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Modulation of clinical expression of plaque-induced gingivitis: response in aggressive periodontitis subjects

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Abstract

Aim: The aim of this study was to characterize the gingival inflammatory response to de novo plaque accumulation in subjects treated for aggressive periodontitis (AP). The gingival inflammatory response of the AP subjects was retrospectively compared with that of periodontally healthy individuals (PH) matched for exposure to plaque and of periodontally healthy subjects previously identified as ''high responders'' (HR) and ''low responders'' (LR).

Materials and Methods: 13 AP subjects and 26 matched PH subjects participated in a 21-day experimental gingivitis trial. Plaque index (PlI), Gingival index (GI), gingival crevicular fluid volume (GCF) and angulated bleeding score (AngBS) were recorded at days 0, 7, 14 and 21. Cumulative plaque exposure (CPE), i.e. PlI over time, was also calculated.

Results: GCF was significantly higher in AP compared with PH group at each observation interval ($p \leqslant 0.001$). In addition, GCF was significantly higher in AP group compared with either LR or HR groups at each observation interval ($p < 0.001$).

Conclusions: These results suggest that susceptibility to gingival inflammation in response to de novo plaque accumulation may be related to susceptibility to periodontitis.

Key words: aggressive periodontitis; gingivitis.

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Despite the universal effect of plaque accumulation on gingival status, there is evidence that the level and consistency of the gingival tissue response to plaque accumulation may vary significantly between individuals with neither quantitative nor qualitative differences in plaque accumulation (Abbas et al. 1986a), suggesting that the inflammatory response of gingival tissues to plaque accumulation is an individual trait possibly dependent on host-related factors, whether genetic or environmental in origin (Tatakis & Trombelli 2004).

This host-dependent variation in gingivitis susceptibility is supported by the results of a large scale, randomized, experimental gingivitis study in periodontally healthy individuals (Trombelli et al. 2004). After 21 days of experimentally induced plaque accumulation, we were able to discriminate two subpopulations, namely ''high responders'' (HR) and ''low responders'' (LR), with significantly different severity of gingivitis in the face of similar amounts of plaque deposits. Specifically, HR individuals, compared with LR individuals, showed significantly higher values for all clinical parameters of gingival inflammation despite the lack of any difference in the extent of plaque accumulation or plaque accumulation rate between the two groups. The identification of individuals with different severity of gingival inflammation in response to similar plaque accumulation rate seems to confirm the hypothesis of a subject-specific effect of neglected oral hygiene on gingival tissues, as suggested by earlier studies on experimental gingivitis (Watts 1978, Wiedemann et al. 1979, Abbas et al. 1986a, van der Weijden et al. 1994) and recent studies on naturally occurring gingivitis (Müller et al. 2000).

Studies by van der Velden and colleagues indicate that susceptibility to experimental gingivitis (in terms of development of bleeding on probing) differs between two groups of patients with apparently different susceptibility to periodontitis. The group with greater periodontitis susceptibility exhibited greater susceptibility to gingivitis (van

der Velden et al. 1985), a result that could not be explained by the age difference between the two groups (Winkel et al. 1987), or by the specific microbial (plaque) or immune (host) parameters examined in these subjects (Abbas et al. 1986b). The concept of a link between susceptibility to periodontitis and susceptibility to gingivitis is also supported by studies on Down's syndrome patients, who exhibit severe periodontal disease early on and also manifest greater gingival inflammation much sooner than age- and sex-matched controls despite similar plaque accumulation (see Tatakis & Trombelli 2004 for a review). Consistently, Brecx et al. (1991) demonstrated that individuals with a history of periodontal disease exhibited a more severe plaque-induced gingival inflammation (determined as either gingival index (GI) or gingival crevicular fluid (GCF) volume) after a period of oral hygiene abstention compared with individuals with a history of long-standing gingival health. In a more recent experimental gingivitis study comparing 10 subjects with a history of aggressive (rapidly progressive) periodontitis against 10 subjects of similar age but resistant to periodontitis (gingivitis control), there was no statistically significant difference between the groups in any of the clinical gingival inflammation parameters (Johnson et al. 1997); nevertheless, the trend was for consistently higher GI and GCF values in the aggressive periodontitis (AP) group. Unlike the study of van der Velden et al. (1985), the other two studies reported significant differences in plaque accumulation between the groups (Brecx et al. 1991, Johnson et al. 1997). Therefore, summarizing the existing experimental gingivitis literature comparing periodontitis-susceptible and periodontitis-resistant subjects, only one study demonstrated significant differences between the groups under similar level of exposure to the etiologic agent (van der Velden et al. 1985).

