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Research Article

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Monocyte Function in the Acquired Immune Deficiency Syndrome Defective Chemotaxis

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Abstract. The ineffective immune response in patients with the acquired immune deficiency syndrome (AIDS) contributes to severe and widespread infections and unrestricted growth by certain tumors. To determine whether monocyte dysfunction contributes to this immunosuppressed condition, we investigated monocyte chemotaxis in patients with AIDS. Using three different chemotactic stimuli, *N*-formylmethionylleucylphenylalanine, lymphocyte-derived chemotactic factor, and C5a des Arg, we studied the chemotactic responses of monocytes from seven homosexual men with AIDS, three homosexuals with lymphadenopathy and an abnormal immunological profile, seven healthy homosexual men, and 23 heterosexual control individuals. Monocytes from each of the AIDS patients with Kaposi's sarcoma and/or opportunistic infection exhibited a marked reduction in chemotaxis to all stimuli compared with the healthy control subjects. The reduced chemotactic responses were observed over a wide range of concentrations for each stimulus. Monocytes from AIDS patients who had clinically apparent opportunistic infection(s) exhibited a greater reduction in monocyte migration to all three stimuli than monocytes from the AIDS patient with only Kaposi's sarcoma. Monocytes from each of three homosexuals with lymphadenopathy and an abnormal immunological profile exhibited decreased chemotactic responses that were intermediate between those of the AIDS patients and the healthy heterosexual control subjects. In contrast to these findings, monocytes from each of seven healthy homosexuals exhibited nor-

mal chemotactic responses to the same stimuli. In addition, monocytes from AIDS patients exhibited reduced chemotaxis to soluble products of *Giardia lamblia*, one of several protozoan parasites prevalent in AIDS patients.

Thus the immune abnormality in AIDS, previously thought to involve only the T-, B-, and natural killer lymphocytes, extends to the monocyte-macrophage. Defective monocyte migratory function may contribute to the depressed inflammatory response to certain organisms and to the apparent unrestricted growth of certain neoplasms in patients with AIDS.

Introduction

The acquired immune deficiency syndrome (AIDS)¹ is a new disease that is characterized clinically by a high incidence of certain neoplasms particularly Kaposi's sarcoma (KS) and/or opportunistic infections (OI) and immunologically by profound immunosuppression (1-5). The disease has a predilection for male homosexuals, intravenous drug abusers, certain Haitians, and residents of certain developing countries (1-6). Thus far there have been no reports of spontaneous or therapeutically induced remission in this disease. The immunosuppression was thought initially to be confined to lymphoid cell dysfunction as evidenced by depressed *in vivo* and *in vitro* T lymphocyte function and by a depletion of the helper/inducer T cell subset leading to a reversal of the T helper to T suppressor ratio (7). In addition, cytotoxic T cell and natural killer (NK) cell

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1. *Abbreviations used in this paper:* AIDS, acquired immune deficiency syndrome; BSS, balanced salt solution; C5a, C5a des Arg, CMV, cytomegalovirus; DMEM, Dulbecco's Modified Eagle's medium; FMLP, *N*-formylmethionylleucylphenylalanine; KS, Kaposi's sarcoma; LDCF, lymphocyte-derived chemotactic factor; MNL, mononuclear leukocyte; NK, natural killer; OI, opportunistic infection; VB, veronal buffer; WBC, leukocyte.

activity are reduced in patients with AIDS (8). Recently, B lymphocytes from AIDS patients were shown to exhibit marked polyclonal activation as manifested by spontaneous Ig production and defective proliferation responses to T cell-independent B cell mitogens (7). The immunosuppression in AIDS thus appears to involve both T and B lymphocyte and NK cell function.

