

Reduced interferon- γ but normal IL-4 and IL-5 release by peripheral blood mononuclear cells from Xhosa children with atopic asthma

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Background: Allergic asthma is increasing in black South Africans, a cohort with inherently high basal IgE levels. Atopy has been linked to an excess of the T helper 2 cytokines IL-4 and IL-5 relative to the T helper 1 cytokine interferon- γ (IFN- γ); however, most studies have utilized T cell clones. Studies on peripheral blood mononuclear cells (PBMC) have shown decreased IFN- γ release in patients with atopic dermatitis. It is uncertain whether this finding extends to atopic asthma.

Objectives: To characterize cytokine release by mitogen-activated PBMC from Xhosa children and to investigate whether reduced IFN- γ release is a feature of atopic asthma and whether there is a relationship between cytokine profiles and asthma severity.

Methods: Cytokine release and proliferation of phytohemagglutinin-stimulated PBMC from 10 patients with severe asthma and 14 patients with moderate asthma (highly allergic to house dust mites) and 17 healthy controls was assessed. Total serum, allergen-specific, and *Ascaris*-specific IgE was measured.

Results: Proliferation did not differ between the groups. The release of IFN- γ was progressively decreased (and the IL-4/IFN- γ ratio increased) in the groups with moderate or severe asthma. Tumor necrosis factor- α release was reduced, but IL-4, IL-5, and granulocyte-macrophage-colony stimulating factor release was unchanged. The presence of *Ascaris*-specific IgE did not influence the cytokine profiles.

Conclusion: Our study extends the findings observed for other atopic disorders and suggests that defective IFN- γ release is a generalized feature of atopic diseases. This study—the first to investigate both severe and moderate asthma, with the groups having similar atopic profiles—indicates that the extent of the defect in IFN- γ release might be related to asthma severity. (*J Allergy Clin Immunol* 1997;100:662-8.)

Key words: Atopy, asthma, African, peripheral blood mononuclear cells, Interferon- γ , IL-4, IL-5, tumor necrosis factor- α , granulocyte-macrophage-colony stimulating factor, *Ascaris*

Abbreviations used

dpm:	Disintegrations per minute
GM-CSF:	Granulocyte-macrophage colony-stimulating factor
HDM:	House dust mite
IFN- γ :	Interferon-gamma
PBMC:	Peripheral blood mononuclear cells
PHA:	Phytohemagglutinin
TNF- α :	Tumour necrosis factor- α

Allergic asthma, the most common chronic disease in children, is increasing in black South Africans.¹⁻³ Asthma is a chronic inflammatory disease of the airways in which mast cells, eosinophils, and T lymphocytes play a role.^{4,5} Atopic inflammation is primarily triggered by excessive IgE-mediated release of mast cell mediators and has been linked to excess production of the T helper 2 (T_{H2}) cytokines IL-4 and IL-5 relative to the T_{H1} cytokine interferon- γ (IFN- γ).⁶ IL-4 is required by B cells for isotype switching to IgE,⁷ and IL-5 is the most specific cytokine for eosinophils⁷; IFN- γ has been shown to negatively regulate IL-4 and IL-5 production.^{8,9}

The hypothesis that the T helper response in allergy and asthma is skewed toward a T_{H2}-type response was based on analysis of long-term T cell clones from a limited number of patients,^{10,11} and the limitations of T cell clones have been highlighted.¹¹ Studies on blood mononuclear cells have suggested that a defect in IFN- γ secretion is a primary component of the atopic state. Mitogen-stimulated mononuclear cells from newborns with a family history of atopic disease^{12,13} or from infants who subsequently developed atopy^{14,15} secreted significantly less IFN- γ than did control cultures. Studies on peripheral blood mononuclear cells (PBMC) from patients with atopic dermatitis¹⁶⁻²³ have also shown decreases in polyclonally stimulated IFN- γ release (but IL-4 release has been found to be either unchanged^{24,25} or significantly increased^{18,21,26}). It is uncertain whether this finding extends to other atopic diseases such as atopic asthma, because the stimulated release of IFN- γ from the PBMC of patients with atopic asthma has only been investigated in a small group of six patients.²⁷ Furthermore, information on the release of other cytokines from the PBMC of atopic individuals is limited.