The aim of the present 21-day experimental gingivitis study was to characterize the subject-based clinical behaviour of the gingiva when exposed to plaque accumulation in subjects previously treated for an aggressive form of periodontitis compared with periodontally healthy individuals matched for exposure to plaque. Moreover, the clinical parameters of gingival inflammation were comparatively analysed in the AP patients with respect to HR and LR individuals.

Materials and Methods

Experimental design

The overall experimental design has been previously detailed (Trombelli et al. 2004). Briefly, a split-mouth localized experimental gingivitis clinical trial was conducted. In each subject one maxillary quadrant was randomly assigned as ''test'' (experimental gingivitis) and the contralateral quadrant as ''control''. Subjects were provided with an acrylic stent customized on the test quadrant, and instructed to wear the stent prior to oral hygiene session throughout the experimental gingivitis period to prevent plaque removal during brushing of the remaining dentition (Putt et al. 1993).

To achieve optimum gingival health (GI = 0) and to standardize gingival baseline conditions all subjects participated in a 2-week pre-trial period, consisting of weekly session of professional scaling and polishing along with oral hygiene instructions. In addition, to exclude the possibility of subclinical ascorbate deficiency, all subjects were provided with a vitamin C (ascorbic acid, 500 mg; Vitamina C Angelini, A.C.R.A.F., Ancona, Italy) supplement to be taken once daily for the entire pre-trial and trial period.

The study design was approved by the local ethical committee and was found to conform to the requirements of the ''Declaration of Helsinki'' as adopted by the 18th World Medical Assembly in 1964 and subsequently revised (www.wma.net/e/policy/17-c_e.html). All participants provided written informed consent.

Tooth and site selection

The following three maxillary teeth were used in each test and control quadrant: lateral incisor, first pre-molar (if missing, replaced by second pre-molar), first molar (if missing, replaced by second pre-molar). For each tooth, parameters were evaluated on the buccal and the mesiobuccal aspect.

Allocation and allocation concealment

In each subject one maxillary quadrant was assigned as ''test'' (experimental gingivitis) and the contralateral quadrant as ''control'' according to a computer-generated randomization list. Examiners were kept unaware of randomization sequence and blinded as to which quadrant was either test or control. A study investigator not involved with examinations informed the participants of quadrant assignment, upon handing them their individual stent. Because of the nature of the study, however, it is not possible to assume that examiners had not become aware of quadrant allocation over the 21-day experimental gingivitis period. Plaque accumulation and gingival status were clinically different between test and control quadrants on days 7, 14 and 21. Whether and to what extent this readily identifiable status of the quadrants may have biased the examiners has not been ascertained.

Clinical parameters

The following clinical parameters, defined in detail previously (Trombelli et al. 2004), were obtained from the selected sites in the following order: GI, PlI, GCF, Angulated Bleeding Score (AngBS), and the derived parameter ''cumulative plaque exposure'' (CPE) was calculated. CPE represents the area under the curve (AUC) of subject-specific PlI over a specific period of time (Trombelli et al. 2004). All clinical parameters were recorded at days 0, 7, 14 and 21 by two trained and calibrated examiners with good to excellent intra- and inter-examiner agreement, as measured by *k* coefficient (Trombelli et al. 2004).

Probing depth (PD), clinical attachment level (CAL) and recession depth (REC) were recorded on six sites (mesio-buccal, bucal, disto-buccal, mesio-lingual, lingual and disto-lingual) on all present teeth with a standard manual-pressure periodontal probe as part of the periodontal record of the patient.

Study populations

AP patients (AP group)

AP group were selected among a pool of patients seeking care at the Research Centre for the Study of Periodontal Diseases, University of Ferrara. Diagnosis of Generalized Aggressive Periodontitis was set on reported clinical criteria (Tonetti & Mombelli 1999). All patients in AP group had received non-surgical therapy with/without surgical periodontal treatment, and had been enrolled in a periodontal supportive programme, based on 3–4-month recall sessions of professional supragingival and subgingival plaque removal.

