

The effects of periodontal therapy on serum antibody (IgG) levels to plaque microorganisms*

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Abstract. The influence of periodontal therapy on serum antibody titers to selected periodontal disease-associated microorganisms was assessed in 23 patients having chronic inflammatory periodontal disease (CIPD). The immunoglobulin G (IgG) titers were determined by the microELISA technique in serum samples obtained prior to treatment; following a hygienic phase which included scaling, root planing, and oral hygiene instruction; following surgical treatment; and one year and two years following hygienic phase (maintenance phase). Considerable individual variability existed in the magnitude of immune response to specific bacterial preparations. Significant reductions in the mean antibody titers were seen to *A. viscosus*, *S. sanguis*, *F. nucleatum*, *S. sputigena*, *B. gingivalis*, *B. intermedium*, *B. melaninogenicus*, *T. vincentii*, and *T. denticola* by the end of the second year of maintenance. There was no consistent response to *Capnocytophaga*. When individual patient responses were examined, 6 of the 23 were found to have elevated titers to at least one of the microorganisms in the interval between pretreatment and the end of the hygienic phase; however, in all but one case, the titers at the end of the second year of maintenance were below pretreatment levels. Antibody levels to bacteria such as *S. sanguis* were modified during therapy. This would indicate that immune responses to microbes not generally considered to be "periodontal pathogens" may be modified by adjuvant activity associated with subgingival plaque or changes in the environment of the sulcus and that subsequent changes in titer do not necessarily reflect a role of that microorganism in the disease process.

Key words: periodontal therapy; antibodies; plaque microorganisms; immunoglobulins; longitudinal study.

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The host immunologic response to the microbial flora of the oral cavity has been studied extensively for a potential role in the etiology of chronic inflammatory periodontal disease (CIPD) (Baker et al. 1976, Baker et al. 1978, Genco et al. 1974, Ivanyi et al. 1972, Page & Schroeder 1982). While its actual role in the disease is still unclear, the host response provides a sensitive indicator of the flora that inhabits the oral cavity, especially the microorganisms that reside in the gingival sulcus (Tew et al. 1985a, b, Vandestein et al. 1984, Willi-

ams et al. 1985). Recently, cross-sectional studies have indicated that levels of certain microbial species are elevated during certain stages of CIPD and that the titers of serum and gingival crevicular fluid antibodies to these microbes are also elevated (Ebersole et al. 1986, Hofstad 1984, Naito et al. 1985, Tew et al. 1985a, b). Other studies have shown that antibodies to many of these species appear normally in the sera during maturation from the neonate to the adolescent (Mouton et al. 1981). Thus, "preinfection" sera do not usually exist and "normal" antibody titers to these microorganisms vary considerably. As a result, one must examine relative changes in levels of antibodies when comparing states of health and disease. An assessment of the success of a particular stage of periodontal therapy is difficult because it is cumbersome to

routinely monitor patients for the presence of periodontal disease associated flora. Monitoring the flora by assessing the host response to it may provide a simple means of assessing patient status during maintenance phase of therapy. We report the results of a longitudinal study on the effects of periodontal therapy on the host antibody response to the microbial flora.

Material and Methods

Subjects

Sera were obtained from 23 patients participating in an ongoing longitudinal clinical trial at The University of Michigan School of Dentistry (Hill et al. 1981). There were nine males and fourteen females in the age range 24-60 years. To be selected for the study, each patient had to fulfill the following cri-

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teria: (1) have at least one periodontal pocket extending 4 mm or more apically to the cement-enamel junction, and (2) have at least twenty treatable teeth. Patients with poor systemic health and those in need of extensive restorative dentistry were excluded from the study.