In the setting of this profound immunosuppression, infection with a wide variety of organisms occurs in patients with AIDS. These organisms include the viruses, cytomegalovirus, Epstein-Barr virus, and *Herpes simplex*; the bacteria, *Mycobacterium avium intracellulare*; the fungi, *Candida albicans* and *Cryptococcus neoformans*; and the protozoans, *Pneumocystis carinii*, cryptosporidia, *Toxoplasma gondii*, *Isospora belli*, *Entamoeba histolytica*, and *Giardia lamblia* (1-6, 9). Although infections with all of these organisms may occur secondary to an underlying primary immunosuppression, certain of them such as cytomegalovirus can induce immunosuppression (10, 11).

The monocyte-macrophage, which has received little attention in AIDS, is involved in the host response to many of the above organisms and participates in many T and B lymphocyte activities (12-16). Therefore, we have initiated a series of investigations into monocyte-macrophage function in patients with AIDS. In the current report, we investigated monocyte chemotactic responses to a variety of defined chemoattractants

in vitro. We report that monocytes from AIDS patients exhibit a marked defect in chemotactic function. This defect may contribute to the depressed immune response to many of the organisms prevalent in AIDS patients. Thus, the immune defect in AIDS, previously thought to involve only the T and B lymphocyte, extends to the monocyte-macrophage.

Methods

Subjects. Ten homosexual males were studied: seven fulfilled the Centers for Disease Control's criteria of AIDS (17) and three had lymphadenopathy with an abnormal immunological profile. The following three groups of age and sex-matched control subjects also were studied: group 1, 23 healthy heterosexual males; group 2, seven healthy homosexual males without evidence of lymphadenopathy or AIDS; and group 3, 12 patients with diseases and/or therapy to control in part for conditions and/or therapy often associated with AIDS. These patients included three with bacterial sepsis on broad spectrum antibiotic coverage, three with Hodgkins' disease on chemotherapy, one with diffuse histiocytic lymphoma on chemotherapy, and five who were anergic as determined by negative skin test reactivity. The anergic patients included three with active tuberculosis on antituberculous drugs, one with sarcoidosis, and one with Wegener's granulomatosis on immunosuppressive therapy. The pertinent clinical and laboratory features of the homosexual patients, the healthy control subjects, and the control patients are presented in Table I.

Mononuclear cell suspensions. Mononuclear leukocytes (MNL)

Table I. Clinical and Laboratory Features of Patients and Control Subjects

Patient no.	Kaposi's sarcoma	Opportunistic infections*	WBC‡	Lymphocytes		Monocytes	
				Total‡	%§	Total‡	%§
1	-	CA, MAI, CMV viremia/esophagitis	2,000	240	12	40	2
2	-	PCP, MAI, HS	2,600	390	15	78	3
3	+	CA, PCP, CS	5,600	1,120	20	280	5
4	+	CN, PCP, HS, CMV viremia	3,000	1,050	35	270	9
5	+	-	5,500	2,475	45	275	5
6	+	CN, MAI, CS, PCP	3,200	384	12	256	8
7	+	PCP, CMV viremia/esophagitis, HS ulcer	4,700	141	3	376	8
M(±SEM)			3,800 (±548)	829 (±311)	20 (±6)	225 (±46)	6 (±1)
8	-	-(LA)¶	4,700	893	19	188	4
9	-	-(LA)	5,900	2,596	44	590	10
10	-	-(LA)	4,400	1,320	30	352	8
M(±SEM)			5,200 (±458)	1,603 (±512)	31 (±7)	377 (±117)	7 (±2)
Healthy homosexuals**			5,733 (±336)	2,035 (±368)	36 (±6)	222 (±46)	4 (±1)
Healthy heterosexuals**			7,129 (±585)	2,378 (±296)	34 (±3)	431 (±55)	6 (±1)
Control patients**			7,770 (±2,150)	678 (±281)	9 (±2)	483 (±120)	10 (±5)

* Abbreviations used in this table: CA, *C. albicans*; CN, *C. neoformans*; HS, *H. simplex*; MAI, *M. avium intracellulare*; PCP, *P. carinii* pneumonia. ‡ Cells/mm³. § % total WBC. || (-) absent, (+) present. ¶ LA, lymphadenopathy. ** M(±SEM).