Patients were included in the study if they met all of the following inclusion criteria:

- *Clinical (oral)*: active (non-surgical/surgical) phase of periodontal therapy completed at least 6 months earlier; no probing pocket depth >5 mm in all teeth; no probing pocket depth >3 mm and GI = 0 at study day 0 in teeth and sites of interest; maxillary lateral incisors, first or second pre-molars and first molars present and suitable for recordings; maxillary central incisors and second/third molars present and suitable for stent retention; able to have maxillary impression taken.
- *Smoking status*: non-smokers or former smokers who had quit smoking at least 3 years before the experimental phase.
- *Other*: able and willing to provide informed consent and to ensure compliance throughout the study.

Patients were excluded from the study if they met any of the following exclusion criteria:

- *Clinical (oral)*: carious lesions and/or inadequate restorations in maxillary lateral incisors, first or second pre-molars and first molars or adjacent teeth, interfering with dental plaque removal in the sites of interest; ongoing dental treatment, except for supportive periodontal therapy; maxillary dental implants, other than central incisor and second molar; maxillary occlusal bite-guard; maxillary orthodontic appliances, fixed or removable (permanent retainers on palatal of maxillary incisors were acceptable); mouthbreathing.
- *Medical*: pregnancy or lactation; physical or mental handicap that can interfere with adequate oral hygiene performance; history of drug abuse; allergy to acrylic material (stent); contraindication for vitamin C supplementation; medications affecting the gingiva and/or oral mucosa (diphenylhydantoin, calcium channel blockers, cyclosporin A, immunostimulants/immuno-modulators); steroidal and non-steroidal anti-inflammatories in the last 6 weeks; systemic or local antimicrobials in the last 6 weeks; systemic conditions (diabetes, quantitative and/or qualitative PMN defects, other immune system disorders, organ transplants, need for antibiotic pre-medication, known genetic defects, e.g., trisomy 21).

Participants were exited from the study immediately upon: requesting to withdraw from further participation; development of acute dental/oral conditions requiring treatment; development of medical conditions conflicting with the exclusion criteria listed above; development of conditions requiring treatment that was in conflict with the exclusion criteria listed above; failure to comply with study instructions/requirements.

Periodontally healthy individuals (PH group)

PH group was retrospectively selected among a cohort of periodontally healthy volunteers who had undergone a randomized, experimental gingivitis trial. Experimental design and inclusion/exclusion criteria for trial participation were described in detail in a previous report (Trombelli et al. 2004).

PH group was matched to AP group with respect to gender and CPE, as assessed on both test and control quadrants on day 21. To improve the statistical power of the comparison between AP and PH groups, two periodontally healthy subjects were matched to every single AP subject. Computer-assisted matching procedure was performed by an examiner who was blinded as to the aim of the study.

Individuals with different susceptibility to plaque-induced gingivitis (HR and LR groups)

Individuals with different susceptibility to plaque-induced gingivitis were identified among a cohort of periodontally healthy volounteers who had undergone a randomized, experimental gingivitis trial. According to GCF values, as recorded on day 21 in test quadrants and standardized on CPE day 21, it was possible to discriminate two sets of individuals, HR and LR groups, with significantly different severity of gingivitis to similar amounts of plaque deposits (Trombelli et al. 2004).

Statistical analysis

The subject was regarded as the statistical unit. For each clinical parameter, the recordings from the six selected sites for either test and control quadrants were added and divided by six to give the mean value for each subject. Therefore, for each clinical parameter at each observational period, the subject was represented by a single test and a single control value. Data were expressed by either median and inter-quartile range (IR) for non-parametric variables, or mean $\pm$ standard deviation (SD) for parametric variables.

Given the 2 : 1 ratio followed in the matching procedure between PH and AP group and a type-I error fixed at 0.05, the statistical power of the study resulted as 69%. At an $\alpha = 0.05$, the difference in GCF – day 21 between PH and AP group had to be 0.131 for test quadrant and 0.076 for control quadrant to be considered statistically significant.

Comparisons between AP and PH groups were performed by using Fisher's exact test for dichotomous variables, and unpaired *t*-test and Mann–Whitney *U*-test for parametric and non-parametric variables, respectively. To compare AP, HR and LR groups ANOVA for repeated measures or Kruskal–Wallis test for parametric and non-parametric variables, respectively, were used. Post hoc comparisons were performed to explore inter-group differences.