Clinical procedures

Clinical examinations were performed prior to treatment and following different stages in therapy. The clinical parameters employed were Plaque Index (Silness & Løe 1964) gingival health according to the criteria of the Periodontal Disease Index (Ramfjord 1959), and pocket depth and attachment level in relation to the cement-enamel junction (Ramfjord 1967). After the pretreatment examination (PT) the hygienic phase (PH) protocol was performed. This included scaling, root planing and oral hygiene instruction for all patients. Approximately 4-6 appointments over a period of one month (total of 5-8 h) were required to complete the hygienic phase for each subject. All initial measurements were repeated for each subject 4 weeks after the completion of the hygienic phase. Following the latter, a periodontist performed surgery or scaling and root planing under local anesthesia in each patient. The details of the surgical and nonsurgical therapeutic procedures have been described elsewhere (Hill et al. 1981). At the completion of the surgical phase, patients were placed on a three month maintenance prophylaxis recall. Patients were rescored annually from the post-hygienic phase evaluation prior to the recall prophylaxis. Clinical parameters were assessed at pretreatment (PT), post-hygienic phase (PH), post-surgical phase (PS, 4 weeks after the removal of the last surgical dressing), maintenance phase I (MP1, one year after the end of the hygienic phase), and maintenance phase II (MP2, two years after the end of the hygienic phase). Whenever the clinical parameters were assessed, 50 ml of peripheral blood were obtained from each patient. Resultant sera were stored frozen at -70°C until used.

Antigen preparation

Isolates of the following microorganisms were used: *Actinomyces viscosus* (AV), *Streptococcus sanguis* (SS), *Fusobacterium nucleatum* (FN), *Selenomonas sputigena* (SEL), *Bacteroides gingivalis*

(BG), *Bacteroides intermedius* (BI), *Bacteroides melaninogenicus* (BM), *Capnocytophaga* sp. (CAP), *Treponema vincentii* (TV) and *Treponema denticola* (TD). Unless otherwise noted, these isolates were obtained from sites of naturally occurring gingivitis or periodontitis during previous clinical studies. Cultural methods for isolation and characterization have been described elsewhere (Loesche et al. 1981, Mangan et al. 1982). The cultures were grown in 500 ml batches and harvested by centrifugation at 12,000 g for 30 minutes. The cell pellets were washed in sterile phosphate buffered saline (PBS, 0.05 M PO_4 , 0.15 M NaCl, pH 7.4) and suspended in sterile distilled water to give a final concentration of 20 mg (wet weight) per milliliter. The washed cells were subjected to a total of thirty minutes of ultrasonic disruption (model W185D, Heat Systems Ultrasonics, Inc., Plainview, New York) delivered in five minute intervals with alternate periods of cooling in an ice bath. The ultrasonicates were centrifuged at 12,000 g for 30 min and the supernatant fraction lyophilized.

Measurement of serum antibody titers

Ultrasonicate preparations of oral microorganisms were diluted ($5 \mu\text{g/ml}$) in sodium carbonate coating buffer (pH 9.6, containing 0.02% Na-N) and then 0.20 ml was added to the wells of round bottom microtiter plates (Immulon, Dynatek Laboratories, Inc., Alexandria, VA). This concentration was previously determined to result in optimal sensitization for the microorganisms tested. The plates were then sealed with cellophane tape and incubated at room temperature ($22-24^{\circ}\text{C}$) overnight in a closed chamber with high humidity. The following morning, the plates were washed with PBS containing polyoxyethylene(20)sorbitan (Tween 20TM, Matheson, Coleman and Bell, Norwood, OH) (PBS-T).

Serum samples were serially diluted in PBS-T (beginning at 1/40). To assure consistency, all samples of a single patient were always analyzed in the same plate. The serum dilutions were added to the sensitized well (0.20 ml/well). In addition, a reference serum, prepared by pooling 20 individual serum samples from healthy donors having no periodontal disease (equal number of males and females, ages 20 to 50 years) was diluted in a similar fashion and added to a row of wells in each plate. This