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TABLE I. Patient characteristics and IL-4 and IFN- γ release

Patient No.	Age (yr)	Sex	Total IgE (kU/L)	<i>Ascaris</i> -specific IgE (kU/L)	HDM-specific IgE (kU/L)	Other allergen-specific IgE (kU/L)	IL-4/IFN- γ values	Ratio IL-4/IFN- γ
S1*	4	M	280	0†	56	E(0.8), P(3.0), M(5.4) D(5.6), C(7.3)	48/10	4.8
S2	12	F	346	2.9	99	—	22/30	0.7
S3	9	F	646	0	91	—	205/47	4.4
S4	6	M	925	0.7	91	E(0.9), P(1.0), S(2.0) C(14.2), D(15.9), G(45.5)	37/89	0.4
S5	8	F	945	0	103	G(43.1)	37/376	0.1
S6	10	M	1440	0.9	47	C(2.4)	91/13	7.0
S7	6	F	1847	9.0	119	M(1.0)	421/17	24.8
S8	14	F	2528	2.1	94	D(1.5), C(3.2), S(4.2) P(49.6), G(104.0)	19/63	0.3
S9	7	F	4697	2.0	80	—	72/78	0.9
S10	11	M	5767	24.9	97	D(0.8), E(1.1), S(1.6) P(4.0), C(5.1), G(5.9)	77/295	0.3
M1	9	M	113	0	43	—	25/153	0.2
M2	7	M	372	1.9	31	—	42/179	0.2
M3	9	F	474	0	76	G(8.4)	58/83	0.7
M4	7	M	614	0	101	—	86/279	0.3
M5	10	M	902	10.7	90	W(1.3)	42/163	0.3
M6	7	F	917	2.1	111	—	79/94	0.8
M7	10	F	1176	2.0	103	C(2.4)	17/159	0.1
M8	14	M	1189	3.3	97	C(0.4), E(0.4), D(5.0) S(9.7), P(14.6), G(62.5)	32/69	0.5
M9	5	F	1206	6.2	124	—	11/25	0.4
M10	10	M	1844	2.0	102	G(1.3)	115/138	0.8
M11	11	M	1946	2.3	83	—	277/147	1.9
M12	11	M	2300	6.0	100	S(0.4), D(0.9), C(1.8) G(12.7)	211/270	0.8
M13	7	F	2395	0	90	P(1.1), G(30.4)	227/155	1.5
M14	7	F	2739	10.7	110	E(0.4), P(2.0)	260/55	4.7

C, Cat; D, dog; E, egg white; G, grass; M, milk; P, peanut; S, soya; W, wheat.

*S, Severe; M, moderate.

†A value of 0 is given to an IgE level less than 0.35 kU/L.

The aims of this study are to characterize cytokine release by mitogen-activated PBMC from Xhosa children, to determine whether reduced IFN- γ release is a feature of atopic asthma, and to investigate whether there is a relationship between cytokine profiles and asthma severity. Xhosa children, in whom allergies and asthma are increasing, have inherently high basal IgE levels^{28,29} and are commonly infected with the intestinal helminth *Ascaris lumbricoides*. No baseline cytokine data are available for this group. We measured the proliferative responses and release of a range of cytokines from PBMCs uniformly stimulated in vitro with the polyclonal activator phytohemagglutinin (PHA).

METHODS

Subjects

Twenty-four chronic asthmatic black (Xhosa) children, who were highly allergic to house dust mite (HDM), were recruited from among the Allergy Clinic patients and classified as having severe ($n = 10$) or moderate ($n = 14$) asthma on the basis of clinical status and prescribed medication.³ The patients with severe asthma included six children receiving inhaled glucocorticoids. No patients had taken oral corticosteroids within the

preceding 5 months. Seventeen healthy controls with no allergic or asthmatic symptoms were recruited from friends of the asthmatic patients and surgical patients. The characteristics of the subjects are presented in Tables I and II. The mean ages of the severe asthma, moderate asthma, and normal groups were 8.7, 8.9, and 9.6 years, respectively.

Ethical approval was obtained for this study from the Ethics and Research Committee of the University of Cape Town Medical School. Informed consent was obtained from subjects or their parents.