All analyses were done with STATISTICA software version 5.5 (StatSoft, Italia s.r.l., Vigonza, Italy). Level of significance was set at 5%.

Results

Demographic characteristics and periodontal status

AP group comprised of 13 patients, six males and seven females, mean age: 35.5 ± 3.3 and PH group comprised of 26 subjects, 12 males and 14 females, mean age: 23.7 ± 1.6. HR group ($n = 24$) comprised of 13 males and 11 females, mean age: 24.1 ± 1.6, and LR group ($n = 24$) comprised of 11 males and 13 females, mean age: 23.4 ± 1.9.

No differences were found among groups in terms of gender distribution. However, AP group was significantly older than PH as well as HR/LR groups ($p < 0.001$).

Periodontal probing parameters were significantly different between AP and PH groups. In particular, AP group presented with greater PD ($p < 0.001$), CAL ($p < 0.0001$) and REC ($p < 0.0001$) compared with PH group (Table 1).

Plaque accumulation

The computer-assisted matching procedure resulted in similar CPE in AP and PH groups in both test and control quadrants at each observation interval (Table 2). Consistently, test-quadrant PlI increased from 0.44 ± 0.22 on day 0 to 1.39 ± 0.34 on day 7, 1.71 ± 0.37 on day 14, and 1.92 ± 0.38 on day 21 in AP group. In PH group, test-quadrant PlI varied from 0.51 ± 0.33 on day 0 to 1.36 ± 0.23 on day 7, 1.62 ± 0.33 on day 14, and 2.0 ± 0.36 on day 21. Mean PlI values for control quadrants at day 0 were 0.51 ± 0.24 and 0.47 ± 0.32 for AP and PH groups, respectively, and did not change significantly over the course of the study. Differences in PlI for test and control quadrants were not statistically significant between AP and PH groups.

When PlI of AP group was compared with LR and HR groups (PlI values for LR and HR as reported in Table 3 of Trombelli et al. 2004) there were no statistical differences either for test or control quadrants. Moreover, no significant differences in CPE were observed when AP, HR and LR groups were compared (CPE values for LR and HR as reported in Table 4 of Trombelli et al. 2004).

Table 1. Descriptive statistics and comparisons for probing depth (PD), clinical attachment level (CAL) and recession depth (REC) (mean ± standard deviation) measured in periodontally healthy subjects (PH group, $n = 26$) and aggressive periodontitis patients (AP group, $n = 13$)

Probing parameters	PH group		AP group		Difference	
	N	mean ± SD	*N*	mean ± SD	*t*-test	*p*-value
PD	26	2.13 ± 0.87	13	3.37 ± 1.14	3.601	<0.001
CAL	26	0.04 ± 0.22	13	4.69 ± 1.21	5.243	<0.0001
REC	26	0.02 ± 0.09	13	1.32 ± 1.35	4.725	<0.0001

Table 2. Descriptive statistics and comparisons for cumulative plaque exposure (mean ± standard deviation) measured in periodontally healthy subjects (PH group, $n = 26$) and aggressive periodontitis patients (AP group, $n = 13$) in test and control quadrants at different observation intervals

	PH group		AP group		Difference	
	N	mean ± SD	*N*	mean ± SD	*t*-test	*p*-value
Test quadrant						
Day 7	26	6.53 ± 1.57	13	6.37 ± 1.44	0.303	0.76
Day 14	26	16.94 ± 2.80	13	17.19 ± 3.21	0.247	0.81
Day 21	26	29.23 ± 4.49	13	29.89 ± 5.35	0.400	0.69
Control quadrant						
Day 7	26	3.39 ± 2.30	13	3.86 ± 1.61	0.659	0.51
Day 14	26	7.00 ± 4.61	13	7.90 ± 3.07	0.633	0.53
Day 21	26	10.95 ± 6.59	13	11.80 ± 4.29	0.422	0.67

Table 3. Descriptive statistics and comparisons for gingival index (median, inter-quartile range (IR)) measured in periodontally healthy subjects (PH group, $n = 26$) and aggressive periodontitis patients (AP group, $n = 13$) in test and control quadrants at different observation intervals