were isolated from heparinized blood by Ficoll-Hypaque density gradient sedimentation (18) and suspended in Dulbecco modified Eagle's medium (DMEM, HEM Research, Rockville, MD) containing 100 U/ml penicillin, 100 µg/ml streptomycin, and 2 mM glutamine. Total MNL and monocyte numbers were determined by Coulter Counter (Coulter Electronics, Inc., Hialeah, FL) and esterase-stained cytospin preparations (19). Suspensions of patient and control MNL were adjusted to yield equal numbers of monocytes (1×10^6 /ml) for each assay.

Chemotactic stimuli. The following products were used as chemoattractants: the synthetic peptide *N*-formylmethionylleucylphenylalanine (FMLP, Peninsula Laboratories, San Carlos, CA) (20); human C5a des arginine (21, 22) prepared from endotoxin-activated human serum in the absence of carboxypeptidase inhibitors (22) and referred to as C5a; and lymphocyte-derived chemotactic factor (LDCF) (23), a 12,500-D heat stable lymphokine prepared from phytohemagglutinin-stimulated human peripheral blood mononuclear cell cultures. In addition, we used a soluble extract from the protozoan parasite, *G. lamblia*, which has defined chemotactic activity (24, 25). The isolation and culture of this organism (WB strain, American Type Culture Collection 30957) and the preparation of the soluble extract have been described previously (26, 27).

Chemotaxis assay. Patient and control mononuclear leukocytes were suspended in Gey's balanced salt solution (BSS; National Institutes of Health Media Unit) containing 2% bovine serum albumin, 100 U/ml penicillin, 100 µg/ml streptomycin, and 0.15 M HEPES and adjusted to a monocyte density of 1×10^6 /ml. The chemotactic stimuli diluted in Gey's BSS with veronal buffer (VB) were placed in the bottom wells of microchamber plates (Neuroprobe, Rockville, MD) that were separated from the upper wells by a polycarbonate filter with 5.0 µm pores (Neuroprobe) (28). Each chamber contained Gey's BSS with VB as a negative control that, along with the stimuli, was tested in triplicate. Following incubation for 90 min in a humidified atmosphere containing 5% CO₂, the filters were removed, fixed, and stained with Diff-Quik (American Scientific Products, Columbia, MD). The cells that had migrated through the filters were then enumerated with an Optomax Image Analyzer (Optomax Inc., Hollis, NH) using a neutral density filter system that readily distinguishes cells from filter pores. Chemotactic activity is defined as the mean (\pm SEM) number of monocytes that migrated through the filter pores in three standard fields determined at low magnification ($\times 16$) by the Image Analyzer, which encompasses most of the field for each of triplicate filters. Standard error of the mean of these nine determinations for each point was routinely $<10\%$ of the mean. Monocyte migration in the absence of stimulus was routinely <12 cells/field. In previous kinetic studies, monocytes were shown not to detach from the distal filter surface until after 2-h incubation. The 90-min incubation used in this study thus minimizes the possibility that differences in cell adherence affected migration.

Statistics. All data are presented as the mean (\pm SEM) number of monocytes that migrated. The mean chemotactic responses among the groups were tested for normality by the Wilk-Shapiro test, and the level of significance was determined using the equal variance and unequal variance *t* tests.

Results

Study population. The clinical and laboratory features of the AIDS patients and the control subjects are presented in Table I. Patients 1 and 2 had only OI whereas patient 5 had KS without clinical manifestation of OI. Cytomegalovirus was subsequently cultured from the urine of patient 5. Patients 3,