reference serum served as an internal standard with which to control for the development of the ELISA and for subsequent calculations of ELISA Units (see below). After a three hour incubation period at room temperature, the plates were washed five times in PBS-T. Alkaline phosphatase (calf intestine, type VII, Sigma Chemical Co., St. Louis, MO) was conjugated to heavy chain-specific rabbit anti-human immunoglobulin G (IgG Bio-Rad Laboratories, Richmond, VA.) by glutaraldehyde treatment. The conjugate was diluted in PBS-T (1:2000; previously determined to be optimal) and 0.20 ml was added to each well. Following an overnight incubation at room temperature, the plates were again washed 5 times in PBS-T. Alkaline phosphatase substrate (Sigma 104TM, Sigma Chemical Co., St. Louis, MO, 1 mg/ml in 0.05 M NaCO_3 and 1 mM MgCl_2 , pH 9.8) was added to each well (0.20 ml/well). After fifteen minutes, the reaction was stopped with 0.025 ml of 6N sodium hydroxide. The absorbancy (405 nm) of each well was then determined (Titertek Multiskan, Flow Laboratories, McLean, VA). Antibody activity in the sera was expressed as ELISA units (EU). This value was defined by a linear regression analysis of the reference serum titration. EU of all the samples were calculated by relating optical density values from each experimental sample to the reference serum, which was assigned a value of 100 EU (Naito 1984). Only absorbance values occurring in the linear portion of the titration curves were used.

Statistical analysis

The significance of the changes in the antibody titers at successive timepoints were assessed by paired *t*-tests. Cross-correlation coefficients were computed to see whether or not the patterns of change of the various titers were similar within each of the patients (Kowalski & Guire 1974).

Results

Changes in clinical parameters during therapy

The clinical status of these patients and their response to treatment has been previously reported (Lopatin et al. 1983). Briefly, a significant reduction in dental plaque (plaque index) and gingival inflammation (gingival index) was

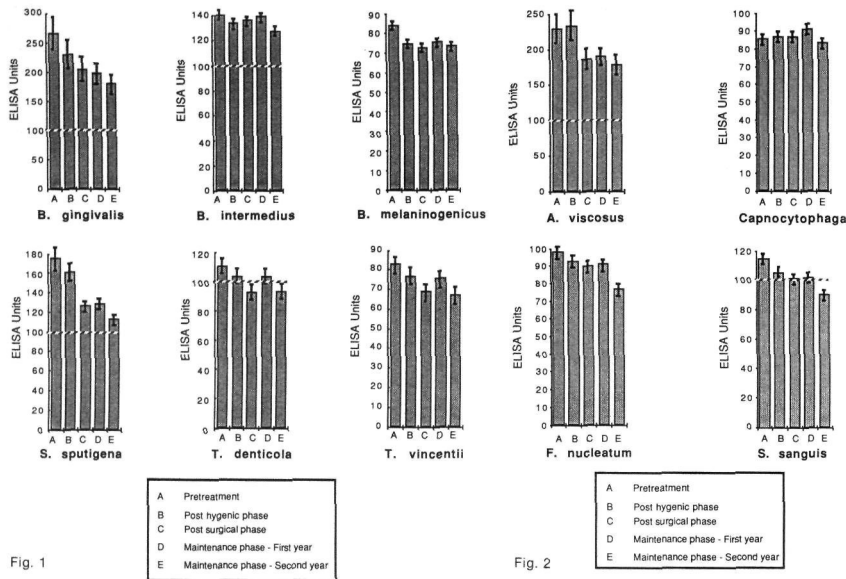


Fig. 1

Fig. 2

Figs. 1, 2. Longitudinal changes in antibacterial antibody titer following periodontal therapy. Each panel shows the mean ELISA unit values (\pm S.E.M.) calculated for the indicated microorganism at five time points during the treatment protocol. Intervals: A. Pretreatment, B. Post hygienic phase, C. Post surgical phase, D. Maintenance phase - first year, E. Maintenance phase - second year. Cross-hatched line indicates healthy pooled sera reference value (100 ELISA units).

observed at all examinations in the patients group following the hygienic phase. In addition, there was a decrease in probing depth in the 4-6 mm and > 7 mm sites over the two years post surgical phase and maintenance of level of attachment in all sites during the same time period.