	PH group		AP group		Difference: *p*-value*
	N	Median (IR)	*N*	Median (IR)	
Test quadrant					
Day 0	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.846
Day 7	26	0.17 (0.0–0.33)	13	0.33 (0.17–0.33)	0.396
Day 14	26	0.50 (0.33–0.67)	13	0.50 (0.50–0.83)	0.190
Day 21	26	0.67 (0.50–0.83)	13	0.83 (0.50–1.0)	0.239
Control quadrant					
Day 0	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.846
Day 7	26	0.0 (0.0–0.17)	13	0.17 (0.0–0.17)	0.185
Day 14	26	0.0 (0.0–0.17)	13	0.0 (0.0–0.33)	0.743
Day 21	26	0.0 (0.0–0.17)	13	0.17 (0.0–0.33)	0.503

*Mann–Whitney *U*-test.

Gingival inflammation

AP group versus PH group

No significant differences were found for GI and AngBS in AP and PH groups in both test and control quadrants at each observation interval (Tables 3 and 4). In contrast, GCF was significantly higher in AP compared with PH group in both test and control quadrants at each observation interval ($p \leqslant 0.001$) (Table 5).

AP group *versus* LR/HR groups

The gingival inflammation parameters of the AP group (Tables 3–5) were compared with the corresponding parameters of LR and HR groups (values reported in Tables 5–7 of Trombelli et al. 2004). When AP, HR and LR groups were compared in test quadrant, GI values were significantly different among groups at days 7, 14 and 21 ($p < 0.001$; Kruskal–Wallis). Post hoc comparisons revealed that GI was significantly higher for AP and HR groups with respect to LR group ($p < 0.01$), while no differences were found between HR and AP groups. In control quadrants, GI was significantly higher for AP compared with LR group at day 7 ($p < 0.05$).

Kruskal–Wallis analysis revealed a significant effect of group on AngBS in test quadrant on days 0, 7 and 21 ($p < 0.05$). However, post hoc comparisons did not detect any significant difference among groups on day 0. The only significant differences found were the HR group presenting with higher AngBS values compared with the LR group on days 7 and 21 ($p < 0.05$).

ANOVA showed a significant difference in GCF among groups at each observation interval in test and control quadrants ($p < 0.001$). Specifically, GCF was significantly higher in AP group compared with either LR or HR groups on days 0, 7, 14 and 21 in both test and control quadrants ($p < 0.001$). Moreover, test-quadrant GCF was significantly lower in LR group with respect to HR group on days 7 ($p < 0.05$), 14 and 21 ($p < 0.001$).

Discussion

The subject-based clinical behaviour of the gingiva when exposed to 21-day de novo plaque accumulation was comparatively evaluated in subjects treated for AP and periodontally healthy indi-

Table 4. Descriptive statistics and comparisons for angulated bleeding score (median, interquartile range) measured in periodontally healthy subjects (PH group, $n = 26$) and aggressive periodontitis patients (AP group, $n = 13$) in test and control quadrants at different observation intervals

	PH group		AP group		difference: *p*-value*
	N	median (interquartile range)	*N*	Median (interquartile range)	
Test quadrant					
Day 0	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.698
Day 7	26	0.0 (0.0–0.17)	13	0.17 (0.0–0.33)	0.356
Day 14	26	0.33 (0.17–0.67)	13	0.17 (0.17–0.50)	0.976
Day 21	26	0.58 (0.33–1.17)	13	0.33 (0.0–0.67)	0.055
Control quadrant					
Day 0	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.846
Day 7	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.698
Day 14	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.0)	0.561
Day 21	26	0.0 (0.0–0.0)	13	0.0 (0.0–0.17)	0.251

*Mann–Whitney *U*-test.

Table 5. Descriptive statistics and comparisons for gingival crevicular fluid volume (in μL; mean ± standard deviation) measured in periodontally healthy subjects (PH group, $n = 26$) and aggressive periodontitis patients (AP group, $n = 13$) in test and control quadrants at different observation intervals