4, 6, and 7 had both KS and OI. These seven AIDS patients were leukopenic ($3,800 \pm 548$ leukocytes [WBC]/mm³) in comparison with seven age- and sex-matched healthy heterosexual control subjects ($7,129 \pm 585$ WBC/mm³), and nearly all AIDS patients had reduced absolute numbers of lymphocytes and monocytes. Although their mean percentage of lymphocytes ($20 \pm 6\%$) was reduced compared with that of the control subjects ($34 \pm 3\%$), the mean percentage of monocytes ($6 \pm 1\%$) was not reduced compared with that of the control subjects ($6 \pm 1\%$). The patients had not received nor were they receiving immunostimulatory therapy at the time this study was performed. One patient had received local radiation therapy and another patient had received local radiation therapy and chemotherapy. Four of the seven patients were receiving one or more antibiotics for their infections. Three homosexuals with only lymphadenopathy (patients 8–10) were also studied. The AIDS patients and the homosexuals with only lymphadenopathy had a depletion of the OKT4 lymphocyte subset leading to a reversal of the OKT4/OKT8 T lymphocyte ratio (data not shown).

The control groups, which consisted of 23 healthy heterosexual males, seven healthy homosexuals, three patients with sepsis, four patients with lymphoma, and five anergic patients (three with tuberculosis, one with sarcoidosis, and one with Wegener's granulomatosis) are described in the Methods. Pertinent laboratory data is presented in Table I where data for the patient control groups is summarized as control patients.

Defective monocyte migration in AIDS. Using three different stimuli, the chemotactic function of monocytes from AIDS patients with KS and/or OI and homosexual patients with lymphadenopathy was compared with that of the healthy homosexual and heterosexual control subjects. As shown in Fig. 1, peripheral blood monocyte chemotaxis was markedly reduced in the AIDS patients with KS and/or OI compared with that of the heterosexual control subjects. This reduction was observed for all three chemoattractants: FMLP ($P > 0.001$), and the inflammatory stimuli, LDCF ($P > 0.0001$), and C5a ($P > 0.0001$). The patients' mean monocyte migration responses to LDCF and C5a were $<20\%$ of the responses of monocytes from the normal subjects. Interestingly, monocyte migration to these stimuli was tested in an eighth patient who was thought initially to have AIDS because of the apparent presence of *M. avium intracellulare* in a lymph node and the history of intravenous drug abuse. Chemotactic activity was normal or near normal for all stimuli, and the individual was subsequently determined not to have AIDS based upon a normal lymphocyte profile and the presence of atypical mycobacterium in the lymph node. This patient's normal monocyte activity emphasizes the relationship between defective monocyte chemotactic function and the presence of the disease. This patient was subsequently excluded from the study.

The chemotactic activity of monocytes from the homosexuals with lymphadenopathy and an abnormal immunological profile was reduced, although not significantly, in response to FMLP, LDCF, and C5a compared with that of the healthy