IgE measurement

Total serum IgE levels and specific IgE to HDM allergen (Der p 1), other common aeroallergens (grass mix and cat and dog dander), food allergens (egg white, milk, peanut, soya), and *Ascaris* were measured in all subjects with the Pharmacia CAP system.

Stimulation of PBMC

PBMC were isolated from heparinized blood by centrifugation on Histopaque - 1077 (Sigma), washed, and resuspended in RPMI-1640 medium supplemented with 10% human AB serum, L-glutamine (2 mmol/L), 2-mercaptoethanol (50 μ mol/L), penicillin (50 units/ml), and streptomycin (20 μ g/ml) (complete

TABLE II. Normal subject characteristics and IL-4 and IFN- γ release

Patient No.	Age (yr)	Sex	Total IgE (kU/L)	<i>Ascaris</i> -specific IgE (kU/L)	Other allergen-specific IgE (kU/L)	IL-4/IFN- γ values	Ratio IL-4/IFN- γ
N1	12	F	23	0*	—	62/147	0.4
N2	3	M	31	0	—	10/59	0.2
N3	9	F	66	0	—	182/234	0.8
N4	11	M	125	0	—	128/217	0.6
N5	10	F	198	0	—	32/284	0.1
N6	15	F	246	0.4	—	34/106	0.3
N7	9	M	338	0.9	—	115/218	0.5
N8	10	F	342	0.6	—	117/157	0.7
N9	5	M	412	0.7	—	117/43	2.7
N10	10	F	439	0.9	—	23/51	0.5
N11	11	F	564	2.7	—	138/806	0.2
N12	9	F	1088	2.7	—	76/82	0.9
N13	10	F	252	0	S(0.8)	42/107	0.4
N14	10	M	273	0	HDM(2.4), C(0.5)	33/711	0.1
N15	8	F	377	0	P(1.2), S(1.3), G(1.4)	507/813	0.6
N16	12	F	566	0	G(0.5)	175/325	0.5
N17	10	M	743	1.8	HDM(2.1)	48/72	0.7

C, Cat; G, grass; HDM, house dust mite; P, peanut; S, soya.

*A value of 0 is given to an IgE level less than 0.35 kU/mL.

RPMI₁₀). PBMC (2×10^5 cells/200 μ L complete RPMI₁₀ per well) were cultured in round-bottomed 96 well plates (Corning) at 37°C in a 5% CO₂ humidified incubator and stimulated with PHA (2.5 μ g/ml final concentration; Wellcome). Preliminary studies showed this was the lowest concentration of PHA to induce maximum proliferation, which, under these conditions, was measured at 68 hours.

Proliferation was assessed by measuring DNA synthesis. Tritiated thymidine (0.8 μ Ci per well; 1 Ci/mmol; ICN Biochemicals) was added to the cultures after 48 hours, and 20 hours later the cells were harvested. Incorporated radioactivity was measured as disintegrations per minute (dpm) and results of triplicate cultures were expressed as delta dpm (mean of wells containing stimulant minus mean of control wells).

Supernatants from parallel cultures (pooled from 5 to 7 wells per subject) were collected 48 hours after stimulation and stored at -80°C. This time interval is associated with peak or plateau secretion of IFN- γ and IL-4.^{19-21, 26, 30} Commercial ELISAs were used to quantitate IL-4, granulocyte-macrophage colony-stimulating factor (GM-CSF) (Medgenix, Belgium) and IL-5 (R&D Systems). IFN- γ and tumor necrosis factor- α (TNF- α) were measured by radioimmunoassay (Medgenix).

Statistical analysis

All results are expressed as means $\pm$ SEM. Mann-Whitney U tests were used to compare cytokine release between groups. Two-tailed Student's *t* tests were used for comparison of IgE levels, IL-4/IFN- γ ratios, and proliferation of PBMC. Correlations were determined using the Pearson coefficient. A Statgraphics 6 computer package was used to analyze the data. Probability (*p*) values of less than 0.05 were considered significant.

RESULTS

IgE levels

Total serum IgE levels. Total serum IgE levels were significantly increased in the group with severe asthma (1942 ± 596 kU/L; *p* = 0.002) or moderate asthma (1299 ± 219 kU/L; *p* = 0.0001) compared with the

normal Xhosa subjects (358 ± 66 kU/L) (see Tables I and II).