	PH group		AP group		difference	
	N	Mean ± SD	*N*	Mean ± SD	*t*-test	*p*
Test quadrant						
Day 0	26	0.07 ± 0.03	13	0.14 ± 0.10	3.566	0.001
Day 7	26	0.18 ± 0.06	13	0.29 ± 0.09	4.182	<0.0001
Day 14	26	0.27 ± 0.12	13	0.43 ± 0.16	3.603	0.0009
Day 21	26	0.37 ± 0.19	13	0.58 ± 0.19	4.159	0.0002
Control quadrant						
Day 0	26	0.07 ± 0.04	13	0.16 ± 0.08	4.653	<0.0001
Day 7	26	0.08 ± 0.03	13	0.18 ± 0.08	5.311	<0.0001
Day 14	26	0.10 ± 0.06	13	0.20 ± 0.11	3.708	0.0007
Day 21	26	0.10 ± 0.05	13	0.22 ± 0.13	4.183	0.0002

viduals matched for plaque exposure. Clinical parameters of gingival inflammation were also analysed in the AP subjects with respect to individuals with different susceptibility to plaque-induced gingivitis (HR and LR groups). The results of the present study indicate that: (1) AP subjects showed a significantly higher gingival inflammatory response, as assessed by GCF, than periodontally healthy patients, a difference that could not be explained by differences in the rate and extent of supragingival plaque accumulation; (2) a significantly higher GCF was observed in AP subjects compared with both HR and LR groups.

In our material, both AP and PH groups showed an increasing exposure to supragingival plaque that, in turn, was associated with an increase in gingival inflammation, as assessed by all clinical parameters in test quadrants. These observations seem to reinforce the validity of this randomized, split-mouth, localized experimental gingivitis model to evaluate the impact of supragingival plaque on gingival status over a 21-day period (Trombelli et al. 2004). Although retrospective in nature, this study was conducted with an identical experimental design for both AP and PH groups, the same clinical examiners, and similarly stringent inclusion/exclusion criteria used to select study populations. Moreover, to minimize the bias from factors that had been shown to affect the gingival inflammatory response to plaque accumulation, the matching procedure between AP and PH group was based on gender distribution and rate of plaque exposure at completion of the experimental period (i.e. CPE on day 21). Male/female ratio has been matched to account for the effect of the physiologic changes in hormone levels associated to the menstrual cycle on gingivitis expression (Mariotti 1994). In this respect, evidence suggests that hormonal cycle variations do not affect clinically normal gingiva but do exacerbate existing chronic gingivitis (Holm-Pedersen & Löe 1967, Kovar et al. 1985, Niemi et al. 1986). The variable CPE, rather than a ''static'' recording such as PlI, has been matched to account for inter-individual differences in plaque accumulation rate. It has been previously shown that CPE exhibited a higher correlation than PlI with GCF assessed on day 21, thus suggesting that CPE may offer a better means of quantifying the biological challenge exerted by plaque on gingival tissues over a specific period of time (Trombelli et al. 2004).

Despite similar CPE values, the AP group presented significantly higher levels of GCF compared with the PH group on both test and control quadrants at each observation interval (Table 4). Moreover, a significantly higher GCF was observed in the AP group even when compared with individuals preselected because of their higher gingival inflammatory response to plaque accumulation (i.e., HR group). Overall, these observations suggest that the presence of an aggressive form of periodontitis is either associated with or may predispose to an increased severity of plaque-induced gingival inflammation. Our findings are consistent with those reported by previous experimental gingivitis trials where the association between susceptibility to gingivitis and susceptibility to periodontitis was investigated (van der Velden et al. 1985, Brecx et al. 1991).

Inclusion of a control quadrant in the examination and analysis was made in order to obtain information on the normal within-subject variation of gingival conditions without abstinence from oral hygiene procedures, thus better determining the specific effects of plaque accumulation (Trombelli et al. 2004). We consider noteworthy that differences in GCF between AP and PH group were evident even when low levels of plaque accumulation were present (control quadrants, Table 4). This finding supports further the hypothesis that the severity of gingival inflammatory response to plaque may be a patient trait (Tatakis & Trombelli 2004, Trombelli et al. 2004), a trait that apparently is not obliterated even when an effective self-performed mechanical plaque control is achieved. The possibility that suscept-

ibility to plaque-induced gingivitis in populations with different susceptibility to destructive periodontitis might be clinically detectable even when an optimum plaque control regimen is either maintained or re-established is also highlighted by the significant differences in GCF between AP and PH groups (for both test and control quadrants) at trial day 0 (Table 4), which was recorded following 2 weeks of strict professional and personal plaque control in all quadrants.