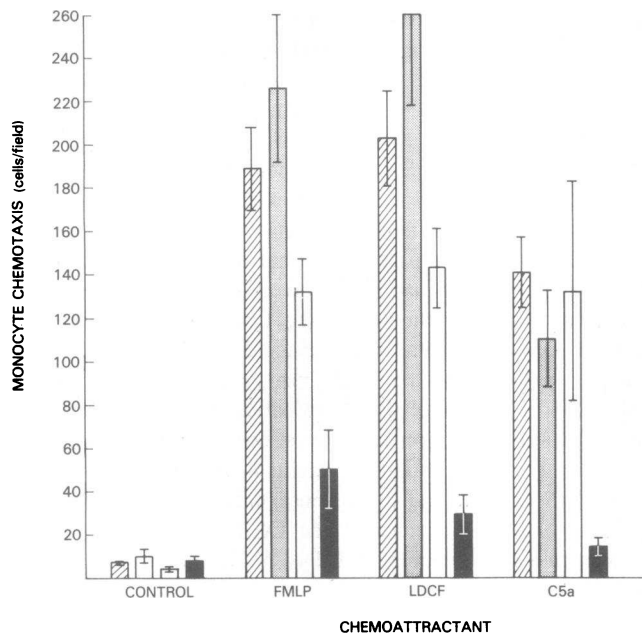


Figure 1. Chemotactic activity of monocytes from 23 healthy heterosexual males (□), 7 healthy homosexual males without AIDS (▨), 3 homosexuals with lymphadenopathy and an abnormal immunological profile (▤), and seven AIDS patients with KS and/or OI (■). Chemotactic stimuli included FMLP (10^{-7} M), LDCF (1:4 or 1:8), and C5a (1:5) as described in Methods. Values represent the mean (\pm SEM) monocyte migration for each population. The difference in monocyte chemotactic activity for the healthy heterosexual control subjects and the AIDS patients with KS and/or OI was statistically significant for each stimulus: FMLP, $P < 0.001$; LDCF, $P < 0.0001$; C5a, $P < 0.0001$. The reduction in activity for the homosexuals with lymphadenopathy and an abnormal immunological profile was not statistically significant in comparison with that of the healthy heterosexual control subjects.

heterosexuals (Fig. 1). There was thus a trend toward depressed monocyte chemotaxis in this subset of homosexual patients, but the depression was not as marked as for that of the homosexuals with AIDS.

In contrast to the responses by monocytes from homosexuals with AIDS, the monocytes from each of seven healthy homosexuals without AIDS exhibited normal chemotactic responses to FMLP, LDCF, and C5a compared with the responses by monocytes from the healthy heterosexual subjects (Fig. 1).

To determine whether the defective monocyte migration response was related to a disease-dependent alteration in sensitivity to the chemotactic stimuli, monocyte chemotaxis was evaluated for a wide range of concentrations of each stimulus. Figs. 2 and 3 present migration dose-response curves for two representative AIDS patients and their control subjects. Monocytes from each normal subject migrated towards each stimulus in a dose-dependent manner; migration increased with increasing concentrations of chemoattractants until excessive doses, which were associated with a decline in chemotaxis, were reached. In contrast, the ability of monocytes from AIDS patients with KS and/or OI to migrate to FMLP, LDCF, and C5a was impaired at all concentrations of these chemoattractants. The patient whose monocytes were still capable of a minimal chemotactic response (Fig. 2) had Kaposi's sarcoma but no clinical manifestation of opportunistic infections. This contrasts to the apparent inability of the monocytes from a patient representative of six patients with one or more opportunistic infections in addition to Kaposi's sarcoma to significantly migrate to any of the chemoattractants (Fig. 3).

Monocyte migration in non-AIDS patients. Monocytes from additional control groups that consisted of three patients with bacterial sepsis, four with lymphoma, three with tuberculosis, one with sarcoidosis, and one with Wegener's granulomatosis were also investigated for their chemotactic responses. As shown in Fig. 4, monocyte chemotaxis was not reduced in these groups compared with that of matched control subjects. Thus, sepsis, cancer, energy-associated conditions, and antibiotic

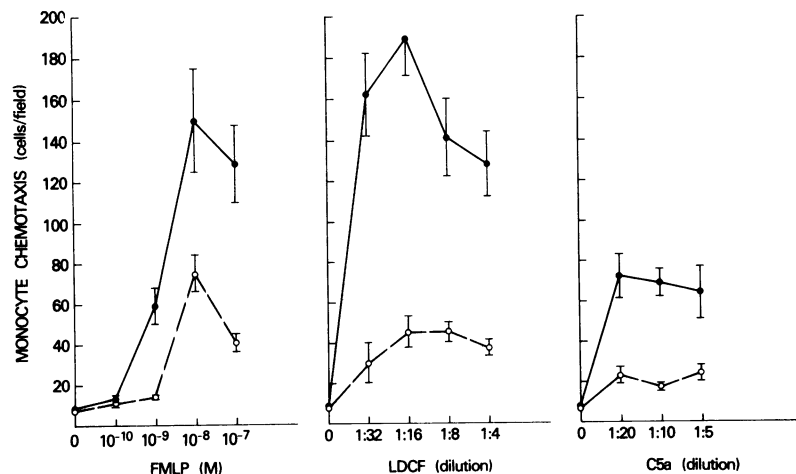


Figure 2. Chemotactic activity of monocytes from an AIDS patient with Kaposi's sarcoma (---○---) and his matched control subject (—●—) to FMLP, LDCF, and C5a over a range of concentrations. Values represent the mean (\pm SEM) number of monocytes that migrated in three fields for each of three filters.

