Neutrophil Chemotaxis Dysfunction in Human Periodontitis

T. E. VAN DYKE, H. U. HOROSZEWICZ, L. J. CIANCIOLA, AND R. J. GENCO*
Department of Oral Biology* and Periodontal Disease Clinical Research Center, School of Dentistry, State University of New York at Buffalo, Buffalo, New York 14226

Polymorphonuclear leukocyte (PMNL) chemotaxis studies of 32 patients with localized juvenile periodontitis (periodontosis or LJP), 10 adult patients with a history of LJP (post-LJP), 8 patients with generalized juvenile periodontitis (GJP), and 23 adults with moderate to severe periodontitis were performed: (i) to determine the prevalence of a PMNL chemotaxis defect in a large group of LJP patients; (ii) to study PMNL chemotaxis in patients with other forms of severe periodontal disease; and (iii) to determine if the PMNL chemotaxis defect seen in LJP patients is a cell-associated defect or is mediated by humoral factors. The effect of periodontal treatment on PMNL chemotaxis was studied in nine LJP patients. The chemotactic response was measured with the Boyden chamber procedure, and patient's peripheral PMNL were compared with those of control subjects, using endotoxin-activated serum, bacterial factor, N-formylmethionyl-leucylphenylalanine, and leukocyte-derived chemotactic factor as the standard chemoattractants. Based upon statistical analysis of chemotaxis assays, most carried out on at least two and often three or more separate occasions, 26 of 32 LJP patients, 7 of 10 post-LJP patients, and 5 of 8 GJP patients exhibited cellular defects of chemotaxis, whereas only 2 of 23 of the patients with adult periodontitis exhibited depressed chemotaxis. Elevated PMNL chemotaxis was occasionally found in subjects with juvenile periodontitis (2 of 32 with LJP and two of eight with GJP); however, it was found in a significant number (10 of 23) of patients with adult periodontitis. In eight of nine LJP patients, depressed PMNL chemotaxis was observed before and after periodontal therapy. The results indicate that the PMNL chemotaxis defect observed in juvenile periodontitis is due to a cell-associated defect of long duration. These studies suggest that the PMNL plays a major protective role against periodontal infection and that the cellular chemotactic defects and may predispose subjects to LJP.

Bacteria and bacterial products have been implicated as important etiological agents in the development of gingival and periodontal disease (11, 23, 35, 40, 41, 44, 48). In the presence of dental plaque, an inflammatory infiltrate is usually present in the gingival tissues, with mononuclear phagocytes, lymphocytes, and polymorphonuclear leukocytes (PMNL) comprising the majority of the infiltrate (37, 38). Cells of lymphocytic origin predominate in the inflamed connective tissue, but the PMNL comprise about half of the leukocytes in the junctional epithelium, and PMNL are prominent cells in the gingival crevice or periodontal pocket. The total number of PMNL in the junctional epithelium increases with the severity of inflammation (34, 36). The cell migration to the area may be in response to chemotactic substances elaborated by bacteria directly or substances such as endotoxin and bacterial antigens that activate the complement system and produce chemotactic factors (21, 28). The gingivitis lesion progresses to an advanced gingivitis lesion which may or may not progress to periodontitis (33). Conceivably, failures of PMNL chemotactic response in the early stages of gingivitis could lead to more rapid advance of the lesion to destructive periodontitis.

Many disorders of PMNL migration have been identified, including decreased locomotor capability of the cell, lowered response to chemoattractants, and the presence of inhibitors to chemotaxis (10, 26, 49). Patients with PMNL migration disorders characteristically have increased susceptibility to infections and, of particular interest, there is severe periodontal disease associated with several of these disorders (16, 18, 24, 31).

Recently, several investigators have demonstrated defective PMNL chemotaxis in a number of patients with periodontosis or localized juvenile periodontitis (LJP), or with rapid, early-onset periodontitis (3, 5, 12, 20) who otherwise appear healthy. Monocyte chemotaxis in most
of these patients is normal (3). The results of these studies implicate both an intrinsic cellular defect of PMNL chemotaxis and serum defects. However, the incidence of humoral inhibitors of chemotaxis in LJP or rapid, early-onset periodontitis is not established.

The present investigation was undertaken to: (i) study the prevalence of a PMNL chemotaxis defect in a large group of LJP patients; (ii) study PMNL chemotaxis in patients with other forms of severe periodontal disease; and (iii) determine if the PMNL chemotaxis defect seen in LJP patients is a cell-associated defect or is mediated by humoral factors. The groups consisted of young patients with LJP, adults with a history of LJP, young patients with generalized juvenile periodontitis (GJP), and adults with moderate to severe periodontitis in which the disease was considered clinically consistent with patient age, plaque accumulation, and occlusion. A group consisting of periodontally healthy subjects served as controls.