Ascaris-specific IgE. Relatively low levels of *Ascaris*-specific IgE were detected in 70% of the patients with severe asthma, in 71% of the patients with moderate asthma, and in 47% of the normal controls (see Tables I and II).

Allergen-specific IgE. The mean levels of HDM (Der p1)-specific IgE were 87.7 ± 6.8 kU/L (range, 47 to 119 kU/L) for patients with severe asthma and 90.1 ± 6.8 kU/L (range, 31 to 124 kU/L) for patients with moderate asthma. The specific IgE response profile of the asthmatic patients to other allergens is shown in Table I. Although they had no symptoms of allergy, two of the normal subjects (N14 and N17; Table II) had HDM-specific IgE levels of 2.4 and 2.1 kU/L respectively. Normal subjects N13 to N16 had low levels of specific IgE to other allergens (range, 0.5 to 1.4 kU/L).

Proliferation

The PHA-induced proliferation of PBMC isolated from normal subjects and patients with severe and moderate asthma was essentially similar. The mean delta dpm was $183,659 \pm 17,007$ (severe asthma), $174,244 \pm 12,963$ (moderate asthma), and $166,261 \pm 12,557$ (normal). Control proliferation (minus Harvester background) was 188 ± 67 dpm.

Mitogen-induced cytokine release

Release of IFN- γ . PHA-induced IFN- γ levels were significantly lower in the patients with severe asthma as compared with the normal group (*p* = 0.02; Fig. 1, *a*; see Tables I and II). The IFN- γ levels were also reduced in the group with moderate asthma, although this was not statistically significant. The mean IFN- γ levels were $98 \pm$

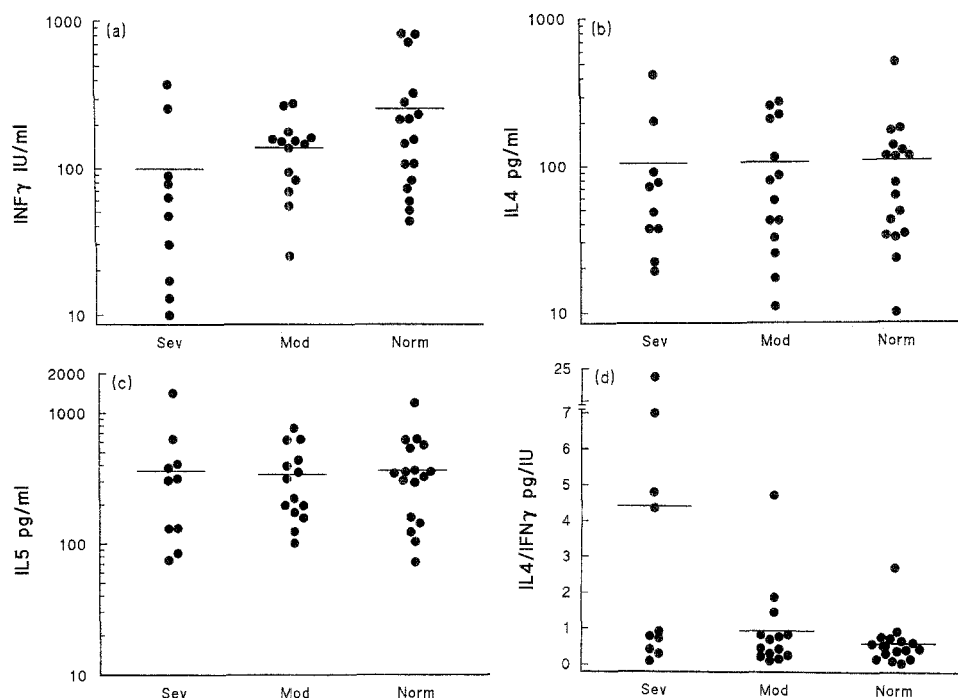


FIG. 1. Release of cytokines by PHA-stimulated PBMC from atopic children with severe (Sev; $n = 10$) or moderate (Mod; $n = 14$) asthma and age-matched normal controls (Norm; $n = 17$). **a.** IFN- γ . **b.** IL-4. **c.** IL-5. **d.** IL-4/IFN- γ ratio. Horizontal lines represent means. In the group with severe asthma, IFN- γ release was significantly decreased ($p = 0.02$) and the ratio of IL-4:IFN- γ release was significantly increased ($p = 0.049$) relative to the controls.