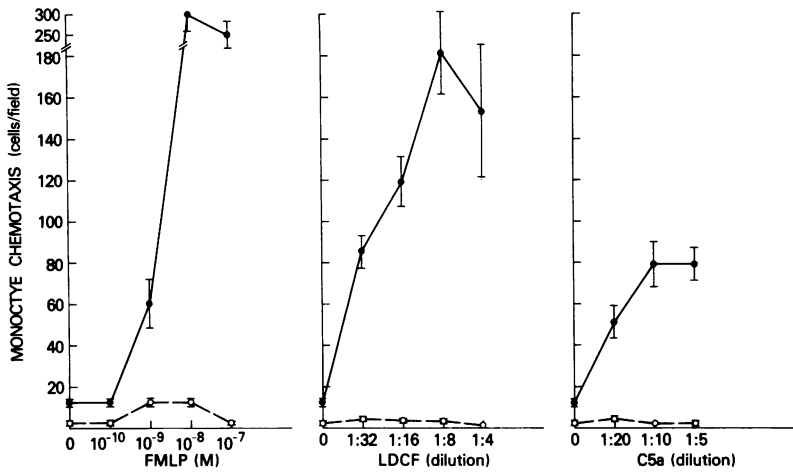


Figure 3. Chemotactic activity of monocytes from a representative AIDS patient with opportunistic infections and Kaposi's sarcoma (---○---) and his matched control subject (—●—) to FMLP, LDCF, and C5a over a range of concentrations. Values represent the mean (\pm SEM) number of monocytes that migrated in three fields for each of three filters.

therapy and/or chemotherapy in these patients did not depress the chemotactic function of their monocytes.

Effect of AIDS serum on monocyte migration. To determine whether a serum factor was responsible for the inhibition of monocyte migratory function in the AIDS patients, monocytes from a healthy control subject were preincubated with different concentrations of serum from three AIDS patients, three healthy homosexuals, and three healthy heterosexuals, and then tested for chemotactic function. As shown in Fig. 5, the migratory response of normal monocytes to C5a was not

inhibited by preincubation with serum from AIDS patients or healthy homosexuals. In addition, monocyte migration responses to FMLP and LDCF were not inhibited (data not shown). Serum from AIDS patients thus did not appear to contain a factor that inhibited monocyte chemotactic function.

Monocyte migration to the protozoan, *G. lamblia*. Recent evidence suggests that products of the extracellular protozoan parasite, *G. lamblia*, serve as chemoattractants for peripheral blood monocytes (25, 26). Since this mechanism of monocyte recruitment may participate in the host response to this parasite (27, 29, 30), and since AIDS patients commonly do not mount an adequate immune response to many protozoan parasites (31) and other infectious agents such as *M. avium intracellulare* (32), we investigated monocyte recruitment to-