MATERIALS AND METHODS

Patient groups. All patients were obtained from the patient population of the State University of New York at Buffalo School of Dentistry and affiliated hospitals. Informed consent was obtained from all patients or, in the case of minors, from their parents or legal guardians. A complete medical history and clinical laboratory procedure including CBC, SMA-12, prothrombin time, and urinalysis were completed on all patients. Patients in all groups were chosen for study based upon medical histories indicating the absence of clinical disease and laboratory tests within normal range. Health questionnaires administered to all patients and controls on each day of PMNL function testing elicited information regarding cigarette use, drug and alcohol consumption, illnesses, and blood loss; for females, additional information regarding birth control medication, menstruation, and pregnancy was gathered. Subjects were not tested who were ill, smoked more than 10 cigarettes, consumed more than 2 ounces (ca. 60 ml) of alcohol, or were taking any medication within the 24-h period before the planned test. Each patient completed a detailed diabetes history which elicited information about the occurrence of diabetes in parents, siblings, or grandparents.

Group I, LJP patients, comprised 32 young patients exhibiting alveolar bone loss localized to molars and incisors and not more than two additional teeth (≤14 teeth including 12 molars and incisors). The mean age was 21.9 years, with a range of 15 to 30 years. There were 12 males and 15 female patients, and the racial distribution was 15 Caucasian and 17 black. This group includes nine which were reported earlier (3) but were restated for this study.

Group II, post-LJP patients, consisted of 10 patients (2 male and 8 female; 5 Caucasian and 5 black). The mean age of these patients was 41.6 years, with a range of 33 to 56 years. These patients exhibited markedly greater alveolar bone loss in the first molar or incisor region (although bone loss was more generalized than in group I) and often had a history of LJP. In four of the patients in this group, we were able to conclusively document prior existence of LJP from radiographs taken in their teenage years.

Group III, GJP patients, exhibited severe alveolar bone loss (>14 teeth and no clear pattern of localization) and were younger than 30 years of age (mean, 21.3; range, 17 to 29) There were eight patients in this group (all female; three Caucasian and five black).

Group IV, the adult periodontitis group, consisted of 23 patients, 11 male and 12 female, who exhibited generalized severe alveolar bone loss with multiple vertical osseous defects; they had a mean age of 41.8 years, with a range of 28 to 62 years. All the patients in this group were Caucasian.

The control group consisted of 85 healthy individuals from laboratory and dental school populations who had no radiographic evidence of bone loss or evidence of periodontal disease other than mild gingivitis. Patients and controls were age and sex matched for most experiments.

Isolation of PMNL and chemotaxis assay. PMNL were isolated and chemotaxis was performed as previously described (46). Briefly, PMNL were separated from heparinized venous blood by Ficoll-Hypaque centrifugation, washed twice in phosphate-buffered saline, and suspended in Gey balanced salt solution (GIBCO Laboratories, Grand Island, N.Y.) containing 2% bovine serum albumin (Sigma Chemical Co., St. Louis, Mo.) at a concentration of 2.5 × 10⁶ cells/ml. The cell suspension was placed in the upper compartment of a modified Boyden chamber separated by a 5-µm micropore filter (Sartorius Membranfilter GmbH, Göttingen, Federal Republic of Germany). The lower compartment contained either endotoxin-activated serum (EAS), Escherichia coli culture supernatant called bacterial factor (BF), the synthetic chemotactic peptide N-formyllimethionylleucylphenylalanine (PMLP), or lymphocyte-derived chemotactic factor, all prepared as previously described (46). Chemotaxis was evaluated by counting the number of cells that accumulated on the distal surface of the filter after a 60-min incubation. Ten high-power fields (×400) were counted for each filter. Each cell population was tested in triplicate chambers. Statistical significance of the difference between patient and control on any given day was determined by analysis of variance (46). Most patients were tested on at least two and often three or more separate occasions with two or three different chemotactic agents on each occasion.