39 IU/ml, 141 ± 20 IU/ml, and 261 ± 63 IU/ml for the severe, moderate, and normal groups, respectively.

Release of IL-4 and IL-5. Release of IL-4 and IL-5 did not differ among the three groups (see Fig. 1, *b* and *c*). The mean IL-4 release was 103 ± 39 pg/ml (severe asthma), 106 ± 26 pg/ml (moderate asthma), and 108 ± 28 pg/ml (normal). The mean IL-5 release was 388 ± 127 pg/ml (severe asthma), 334 ± 56 pg/ml (moderate asthma), and 379 ± 66 pg/ml (normal). For the asthmatic patients (severe plus moderate), there was a highly significant correlation between the PHA-stimulated release of IL-4 and IL-5 ($r = 0.78$; $p < 0.00001$).

IL-4/IFN- γ ratio in patients with asthma. The IL-4/IFN- γ ratio was increased in patients with asthma. The ratio was greater than 1 pg/IU in 4 out of 10 patients with severe asthma, 3 out of 14 patients with moderate asthma, and 1 out of 17 controls (see Fig 1, *d* and Tables I and II). These increased ratios were not associated with increased atopic status as indicated by the levels of allergen-specific IgE. The mean IL-4/IFN- γ ratio was 4.4 ± 2.4 pg/IU (severe asthma), 0.94 ± 0.32 pg/IU (moderate asthma), and 0.60 ± 0.14 pg/IU (normal). The ratio for the severe group was significantly increased relative to the control group ($p = 0.049$).

Correlation between increased proliferation and release of IL-4 or IFN- γ . No correlation was found in the three groups, except in the group with severe asthma, in which IL-4 release tended to increase with increasing prolifer-

ation. This correlation was significant if the one outlier was omitted ($r = 0.7$; $p = 0.03$) (Fig. 2).

Correlation between Ascaris-specific IgE levels and IL-4 or IFN- γ release or IL-4/IFN- γ ratio. No correlation was found in the severe, moderate, or normal groups. In each group, the range of values for IL-4, IFN- γ , and IL-4/IFN- γ ratio was similar for subjects with or without *Ascaris*-specific IgE (see Tables I and II).

TNF- α and GM-CSF levels. The mean and range of values for TNF- α tended to reduce progressively in the groups with moderate or severe asthma. However, these differences were not statistically significant. The mean TNF- α release was 2635 ± 287 pg/ml ($p = 0.083$) for the patients with severe asthma and 3473 ± 357 pg/ml ($p = 0.77$) for the patients with moderate asthma compared to 3776 ± 436 pg/ml for the controls. The release of GM-CSF was similar in the severe, moderate, and normal groups, with means of 8330 ± 1510 pg/ml, 7533 ± 715 pg/ml, and 8222 ± 956 pg/ml, respectively.

Spontaneous cytokine release

Supernatants from unstimulated cultures were collected after 6 days, that is, at a time when antigen-stimulated cytokine release becomes measurable. Samples (5 to 8 per subject group) were chosen at random for assay. The spontaneous release of IL-4, IL-5, and IFN- γ was very low or undetectable in all cases. The

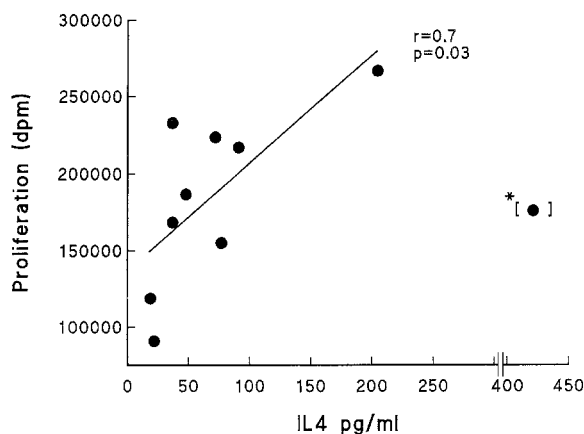


FIG. 2. Significant correlation between proliferation and IL-4 release for the group with severe asthma. PBMC were stimulated with PHA, and proliferation was assessed in parallel cultures as described in Methods. (* = outlier omitted.)

spontaneous release of TNF- α and GM-CSF was not measured.