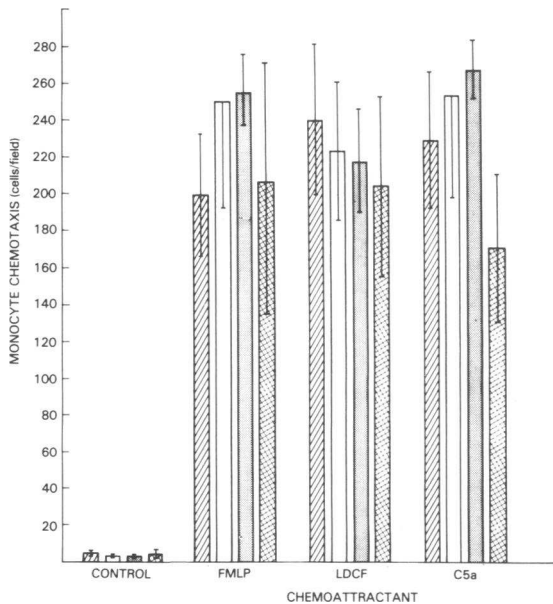


Figure 4. Chemotactic activity of monocytes from the following groups: seven healthy control subjects (\square); three patients with bacterial sepsis (\boxplus); four patients with lymphoma (\square); and five anergic patients including three with tuberculosis, one with Wegener's granulomatosis, and one with sarcoidosis (\blacksquare). Values represent the mean (\pm SEM) monocyte migration for each population.

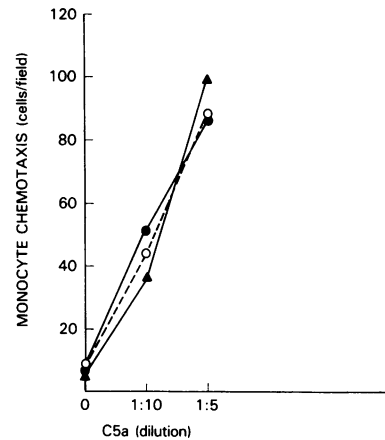


Figure 5. Chemotaxis of monocytes from a healthy control subject in response to C5a after a 2-h preincubation of suspensions of the monocytes in 20% sera from either three AIDS patients with KS and/or OI (—●—), three healthy homosexuals (---○---), or three healthy heterosexuals (—▲—). Monocyte migration was quantitated as described in Methods. Individual points represent the mean chemotaxis response of the three preincubated monocyte suspensions in each group.

wards soluble products of *G. lamblia*. As shown in Table II, monocytes from seven patients with AIDS exhibited significantly reduced migration to the optimal concentration of soluble *G. lamblia* in comparison to migration by monocytes from the control subjects and the healthy homosexuals ($P < 0.025$). Thus, in addition to an inability of monocytes from AIDS patients to respond normally to FMLP and inflammatory chemotactic stimuli (C5a, LDCF), monocytes from these individuals also do not respond normally to chemotactic products of a protozoan parasite.

Discussion

We investigated the chemotactic capability of peripheral blood monocytes from patients with AIDS. In contrast to the chemotactic responses of monocytes from healthy heterosexuals, monocytes from homosexuals with AIDS exhibited reduced directed migration to three distinct chemoattractants, FMLP, LDCF, and C5a. Monocyte chemotaxis in homosexuals with lymphadenopathy and an abnormal immunologic profile was intermediate between that of the AIDS patients and the healthy heterosexual control subjects. Monocyte chemotaxis in healthy homosexuals without evidence of lymphadenopathy or AIDS was not reduced.

The inability of monocytes from AIDS patients with KS and/or OI to respond to any of the three stimuli studied suggests that the defect is not limited to a single receptor-stimulus interaction, but is likely the consequence of a more generalized defect. In addition, since the suppressed chemotactic response occurred at all concentrations of each stimulus, the reduced migration is not the consequence of a shift in monocyte sensitivity to the stimuli. Also, the observations indicate that the reduced monocyte migration is due to a defect in monocyte chemotactic function and not a serum factor that inhibits chemotaxis. Furthermore, random migration of patients' monocytes exhibited no significant decrease or increase in activity in the absence of defined chemoattractants compared with that of the control subjects (Figs. 1-3, Table II).

Table II. Chemotactic Response to *G. lamblia* by Monocytes from Normal Subjects and Patients with AIDS

Stimulant	Chemotactic activity by group*		
	Normal subjects	Healthy homosexuals	AIDS patients
Control‡	9±1	7±2	8±2
<i>G. lamblia</i> §	45±10	41±11	13±5 [¶]

* No. = 7.

‡ Media alone.

§ A soluble extract of *G. lamblia* (50 µg/ml protein).

^{||} Mean number of cells per field±SEM.

[¶] Statistically different from the normal subjects and the healthy homosexuals ($P < 0.025$).