Day-to-day variability of absolute values for chemotaxis precluded pooling of patient group data; therefore, nonparametric statistics were applied to evaluate patient population differences as follows: a patient’s chemotactic response was graded as depressed (−1), normal (0), or elevated (+1), based upon the statistical analysis of the comparison with the paired control. Differences that were not significant at the 5% level were graded as normal. A mean value for the patient response was obtained for each chemotactic agent.
tested by averaging the nonparametric grades for that agent tested on several occasions and then the mean value of all agents obtained for each patient. Based upon the overall mean of nonparametric grades ±5%, the expected error (see Results), each patient was categorized as depressed, normal, or elevated. All experiments are reported.

Population differences were assessed by using a chi-square analysis by comparing the observed population distribution to the expected population distribution (43). Thirty-six controls were paired, and their chemotaxis results were compared to assess the accuracy of the assay. The expected population distribution was calculated from the number of statistically significant differences observed when the 18 paired controls were tested with three different chemotactic agents, for a total of 54 paired control tests.

**Serum inhibitors of chemotaxis.** Cell-directed inhibitor (CDI) is a heat-stable substance which interacts directly and reversibly with PMNL to block chemotaxis (28). The presence of CDI in serum was evaluated by preincubating isolated PMNL in 100 μl of fresh serum for 30 min at 37°C. Cells were then diluted to 50 ml with phosphate-buffered saline, centrifuged, suspended in Gey medium as above, and assayed. Normal cells were placed in patient serum to assess CDI activity; autologous serum served as control. Washed cells from patients were placed in normal serum to assess recovery of chemotactic response (26). Cells in autologous serum served as control. The A, B, and O blood types for patient and control were matched for these experiments to minimize the potential for agglutination of PMNL.

**Checkerboard experiments.** The effects of various concentrations of chemotactic factor above and below the filter were investigated, using an experimental protocol similar to that described by Zigmond and Hirsch (51). Random migration was studied in the absence of chemotactic factors; chemokinesis was studied when equal concentrations of chemotactic factor were above and below the filter; and chemotaxis was studied when a higher concentration of chemotactic factor was present in the lower compartment. Negative chemotaxis (higher concentration of chemotactic factor in the upper cell compartment) was not studied. All experiments were incubated for 60 min. The leading-front technique (51) was used to quantitate random migration and chemokinesis, since cells do not migrate to the distal surface in 60 min under those conditions. Previous work has demonstrated that the automatic counting techniques we used are comparable to visual measurements (45).

**Dose response and kinetics of the PMNL chemotaxis defect.** The response of LJP patient cells and normal control cells was evaluated at various concentrations of chemotactic factor (EAS) and at various incubation times. The patient and normal cells were always assayed under identical conditions.

**Effect of therapy on the PMNL chemotaxis defect.** PMNL chemotactic response was evaluated after conventional therapy in nine LJP patients. Treatment consisted of repeated scaling and root planing and in some cases antibiotic therapy (2 weeks of tetracycline administration, 1 g/day orally at 6-week intervals for the first 15 months). Chemotaxis was evaluated from 6 months to 2 years after such therapy was initiated. Since tetracycline has been reported to affect PMNL chemotaxis (27), patients in this series were tested several weeks after the cessation of tetracycline administration.

### RESULTS

**Control group.** The chemotactic response to three different chemotactic agents (EAS, BF, FMLP) was assessed in 18 pairs of control subjects. In all, 54 paired PMNL chemotactic tests were analyzed. Significance of differences at the 95% confidence level was determined by analysis of variance. Nine of the 54 paired control tests were significantly different from each other, and these differences were normally distributed, with four showing elevated chemotaxis and five showing depressed chemotaxis (Fig. 1). Of the tests that were different, no member of a pair of controls was different with more than one agent at a time, suggesting experimental error rather than true differences between the PMNL. Based upon this analysis, the expected values for the chi-square analysis for population differences were computed, and an experimental error of 8% of the tests showing depressed chemotaxis and 8% of the tests showing elevated chemotaxis was established.

**Group I.** The PMNL chemotaxis of the LJP patients was compared, on a day-to-day-basis, with that of periodontally normal, healthy, age-
and sex-matched controls. Significant differences between patient and control for each test were determined by analysis of variance. It was found that in 26 of 32 LJP patients, PMNL chemotaxis was significantly depressed compared with matched controls. Individual LJP patients were frequently depressed to all agents tested (Table 1). When taken as a group, the chemotactic response of LJP patients was statistically significantly depressed, with a $P$ value of less than 0.001 (Fig. 2). There was no difference in the percentage of defective subjects when tested with different chemotactic agents; however, chemotactic depression was most consistently observed with EAS.

Of the 26 LJP patients who are described as having depressed chemotaxis, 8 were depressed to all agents every time they were tested. The others were depressed a majority of times tested but did test normal to individual agents occasionally (Fig. 3).