Changes in antibody titers during therapy

As shown in Figs. 1, 2, with the exception of *Capnocytophaga*, periodontal therapy produced a reduction in the mean antibacterial antibody titers, which was significant ($p < 0.05$), when the pretreatment (PT) measurements were compared to those of the 2-year post surgical phase (MP2). Since all of the antibody titrations were compared to a reference serum pool (arbitrarily defined as possessing a titer of 100 EU), obtained from an age-matched group of healthy individuals who had no evidence of inflammatory periodontal dis-

ease, the humoral responses of the patients to these microorganisms could be clearly categorized by whether a decrease in titer occurred from a supranormal value, i.e., the pretreatment ELISA titer was significantly in excess of 100 EU, or whether the periodontal therapy caused a decrease from a relatively normal value, i.e., pretreatment titer less than or equal to 100 EU. As shown in Figs. 1, 2, the mean antibody titers to 4 oral microorganisms were clearly elevated over normal control values (indicated by cross-hatched bars at 100 EU). These included *B. gingivalis* (BG, 260 EU), *S. sputigena* (SS, 175 EU), *A. viscosus* (AV, 240 EU), and *B. intermedius* (BI, 140). There were significant ($p < 0.05$) reductions in the mean antibody titers to the remaining microorganisms, however, those changes were all relative to the values one would expect to find in healthy, non-periodontally diseased control subjects.

The intervals during which the de-

creases in antibody titers occurred were not the same for each microorganism. Table 1 indicates the % changes in the antibody titers (and significance of the changes) between each treatment interval. In the interval between PT and PH, there is a significant reduction in the titer to SS (8.7%, $p < 0.003$), BG (13.5%, $p < 0.01$), and BM (10.7%, $p < 0.02$). In the interval between PH and PS, there was another significant decrease in the titer to BG (12.4%, $p < 0.02$). In no case was there a significant change in the antibody titer between PS and MP1. In the final interval examined, MP1 to MP2, decreases in the mean titers occurred with all of the microorganisms tested, however, only those decreases associated with AV (12.8%, $p < 0.03$), FN (15.4%, $p < 0.02$), SEL (18.1%, $p < 0.01$), and TV (13.9%, $p < 0.02$) were significant. In general, a change in the mean antibody titer less than 8% did not appear to be statistically significant.

Table 1. Relative changes in antibacterial antibody titers between treatment intervals*

Antigen	PT → PH	PH → PS	PS → MP1	MP1 → MP2	PT → MP2
<i>A. viscosus</i>	1.3	8.8	0	12.8 (0.03)	24.8 (0.02)
<i>F. nucleatum</i>	5.1	0	0	15.4 (0.02)	21.2 (0.01)
<i>S. sanguis</i>	8.7 (0.003)	6.5	0	7.8	20.3 (0.02)
<i>S. spjutigena</i>	8.5	6.6	1.6	18.1 (0.01)	35.4 (0.0002)
<i>B. gingivalis</i>	13.5 (0.01)	12.4 (0.02)	0	29.8 (0.01)	
<i>B. intermedius</i>	4.3	1.5	0.7	6.5	7.9 (0.02)
<i>Capnocytophaga</i>	0	1.1	-3.3	7.5	3.4
<i>T. vincentii</i>	6	2.8	-4.3	13.9 (0.02)	20.2 (0.002)
<i>T. denticola</i>	6.4	7.9	-7.1	4.9	15.5 (0.02)
<i>B. melaninogenicus</i>	10.7 (0.02)	-0.3	-3.6	3.9	10.8 (0.02)

* % decrease in ELISA Units. *P*-value indicated by parentheses. Boxed value indicates a significant change with Bonferroni correction applied ($p < 0.05$).

Abbreviations: PT, pretreatment; PH, post-hygienic phase; PS, post-surgical phase; MP1, maintenance phase 1st year; MP2, maintenance phase 2nd year.

We might remark that since several tests were performed in Table 1 for each microorganism, *viz.*, one for each pair of successive timepoints for a total of five tests, some investigators might suggest the Bonferroni's approach (Glantz 1981) to "correct" the individual *P*-values to ones more appropriate for the situation in which multiple, related tests are performed. This correction amounts to multiplying each of the *P*-values shown in Table 1 by 5 (the number of tests performed). Thus, the only contrasts shown to be significant are those for which the uncorrected *P*-values are ≤ 0.01 .