DISCUSSION

We investigated PHA-induced proliferation and release of cytokines from PBMC of South African Xhosa children. This is the first study to compare groups with either severe or moderate asthma (both groups being highly atopic) with healthy controls. The release of IFN- γ progressively decreased in patients with moderate or severe asthma but was statistically significant only in the severe group. The proliferation results indicate that the PBMC from the three groups of subjects are similarly activated in vitro and that differences in cytokine release between the groups are not due to differences in the degree of cellular activation or proliferation. There was also no evidence of preactivation in vivo or during isolation because there was no excess spontaneous proliferation, and spontaneous cytokine release was negligible. Our finding of decreased IFN- γ release in children with asthma agrees with studies on polyclonally stimulated PBMC from children and adults with other atopic diseases, such as cow's milk allergy,³¹ severe atopic dermatitis,¹⁶⁻²⁰ or moderate to severe atopic dermatitis.²¹⁻²³ In these studies, PHA, which cross-links T cell receptors, was most commonly used as the stimulus,^{17-20, 23} although similar results were obtained with other polyclonal activators.^{16, 20-22}

We found the PHA-induced release of IL-4 to be substantially similar in the three groups. In comparison with studies investigating IFN- γ release, there have been fewer reports on IL-4 release from mitogen-stimulated PBMC of atopic individuals, and the results have not been as consistent. Significantly increased release of IL-4 was found in children¹⁸ and adults^{21, 26} with atopic dermatitis, whereas no significant difference was reported in patients with cow's milk allergy,³¹ mild atopy,¹⁸ or atopic dermatitis.^{24, 25} Only two studies on the mito-

gen-induced release of IFN- γ or IL-4 from PBMC of patients with asthma have been published. Recently Park et al.³² found that the release of IL-4 was significantly increased in patients with atopic asthma, as well as in atopic patients without asthma. Tang et al.²⁷ reported that PBMC from children with atopic asthma released significantly more IL-4 and less IFN- γ than did PBMC from either patients with intrinsic asthma or healthy controls. However, in this study, there were only six patients in each of the groups with asthma.

Our finding that IL-4 release was not increased in patients with atopic asthma could be related to the high basal IgE levels found in healthy black subjects, independent of atopic family history, allergic symptoms, or parasitic infection.^{28, 29} Our results support previous observations that serum IgE levels in healthy control black South African children are higher than accepted reference values for white subjects and that there is considerable overlap with the values for the atopic asthma patients.

Although we did not observe increased IL-4 release, we did find, in similarity with other studies,^{18, 27} raised IL-4/IFN- γ ratios in the highly atopic subjects, and this was significant in the group with severe asthma. Because IL-4 and IFN- γ are mutually cross regulatory,^{8, 9} it is suggested that the ratio of IL-4 release to IFN- γ release in each individual is more important than the absolute levels. The extended range of individual values for the stimulated release of IFN- γ and IL-4 and for the IL-4/IFN- γ ratio and the overlap of values between the groups that was found in the present study are also similar to the results of all other studies on cytokine release from the PBMC of atopic individuals.

A further difference between the groups in our study was that the only correlation between increased proliferation and IL-4 or IFN- γ release was that of increasing IL-4 release in the group with severe asthma. Other studies have not investigated the relationship between proliferation and cytokine release.

Our study found no relationship between levels of *Ascaris*-specific IgE and the mitogen-stimulated release of either IL-4 or IFN- γ or the IL-4/IFN- γ ratio. Previous studies^{33, 34} on mitogen-stimulated PBMC from helminth-infected individuals and normal controls reported no difference in IFN- γ release and also showed that IL-4 release was not increased in helminth-infected individuals with moderately elevated serum IgE levels.³³ In mice, infection with intestinal helminth parasites has been shown to cause increased IL-4 expression in the enteric region only.³⁵