The LJP group was 60% black, whereas the control group was >95% Caucasian. To assess the possibility of racial differences accounting for the observed distribution of PMNL chemotaxis defects, the two racial groups were analyzed separately. Chi-square analysis indicated that there was no relationship between race and PMNL chemotaxis ($P > 0.05$) for this group of subjects.

It is interesting to note that two patients with LJP had an elevated chemotactic response. One of these patients, a 22-year-old female, was tested four times with three different agents against four different control subjects over an 8-month period. The chemotactic response of the patient was never lower than that of the control and was significantly elevated in the majority of tests. Clinical data were obtained on this patient, who was treated by scaling, root planing, and oral hygiene measures during the 8-month period in question. There was no correlation found between chemotactic response and clinical condition of this patient. The other patient, also a female, exhibited elevated PMNL chemotaxis; however, the degree or consistency of elevation was not nearly as marked as with the first.

Of the four LJP patients who appeared to exhibit normal PMNL locomotion, two females, aged 19 and 29, tested normal on all occasions. One female and one male, aged 23 and 28, tested erratically, showing significant elevation with some agents and significant depression with others, often on the same day.

**Group II.** Of the 10 patients in the post-LJP group, 7 were found to exhibit depressed PMNL chemotaxis (Fig. 4). The four patients in this group with documented previous LJP all ex-

![Fig. 2. Chemotactic responsiveness of PMNL from LJP patients. Patients were designated as depressed, normal, or elevated as described in the text. Statistical significance of differences between individual patients and controls was assessed by analysis of variance. Statistical significance of the number of patients with depressed chemotaxis was assessed by chi-square analysis (n = total number of patients).](http://iai.asm.org/)

**Table 1. Chemotaxis of PMNL from LJP patients**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Chemotaxis (% of Control) in patient no.:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>1  2  3</td>
</tr>
<tr>
<td></td>
<td>12-21-77 3-6-78 12-21-78 3-6-78 10-6-76 5-5-77 6-2-77</td>
</tr>
<tr>
<td>EAS</td>
<td>51' 32' 46' 28' 24' 9' 7'</td>
</tr>
<tr>
<td>BF</td>
<td>17' 23' 10' 20' 14' ND' ND</td>
</tr>
<tr>
<td>FMLP</td>
<td>12' 24' 9' 19' 10' 46' 38</td>
</tr>
</tbody>
</table>

* Representative data from 3 of the 32 LJP patients tested. Patients 1 and 2 exhibited depressed chemotaxis to all agents on each day tested. Patient 3 was not significantly depressed on all occasions; however, all tests were below control values.

† Day of test.

Significantly different from control as assessed by analysis of variance at $P \leq 0.05$.

ND, Not done.
Iodontal therapy.

8-month antaxis. Group 10 showed depressed chemotaxis. Group 128 exhibited elevated chemotaxis of patients). The dose-response behavior of the same patient's PMNL to EAS was evaluated, and depressed chemotaxis was observed at all concentrations tested. Similar results were obtained on six randomly selected LJP patients compared with normal controls.

Of the 26 LJP patients exhibiting depressed chemotaxis, five of the eight patients showed depressed chemotaxis, one tested normal, and two showed elevated chemotaxis.

Group IV. Eleven of the 23 patients in the adult periodontitis group were normal, and two showed depressed chemotaxis. However, a significant number ($P < 0.001$) of patients in this group exhibited elevated chemotaxis (Fig. 5). Of the 10 patients that exhibited elevated chemotaxis, 4 were tested on 6 or 7 separate days over an 8-month period both before and during periodontal therapy. The number of elevated tests to individual agents exhibited by each patient over this period of time was significant ($P < 0.05$) and did not appear to relate to periodontal disease status. Other elevated patients in this group, although tested fewer times, showed consistent elevation of PMNL chemotaxis.

**Serum effects on PMNL chemotaxis.** CDI was found in the serum of 4 of 21 randomly selected LJP patients with chemotaxis defects ($P > 0.05$). LJP patient cells did not recover activity in normal serum.

**Checkerboard experiment.** The checkerboard experiment compared six randomly selected LJP patients with six separate controls, and depression of chemotaxis of the LJP patients' neutrophils was observed. The random migration of LJP PMNL was the same as for controls, and the chemotaxis defect was apparent at all chemotactic factor concentrations tested (Table 2).