Monocytes from patients with sepsis, lymphoma, and anergy-associated conditions did not exhibit defective chemotactic function, even in the setting of in vivo antibiotic therapy and chemotherapy. Also, monocytes from the three AIDS patients with KS and/or OI who were not receiving antibiotics exhibited defective migratory responses comparable to those of the four AIDS patients receiving antibiotics. These observations suggest that the defective chemotactic function that we have observed in AIDS patients with KS and/or OI is not solely the consequence of bacterial infections, neoplasms, anergy, chemotherapy, or drug therapy.

In addition to impaired chemotaxis to FMLP, C5a and LDCF, monocytes from the AIDS patients were defective in their migration response to *G. lamblia*. Patients' monocytes thus exhibited impaired chemotaxis to the inflammatory stimuli (LDCF and C5a), the bacterial analogue FMLP, as well as products of a protozoan parasite. This defect in migratory capability could contribute to the reduced immune-mediated inflammatory reaction to some organisms that has been observed in patients with AIDS. For example, *M. avium intracellulare*, which occurs frequently in AIDS patients, elicits minimal or no granulomatous reaction (32). A potential mechanism for this impaired granuloma formation is that as these ubiquitous bacteria invade the host, monocytes are not appropriately recruited in sufficient numbers to elicit a macrophage-mediated granulomatous reaction. In addition, defective T cells may not generate sufficient quantities of lymphokines, such as LDCF and macrophage activating factors, to recruit adequate monocytes/macrophages to the inflammatory foci. With impaired granulomatous responses to control the infection, the organisms disseminate to virtually every body organ.

Although the mechanisms responsible for this suppressed monocyte migratory function are unclear, a number of possibilities warrant further investigation: reduced numbers of membrane chemoattractant receptors, prior in vivo desensitization, reduced transmission of the chemotactic signal, and/or impaired cytoskeletal function. In this regard, Snyderman et al. (33, 34), have shown that a low molecular weight material from tumor cells and certain oncogenic murine leukemia viruses inhibits macrophage migration. In addition, these investigators recently showed (35) that the low molecular weight material secreted by tumor cells that inhibits monocyte migration is physicochemically and antigenically related to the immunosuppressive retroviral protein, P15E. Also, P15E-related proteins were recently shown (36) to be present in human malignant cell lines and blast-transformed cells. These observations may be of particular relevance to the depressed migratory response that we have observed in AIDS patients since cytopathic human T-lymphotropic retroviruses (HTLV-III) have been detected and isolated from patients with AIDS and pre-AIDS (37-40). The expression of a protein similar to P15E by either this virus or transformed cells could suppress macrophage accumulation at sites of inflammation or neoplastic transformation. This suppression in chemotaxis could then

contribute to or potentiate the progression of various infections and neoplastic processes in patients with AIDS since monocytes have been shown to limit the growth of certain neoplastic tumors (41, 42).

In a preliminary report (43), decreased random locomotion by monocytes was observed in 10% of symptom-free homosexual men. In contrast, we studied directed migration to four specific chemoattractants over a wide dose-response range and observed that monocyte chemotaxis was normal in healthy homosexuals without lymphadenopathy or AIDS. However, homosexuals with lymphadenopathy and an abnormal immunological profile demonstrated a decrease, although not significant, in monocyte chemotactic function. Furthermore, although chemotaxis was clearly reduced in AIDS patients with only Kaposi's sarcoma, the defect was most apparent in those AIDS patients with clinically defined opportunistic infections. These observations suggest that the defect in monocyte function is not secondary to the clinically apparent opportunistic infections, although opportunistic infections may potentiate the defect. Regardless of whether suppressed monocyte chemotaxis is a primary or secondary event in patients with AIDS, the inability of peripheral blood monocytes to migrate to inflammatory stimuli and to chemotactic products of infectious organisms could contribute to the inadequate host response to certain opportunistic organisms and neoplasms characteristic of this disease.

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