If results of individual patients are examined, however, a slightly different picture of the change in the humoral immune response to these microorganisms was seen. While it is difficult to present such individual results in simple tabular form, several observations can be made. There was no unique pattern of humoral responses following treatment. Attempts to demonstrate relationships between antibody responses to different microorganisms did not reveal typical patterns. With the exception of one patient, the trend was a general reduction in antibody titers with treat-

ment. In this patient and 5 others, there were increases in antibody titers to selected microorganisms immediately following the hygienic phase. In most cases, these increases represented a response to a single microorganism and this early increase was not predictive of the ultimate antibody titer at the end of two years. The responses of patient no. 10 are shown in Fig. 3. This individual's response to therapy was unique in this group, since although a modest increase in titer was found to occur in five other patients (for 1-2 bacteria), which by MP2 was decreased below pretreatment levels in three subjects, this patient demonstrated significantly elevated antibody titers to six of the ten bacteria, and he did not ultimately demonstrate a significant decrease in titer over the entire course of treatment to any bacteria. The case history and response to therapy of this patient was unremarkable when compared to the other patients in this study.

Discussion

Numerous studies have attempted to correlate patient systemic immunity to specific oral microorganisms with the severity of inflammatory periodontal disease (Baker et al. 1976, Baker et al. 1978, Genco et al. 1974, Ivanyi et al. 1972, Page & Schroeder 1982). Lymphocyte blastogenic responses to disease-associated microorganisms have been examined in longitudinal studies (Lopatin et al. 1983, Osterberg et al. 1983), however, their value in predicting or establishing the severity of disease is questionable.

The humoral immune response has also been studied for its ability to correlate with disease activity. High corre-

lations between antibody titers and disease activity has been demonstrated for selected microorganisms in cross-sectional studies. For example, there is a particularly high degree of association between the presence of antibodies to *Actinobacillus actinomycetemcomitans* and the occurrence of localized juvenile periodontitis (Ebersole et al. 1982). In contrast, patients with adult or with rapidly progressive periodontitis frequently have increased levels of IgG antibodies to *Bacteroides gingivalis* (Mouton et al. 1981).

However, the predictive value of single time point antibody measurements in assessing disease, or its utility in assessing treatment is not clear because, even with a high correlation between disease severity and antibody titer, numerous subjects possess antibody titers that fall above and below the ranges that identify health and disease, irrespective of their oral health status. This situation is due to fact that most of the members of the oral flora associated with chronic inflammatory periodontal disease states can be identified in healthy subjects (Loesche & Syed 1978, Loesche et al. 1985), and that antibody titers to this flora appears in adolescence (Mouton et al. 1981) and can be demonstrated in health (Doty et al. 1982).

Since it is virtually impossible to obtain pre-disease sera from individuals who have developed CIPD, normal baseline antibody levels to the oral flora are not usually available. We therefore measured the antibody levels to a select group of oral microorganisms in a longitudinal fashion in order to assess treatment effects. Presumably, a return to health would result in a reduction of the oral immune sensitization to the

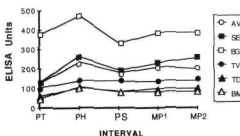


Fig. 3. Changes in humoral antibody titers during therapy to selected oral microorganisms in patient no. 10. Patient no. 10 represented a unique pattern of humoral immune response during periodontal therapy.

periodontal disease associated microorganisms.

The results suggest that scaling and root planing result in general reduction of antibody titers to the oral microorganisms, in many cases to levels below those of normal subjects. The humoral response appears to be elevated to suspected periodontal "pathogens" such as BG, as well as "innocuous" oral flora such as SS, suggesting that there is a general sensitization to most of the flora. 2 characteristic types of responses were observed (Table 1). First, significant early (PT-PH) decreases in antibody titers were associated with BG, SS, and BM. Second, progressive, cumulative changes that resulted in a significant decrease in titers by the end of the maintenance phase (MP2) were seen with the remaining microorganisms, with the exception of CAP. In this table, CAP is the sole species not resulting in a significant mean group change in response to treatment. CAP titers were found to be the most variable in response to treatment.