**Characterization of the PMNL chemotaxis defect.** The depressed chemotactic response of an LJP patient was observed at incubation times ranging from 30 to 120 min (Fig. 6). The dose-response behavior of the same patient's PMNL to EAS was evaluated, and depressed chemotaxis was observed at all concentrations tested. Similar results were obtained on six randomly selected LJP patients compared with normal controls.
PMNL chemotaxis, 9 were tested both before and after conventional therapy to determine whether the disease state was causing PMNL dysfunction or whether the PMNL migration defect was independent of disease status. The chemotaxis defect persisted after therapy in eight of the nine patients tested \((P < 0.001; \text{Table } 3)\).

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Bottom compartment/top compartment}\textsuperscript{b} & 0:0 & 1:1 & 2:2 & 4:4 \\
\hline
103.5 ± 7.7 & 105.2 ± 2.2 & 120.8 ± 6.2 & 133.7 ± 8.3 \\
105.5 ± 7.5 & 105.3 ± 3.6 & 117.6 ± 5.9 & 133.7 ± 0.2 \\
\hline
\end{tabular}
\caption{Checkerboard experiment\textsuperscript{a}}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Bottom compartment}\textsuperscript{c} & 0 & 1 & 2 & 4 \\
\hline
7.3 ± 0.25 & 30.1 ± 6.4 & 128.6 ± 24.6 & 108.3 ± 14.8 & 84.7 ± 19.6 \\
24.3 ± 7.3 & 30.7 ± 6.5 & 38.4 ± 9.2 & 63.8 ± 15.8 & 106.1 ± 12.5 \\
& 23.3 ± 1.6 & 32.6 ± 4.5 & & \\
\hline
\end{tabular}
\caption{Representative experiment in which LJP and control PMNL are compared. LJP values appear at the top of each cell, and normal values are at the bottom.}
\end{table}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Chemotaxis (% of control)} & \textbf{Before} & \textbf{After} & \textbf{Agent} \\
\hline
1 & 16\textsuperscript{a} & 70 & FMLP & \\
2 & 20\textsuperscript{a} & 77\textsuperscript{a} & FMLP & \\
3 & 10\textsuperscript{a} & 38 & FMLP & \\
4 & 46 & 27\textsuperscript{a} & FMLP & \\
5 & 23 & 74\textsuperscript{a} & FMLP & \\
6 & 77\textsuperscript{b} & 99 & FMLP & \\
7 & 50\textsuperscript{a} & 51\textsuperscript{a} & FMLP & \\
8 & 22\textsuperscript{a} & 17\textsuperscript{b} & FMLP & \\
9 & 21\textsuperscript{b} & 54\textsuperscript{b} & FMLP & \\
\hline
\end{tabular}
\caption{Chemotactic response of LJP patients before and after periodontal therapy\textsuperscript{a}}
\end{table}

\textbf{DISCUSSION}

The present study demonstrates that in a group of 32 LJP patients, most (81%) exhibited a PMNL chemotaxis defect. These results extend and confirm earlier studies in which defective PMNL chemotaxis was reported in nine patients with LJP by Cianciola et al. (3) in seven of nine LJP patients by Clark et al. (5), and in 12 of 14 patients by Lavine et al. (20).

Previous reports discuss a group of patients whom we classify as having GJP (rapid, early-onset periodontitis). The criteria established for placing patients into this group are similar among investigators; however, firm criteria for diagnosis are not available. The present study describes the presence of a PMNL chemotaxis defect in young patients with GJP. The high incidence (62%) of impaired PMNL chemotaxis in this group is consistent with the concept that the two disease states are related and that LJP may progress to GJP in certain cases (9).
Twenty-three adult patients with severe periodontitis were studied, and 43% exhibited elevated chemotaxis. Four of the patients exhibited elevated chemotaxis when tested repeatedly over an 8-month period, during which time they underwent conventional periodontal therapy. Hill et al. (13, 14, 17) have reported similar elevations in chemotactic response during episodes of acute bacterial infection. A possible mechanism may be a shift within the PMNL population to more mobile cells (19) in response to infection. We were unable to discern any pattern between chemotactic response and periodontal clinical indices. However, the standard periodontal clinical indices measure surface inflammation and may not be indicators of infection of deeper periodontal structures. To determine whether PMNL chemotaxis may be used as an indicator of periodontal infection or activity of disease requires further study.