Investigations of bronchoalveolar lavage fluid and tissue samples have consistently shown increases in IL-4, IL-5, and activated T cells in patients with atopy or allergic asthma,^{4, 36} and have also demonstrated that T cells are the main source,^{37, 38} although mast cells and eosinophils can also release these cytokines. However, there is little evidence as to whether under conditions of uniform activation, T cells are preprogrammed to release more IL-5 in asthmatic or atopic patients. We

found that the stimulated IL-5 release from PBMC of patients with allergic asthma and control subjects was substantially identical. This is in agreement with the findings that IL-5 mRNA expression by CD4⁺ T cells was highly significantly increased in patients with acute asthma but not in those with stable asthma,³⁹ and that there was no difference in IL-5 release from PBMC of patients with atopic dermatitis and healthy subjects.²⁵ Although spontaneous release of IL-5 and IL-4 from purified T cells has been found to be increased in atopic patients,^{40, 41} our study found no spontaneous release of IL-5 or, in agreement with other studies on PBMC, of IL-4 or IFN- γ .^{13, 16-20, 24, 25, 27, 31}

Our finding of similar release of IL-4 and IL-5 from PBMC of either atopic asthma patients or normal subjects does not preclude increased release of these cytokines from T cells in inflammatory lung tissue in the patients with atopic asthma. Evidence suggests that the role of T cells that release high amounts of IFN- γ is to antagonize the release of IL-4 in inflammatory tissue,⁴² and that therefore, the defective release of IFN- γ in atopic patients could result in uncontrolled release of IL-4 in the lung. It has also been demonstrated recently that the cytokine profile of CD4⁺ memory T cells can be altered by macrophage-released cytokines such as IL-12.^{43, 44} This opens up the question of the extent to which circulating memory T cells are committed to a predetermined T_{H1}- or T_{H2}-type response on activation and to what extent cytokine release is modified in the inflammatory tissue environment.

In asthma there is a disease-related increase in TNF- α in lung tissues⁴⁵; however, TNF- α is produced by many cell types including macrophages, T cells, neutrophils, epithelial cells, and lung mast cells.⁴⁵ In this study we have shown that the capacity of stimulated PBMC to release TNF- α is not increased in asthmatic patients. GM-CSF, a known hematopoietic growth factor with eosinophil-activating function, is also produced by multiple cell types,³⁸ but in stimulated PBMC it is released by the T cells and not by the macrophages.⁴⁶ Our finding that GM-CSF release from PBMC was broadly similar in the asthmatic and normal groups, agrees with the recent findings that GM-CSF mRNA expression from polyclonally stimulated T cells did not differ between stable asthmatic patients and normal controls.⁴⁷ GM-CSF has been suggested to be of minor importance in asthma.³⁶

We considered it possible but not likely that our findings in this study were influenced by the use of inhaled steroids. In vitro addition of glucocorticoids inhibits synthesis of various cytokines.^{48, 49} Although the levels of circulating steroids achieved with inhalation therapy are not known, it is unlikely that meaningful levels of steroids remain in the isolated and washed PBMC preparations used in in vitro studies. This is supported by the finding of similar proliferation of PBMC from the three groups in vitro. Six of the 10 severe asthmatic patients received inhaled steroids. There was no tendency for steroid use to be associated with decreased or increased IL-4, IFN- γ , or IL-4/IFN- γ

ratio relative to the non-steroid users among the patients with severe asthma. Recent evidence suggests that in asthma, glucocorticoids exert their therapeutic effect at least partly by reducing the synthesis of IL-4 and IL-5 and by upregulating IFN- γ .⁵⁰

Our study has shown that mitogen-stimulated PBMC from asthmatic Xhosa children have cytokine profiles that are similar to those documented for other atopic cohorts with respect to IFN- γ but not to IL-4 release and that these cytokine profiles are unrelated to the presence of *Ascaris*-specific IgE. This study also provides new data on IL-5, GM-CSF, and TNF- α release by PBMC from asthmatic children.

The major finding of this study was that decreased IFN- γ release is a feature of atopic asthma. This extends the findings for other atopic disorders and suggests that defective IFN- γ release is a generalized feature of atopic diseases. The significantly decreased IFN- γ release in the patients with severe asthma confirms a recent study with a small group of patients with severe atopic asthma.²⁷ Our finding that IFN- γ release was reduced but not significantly decreased in the group with moderate asthma, which had a similar atopic profile to the group with severe asthma, suggests that the extent of the defect in IFN- γ release might be related to asthma severity.

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