the upper tertile of bleeding on probing around third molars detected at enrollment, increased the odds of periodontal disease progression throughout the mouth during pregnancy, at least 4 probing sites with increased PD greater than 2 mm with resulting PD greater than 4 mm.⁵ More than half of the third molar probing sites were affected by periodontal progression in the relatively few months of pregnancy, compared with a third of first and second molar sites.

Table 5. MEAN (SD) PERIODONTAL PROBING DEPTH BY TOOTH TYPE, JAW, AND EXAMINATION*

	Maxillary		Mandible	
	Antepartum	Postpartum	Antepartum	Postpartum
Central incisor	1.27 (0.56)	1.32 (0.54)	1.18 (0.54)	1.26 (0.56)
Lateral incisor	1.29 (0.56)	1.36 (0.55)	1.22 (0.55)	1.29 (0.56)
Canine	1.36 (0.57)	1.41 (0.55)	1.26 (0.54)	1.35 (0.56)
First premolar	1.57 (0.56)	1.65 (0.54)	1.48 (0.56)	1.59 (0.56)
Second premolar	1.73 (0.61)	1.81 (0.60)	1.68 (0.61)	1.77 (0.59)
First molar	1.93 (0.66)	2.03 (0.60)	1.99 (0.64)	2.07 (0.61)
Second molar	2.10 (0.69)	2.18 (0.64)	2.21 (0.71)	2.25 (0.66)
Third molar	2.44 (0.74)	2.45 (0.72)	2.57 (0.76)	2.60 (0.71)

Mean periodontal probing depth was significantly greater in the molar region, both at enrollment and postpartum, $P < .01$.

*Subjects with visible third molars: antepartum n = 405, postpartum subjects n = 360.

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Table 6. ADJUSTED LOGISTIC REGRESSION MODEL FOR POSTPARTUM MAXILLARY AND MANDIBULAR PERIODONTAL DISEASE AND PRETERM BIRTH, GESTATION AGE LESS THAN 37 WEEKS FOR SUBJECTS WITH VISIBLE THIRD MOLARS*

Variable	Odds Ratio (95% CI)
Maxillary periodontal disease severity	2.6 (1.1-6.8)
Mandibular periodontal disease severity	0.5 (0.2-1.2)
Non-Caucasian	5.6 (2.0-16.7)
Previous preterm birth	1.4 (0.7-2.7)
Smoke during pregnancy	1.4 (0.7-3.0)
WIC/food stamps	1.2 (0.6-2.5)
No insurance	1.5 (0.7-3.1)

*n = 360 subjects; preterm birth, n = 61 (17%). Also adjusted for maternal age, maternal weight, marital status, alcohol use, previous preterm delivery in the same model.

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In a longitudinal clinical study of asymptomatic young adult subjects in the same age range as the OCAP study subjects, White et al reported that periodontal pathology in the third molar region was significantly associated with elevated levels of periodontal pathogens.³ Blakey et al have suggested that third molar periodontal pathology initiated in the mandible and preceded periodontal disease detected more anterior in the mouth.^{1,2}

The clinical findings we report are consistent with the data reported by Blakey et al and White et al, and are compatible with current biological models of periodontal disease indicating that the acquisition of recognized periodontal pathogens is critical for the initiation and progression of periodontal pathology.^{1,3,11}

The proportion of OCAP subjects with moderate/severe periodontal disease affecting both jaws similarly, changed very little during pregnancy. Clinical and animal model data linking chronic oral inflammation with periodontal disease to unwanted obstetric outcomes were recently summarized by Offenbacher.¹² Chronic oral inflammation indicative of periodontal disease opens a portal to the blood stream for the pathogenic bacteria unique to the oral region. Thus, it is plausible that the oral cavity, an anatomically distant site with chronic inflammation and chronic exposure of pathogenic bacteria to the blood-stream, may induce a systemic response affecting the developing human fetus in a manner similar to more proximal anatomic exposure documented with genitourinary tract inflammation. In the data we report from OCAP, the severity of periodontal pathology was greater in subjects with visible third molars, increasing the odds of an accompanying systemic response to this chronic oral inflammation.

The subjects studied over time in the trial by Blakey et al cited above were in a similar age range as the OCAP subjects we studied, mean ages at enrollment 28.2 ± 8.2 years versus 28.2 ± 6.6 years, respectively. However, the OCAP subjects had considerably more periodontal pathology, disease in the maxilla being as prevalent as in the mandible, while few of Blakey et al's subjects had PD greater than 4 mm detected in the maxilla.²

Based on the data reported by Blakey et al, which indicated that periodontal disease in the mandible contributed to subject level periodontal pathology more than maxillary disease, it would be logical to conclude that systemic exposure and an accompanying systemic inflammatory response would more likely emanate from the lower jaw.² In the OCAP subjects, the increased risk of a systemic response, an unwanted obstetric outcome, preterm birth, or an elevated serum CRP postpartum, were associated with the level or severity of maxillary periodontal disease, controlling for levels of mandibular periodontal disease.

Is this logical clinically when disease severity in both jaws is not significantly different? Certainly, the maxilla has a greater blood supply than the mandible, including more extensive venous drainage. This could be the explanation. Once periodontal disease is established in the maxilla, affected patients may be more at risk for a systemic response from oral inflammation and periodontal pathogens. Clearly, this topic deserves further investigation.

Our data should be viewed with some caution. Subjects enrolled in OCAP and those studied by Blakey et al in the longitudinal study are not representative of the entire United States population.^{1,2,6}

Table 7. ADJUSTED LOGISTIC REGRESSION MODEL FOR POSTPARTUM MAXILLARY AND MANDIBULAR PERIODONTAL DISEASE AND ELEVATED SERUM CRP, UPPER QUARTILE AT TERM AT LEAST 23.0 mg/L POSTPARTUM, FOR SUBJECTS WITH VISIBLE THIRD MOLARS*

Variable	Odds Ratio (95% CI)
Maxillary periodontal disease severity	2.5 (1.2-5.1)
Mandibular periodontal disease severity	0.6 (0.3-1.2)
Non-Caucasian	0.6 (0.4-1.0)
Smoke during pregnancy	1.0 (0.6-1.7)
WIC/food stamps	1.5 (0.9-2.4)
No insurance	1.4 (0.8-2.5)

*n = 360 subjects; preterm birth, n = 61 (17%). Also adjusted for maternal age, maternal weight, marital status, alcohol use in the same model.

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In addition, few clinical studies have been conducted on young adults, and until recently, PD data have not been collected from the third molar region. However, clinicians and their patients should be aware that periodontal pathology most often affecting molars in young adults, accompanied by chronic oral inflammation, may lead to oral disease of increasing severity and a potential risk of exposure for systemic disease.

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