The observed PMNL chemotaxis defect could be due to an intrinsic cellular defect or to humorally mediated effects. Studies of patients with recurrent infections (6) and hyperimmunoglobulinemia E (7, 15) indicate an intrinsic cellular defect in which humoral factors appear to have no role. In some diseases where the intrinsic cellular defect is permanent, such as Chediak-Higashi syndrome (4), random migration is normal. In other conditions of intrinsic cellular defects, such as measles (1) or hypovitaminosis D (rickets) (24), random migration is also defective, implying a generalized locomotion defect which is reflected in chemotaxis rather than a specific defect in the directional response to chemotactic agents.

Study of the serum of cirrhotic patients (8, 25) revealed a cell-directed inhibitor of chemotaxis which reversibly binds to PMNL. This naturally occurring factor is characterized by its effect on normal cells and the ability of neutrophils from cirrhotic patients to recover normal activity in normal serum. This factor may be in excess in serum, or its natural antagonist may be deficient (42, 45). In studies where the antagonist is deficient, normal plasma added to the deficient PMNL will correct the defect, but patient serum or plasma has no effect on normal cells. Another type of serum inhibitor has been described that inactivates chemotactic factors from complement or bacteria (2, 49, 50) (CFI). There is also evidence of natural inhibitors to these chemotactic factor inactivators (47).

The present studies of LJP patients revealed that the defect was detected when the PMNL were tested in a serum-free system. Additionally, patient serum had no effect on normal cells in 81% of the cases tested, and patient cells did not recover chemotactic activity when incubated in normal serum. This evidence strongly suggests that there is an intrinsic PMNL defect in chemotaxis and that for most patients CDIs do not contribute to the PMNL chemotaxis defect.

The presence of humoral inhibitors was reported in two earlier studies, although the incidence of these inhibitors differed somewhat. Clark et al. (5) reported five of nine LJP patients with CDI in their serum and four of nine with reduced chemotactic factor generation. Lavine et al. (20) found that 2 of 14 LJP patients had CDI, 1 of 14 had CFI, and 1 of 14 had reduced chemotactic factor generation.

Further evidence as to the nature of the chemotaxis defect was obtained from the study of post-LJP patients. The finding of a PMNL chemotaxis defect in these patients in the absence of CDI provides indirect evidence that the chemotaxis defect observed in LJP patients persists for many years. This concept is further supported by the fact that treatment of the disease did not reverse the defect in 91% of the cases treated. These data suggest that the chemotaxis defect in LJP patients is not cell associated and long lasting.

We have demonstrated PMNL chemotaxis defects in periodontal disease-free younger siblings of LJP patients, suggesting that the chemotaxis defect is familial and may precede overt disease. If this is indeed the case, the neutrophil dysfunction may predispose or increase susceptibility to LJP (L. J. Cianciola, R. J. Genco, M. R. Patters, and J. McKenna, Am. Assoc. Dent. Res. Abstr., 1977). Genetic determination of neutrophil chemotaxis defects has been described in several instances, for example, in the family described by Nietherammer et al. (32) in which depressed neutrophil chemotaxis was inherited as an autosomal recessive characteristic.

Random migration as measured by the checkerboard experiments (Table 2) show that this parameter is normal in LJP patients. This information plus the chemotaxis data suggest that the defect is one of directed migration, namely, the inability to respond to a chemotactic gradient. In addition, the kinetic and dose-response data (Fig. 6) demonstrate that the chemotaxis defect is not simply a function of time of incubation or concentration of chemotactic factor used in the in vitro tests. The fact that the patient's cells continue to migrate, accumulate, and exhibit increased locomotion in increased chemotactic factor concentrations suggest that the PMNL are capable of normal locomotion, but that oriented or directed locomotion (true chemotaxis) is compromised.

Evidence that the PMNL chemotaxis defect
in LJP patients is a long-lasting, cell-associated defect of cell migration in response to chemotactic factor gradients can be summarized as follows: (i) the defect is observed with washed cells in a serum-free system; (ii) patient serum does not affect chemotaxis of normal cells; (iii) patient cells do not recover in normal serum; (iv) random migration is normal; (v) the defect persists after conventional therapy; and (vi) the defect persists into adulthood in post-LJP patients.

Further studies are underway to define the biochemical basis of this defect.

The study of PMNL chemotaxis defects in humans may be limited by illness or death of the patient. The LJP group is an excellent group for the study of cell-associated cellular defects of chemotaxis and may aid in the further description of the mechanisms of cell movement, since the patients appear to be healthy except for the periodontal disease, and the PMNL defect appears to be of long duration. This study and others (3, 5, 11, 19) suggest that the PMNL contributes to more severe disease.

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LITERATURE CITED