Presumably, the changes in antibody titers seen during this study result from reductions in the numbers of specific members of the microflora. Microbiological studies (reviewed by Page & Schroeder 1982) describe the presence of high levels of BG in untreated lesions of adult periodontitis. Although the microbiota of the gingival sulcus was not monitored in this study, the progressive decrease in antibody titers to BG and other CIPD-associated microorganisms probably reflects reductions in levels of these microorganisms during therapy.

A recent report (Ebersole et al. 1985) also examined the humoral immune response to selected oral microorganisms following therapy. In their study, patients treated with scaling and root planing demonstrated increased antibody titers to certain microorganisms, while their responses rarely decreased below pretreatment values within the timeframe examined. Their findings were explained as a re-immunization to the oral flora resulting from the trauma of the treatment protocol. Since the sampling intervals and methods of therapy differed significantly between our study and theirs, it is difficult to make a comparison between the results. However, a comparison between the studies does suggest that the antibody levels are quite sensitive to the therapy. In our study, six patients demonstrated an increase in antibody titer to selected

plaque microorganisms during the PT-PH phase of treatment. Since the mode of therapy might be expected to result in a certain level of additional sensitization, and bacteremias have been shown to accompany such procedures (Hockett et al. 1977), increasing levels of antibodies to the oral flora would not be unexpected. However, three of the six patients ultimately demonstrated reduced antibody titers by the end of the second maintenance phase. It is not clear at present what is unique about the remaining patients, especially patient 10 who demonstrated increased titers to six out of ten of the bacteria. Their (clinical) response to therapy did not differ from that of the other patients.

Our findings do not shed light on the role of the periodontal disease associated microorganisms in the etiology of CIPD. In fact, since antibody levels to bacteria such as *S. sanguis* were also modified during therapy, one must consider the possibility that immune responses to microbes not generally considered to be "periodontal pathogens" are modified by adjuvant associated with subgingival plaque. Alternatively, the levels of these "non-pathogens" in the sulcus may be influenced by the environment created by the "pathogen". Thus, changes in antibody titers to a microbial antigen preparation would not necessarily identify a role for that microorganism in the disease etiology. The results of this study, however, tend to support the concept that periodontal treatment reduces the antigenic stimuli in the periodontium, resulting in decreased antibody titers to the plaque flora, in general. In many cases, the antibacterial titers were quite resistant to change, and the time elapsed between initiation of therapy and occurrence of significant changes in antibody level exceeded one year. This was also suggested by observations in edentulous subjects where the length of time the individuals were totally edentulous has a significant influence upon the levels of circulating antibodies to oral microorganisms (Jacob et al. 1982). One might expect that once sensitized to a particular antigen, maintenance of that im-

mune response would require minimal levels of antigen in the gingival sulcus, because of the sensitivity of the anamnestic response. As a result, those responses which are most easily eradicated might be thought to be bacteria that were most easily eliminated or which are the poorest immunogens. The more persistent immune responses might, thus, be considered to be associated with more difficult to eliminate flora, or those associated with health. The more significant use of this type of analysis might be the monitoring of the maintenance patient who has demonstrated reduced antibody titers as a result of therapy. In a patient primed immunologically to the CIPD-associated microorganisms, one might expect a very rapid rise in the antibody titer if the crevicular flora increases, possibly suggesting that additional therapy is desirable. One cannot overstate, however, that because of individual variability in the magnitude of immune responses to specific bacterial preparations, pretreatment sera from each patient must serve as that individual's baseline reference.