It should be noted that in our study there was a statistically significant age difference between AP and PH groups, a discrepancy that mainly relates to the inclusion criteria to select study populations. Although other studies offer evidence suggesting that differences in age may partly account for the observed variability in gingival inflammatory response between individuals with different periodontal conditions (Fransson et al. 1996), it is unlikely that a mean age difference of 12 years between two groups of mean age of 23 and 35 years (present study) is of the same biological significance as a mean age difference of over 40 years between two groups of subjects under 26 and over 65 years of age (Fransson et al. 1996). Furthermore, data stemming from experimental gingivitis trials in patients of similar age with different susceptibility to destructive periodontal disease (Brecx et al. 1991, Johnson et al. 1997) suggest that other individual characteristics, rather than age, may explain differences in gingival inflammatory response to de novo plaque accumulation.

Because of the experimental design of the study (effect of progressive plaque accumulation on clinical parameters of gingival inflammation), an influence of qualitatative characteristics of the supragingival microbiota as well as inflammatory response profile of the host on the observed inter-group variability in GCF levels cannot be excluded. In this respect, all studies reporting on experimental gingivitis in individuals with variable susceptibility to periodontal breakdown showed that differences in gingival inflammatory response to accumulated plaque could only be detected by means of clinical parameters, e.g., bleeding elicited by probing pressure (van der Velden et al. 1985), GI (Brecx et al. 1991) and/or crevicular fluid volume (Brecx et al. 1991, Johnson et al. 1997). However, significant differences between variably susceptible subjects could not be found when other parameters potentially associated with the inter-individual variability in plaque-induced gingival inflammation, such as microbiological profile (Abbas et al. 1986b, Johnson et al. 1997), histopathological features of the gingival lesion (Abbas et al. 1986b) or GCF inflammatory mediators (Johnson et al. 1997), were investigated.

Although this study corroborates the notion of a link between susceptibility to gingivitis and susceptibility to periodontitis, the potential significance of the inter-individual variability in plaque-induced gingival inflammatory response for the onset and progression of the destructive periodontal lesion remains uncertain. Recently, studies demonstrated that persistent gingival inflammation in a well-controlled, well-educated population results in a greater risk for tooth mortality and attachment loss on a long-term basis, and that the risk for tooth/attachment loss increases with an increasing severity of the gingival inflammation (Schätzle et al. 2003, 2004). In contrast, a study in non-human primates failed to find that animals with high and low inflammatory response to long-standing plaque accumulation have any disparity in susceptibility to ligature-induced periodontal destruction (Ebersole et al. 2000).

All of the available studies, including the present one, on the effect of periodontal status on the modulation of experimentally induced gingival inflammation are retrospective in nature, i.e., the experimental gingivitis trial is conducted after the clinical manifestation (and treatment) of periodontitis (van der Velden et al. 1985, Brecx et al. 1991, Johnson et al. 1997). Therefore, and despite the apparently consistent association of greater inflammatory response to de novo plaque accumulation in subjects with a history of periodontitis, the lack of a temporal sequence between the onset of gingival inflammation and the onset of destructive periodontal lesions prevents any definitive conclusion on whether a more severe inflammatory response of the marginal gingiva would manifest prior to the onset/progression/treatment of periodontitis or, rather, whether such a heightened response is a mere effect of the periodontal status of the subject (e.g., anatomical differences between reduced but healthy periodontium and intact healthy periodontal tissues).

In summary, within the limitations of the present study, subjects with a history of aggressive periodontitis demonstrate significantly higher gingival inflammatory response, as assessed by gingival crevicular fluid volume, in response to de novo plaque accumulation when compared with periodontally healthy subjects matched for extent and rate of supragingival plaque accumulation; AP subjects demonstrate a significantly higher gingival crevicular fluid response even when compared with a subgroup of periodontally healthy subjects predetermined to have a high response to plaque accumulation. These results suggest that susceptibility to gingivitis might be related to susceptibility to periodontitis.

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Clinical Relevance

Increasing evidence supports an association between gingivitis susceptibility and periodontitis susceptibility. Therefore, we designed an experimental gingivitis study to characterize the subject-based clinical behaviour of the gingiva to de novo plaque accumulation in periodontally-healthy subjects and AP patients. After 21 days of plaque accumulation, AP patients showed a significantly higher gingival inflammatory response, as assessed by GCF, than periodontally healthy subjects. These results reinforce the hypothesis that susceptibility to gingivitis might be related to susceptibility to periodontitis.

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