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Zusammenfassung

Die Auswirkung parodontaler Therapie auf die Serum-Antikörper (IgG) - Niveaus von Plaque-Mikroorganismen

Der Einfluß parodontaler Therapie auf die Serum-Antikörpertiter von selektierten, mit der Krankheit assoziierten parodontalen Mikroorganismen, wurde bei 23 Patienten mit chronisch entzündlicher Parodontalkrankheit (CIPD) beurteilt. In Serum-Stichproben wurde der Immunglobulin G (IgG)-Titer mit der Mikro-ELISA-Technik vor der Behandlung bestimmt und zwar nach der Hygienephase mit Zahnsteinentfernung, Wurzelglättung und Instruktion in oraler Hygiene; nach der chirurgischen Behandlung, sowie 1 Jahr und 2 Jahre nach der Hygienephase (Nachsorgephase). Die Immunitätswerten gegenüber speziellen bakteriellen Zubereitun-

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gen schwanken beträchtlich. Gegenüber *A. viscosus*, *S. sanguis*, *F. nucleatum*, *S. spuitigena* und *B. gingivalis*, sowie *B. intermedius*, *B. melanogenicus*, *T. vincentii* und *T. denticola* wurden gegen Ende des 2. Nachsorgejahres signifikante Reduktionen der mittleren Antikörper-Titer beobachtet. Auf *Capnocytophaga* kam es zu keiner gleichbleibenden Niveau-angabe. Bei näherer Untersuchung der Antworten der einzelnen Patienten zeigte es sich, daß bei 6 Patienten in der Zeit zwischen Vorbehandlung und dem Ende der Hygienephase ein erhöhter Titer gegen zumindest einen der Mikroorganismen vorlag. Mit einer Ausnahme lagen jedoch in allen Fällen die Titer gegen Ende des 2. Nachsorgejahres unterhalb der Niveaus, die vor der Behandlung konstantiert worden waren. Antikörpertiterniveau gegenüber Bakterien wie *S. sanguis* änderten sich während der Behandlung. Das könnte bedeuten, daß Immunantworten auf Kleinstlebewesen, die generell nicht als "parodontale Pathogene" angesprochen werden, durch Stützmaßnahmen hinsichtlich der subgingivalen Plaque oder durch Veränderungen des Sulkus-Milieus modifiziert werden können und daß die dann zu beobachtende Veränderung des Titers nicht unbedingt die Rolle widerspricht, die dieser Mikroorganismus in dem Krankheitsprozess spielt.

Résumé

Effets du traitement parodontal sur les taux d'anticorps sériques (IgG) aux microorganismes de la plaque

L'influence du traitement parodontal sur les taux d'anticorps sériques à certains microorganismes associés à la maladie parodontale a été déterminée chez 23 patients souffrant de parodontite chronique. Les taux d'IgG ont été déterminés par la technique micro-ELISA d'échantillons de sérum obtenus avant le traitement, après une phase d'hygiène (détartrage, lissage radiculaire et instruction en hygiène buccale), après la chirurgie parodontale ainsi qu'une et deux années après la phase de maintien. Une variation individuelle considérable existait dans l'ampleur des réponses immunitaires aux préparations bactériennes spécifiques. Des réductions significatives dans les taux d'anticorps moyens ont été notées pour *A. viscosus*, le *S. sanguis*, le *F. nucleatum*, le *S. spuitigena*, le *B. gingivalis*, le *B. intermedius*, le *B. melanogenicus*, le *T. vincentii* et le *T. denticola* à la fin de la seconde année de maintien. Il n'y avait aucune réponse cohérente au *Capnocytophaga*. Lorsque les réponses individuelles des patients étaient examinées, six des 23 sujets possédaient des taux élevés à au moins un des microorganismes, dans l'intervalle entre le pré-traitement et la fin de la phase d'hygiène; cependant, dans tous les cas sauf un, les taux à la fin de la seconde année de maintien étaient en dessous des taux pré-traitement. Des taux d'anticorps aux bactéries telles que le *S. sanguis* ont été modifiés durant le traitement. Ceci indiquait que les réponses immunitaires

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res aux microbes qui ne sont généralement pas considérés comme "pathogènes parodontalement" peuvent être modifiées par une activité supplémentaire associée à la plaque sous-gingivale ou des changements dans l'environnement du sillon et que les variations ultérieures dans les taux n'impliquent pas nécessairement un rôle de ce microorganisme dans le processus de la maladie.

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