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Nasal eosinophilia induced by PAF-acether is accompanied by the release of eosinophil cationic protein

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Nasal eosinophilia induced by PAF-acether is accompanied by the release of eosinophil cationic protein. A. Tedeschi, N. Milazzo, A. Miadonna. ©ERS Journals Ltd 1994.

ABSTRACT: It has been demonstrated that platelet-activating factor (PAF)-acether can induce nasal neutrophilia and eosinophilia, with a different degree of responsiveness in atopic and in nonatopic subjects. The aim of this study was to evaluate whether PAF can also induce the release of secondary mediators in the human nose.

Ten patients with allergic rhinitis and 10 normal subjects underwent nasal challenge with PAF (500 nmol), lyso-PAF (500 nmol) and saline solution. Nasal lavages were performed before and after challenge to evaluate changes in nasal cytology and release of histamine, immunoreactive leukotriene (iLT) C_4 and eosinophil cationic protein (ECP).

PAF caused neutrophilia and eosinophilia, which appeared earlier in atopic than in nonatopic subjects (30 min *vs* 1 h), and peaked 3 h after challenge in both groups. Lyso-PAF caused mild neutrophilia, which appeared 3 h after challenge in both groups; an increase in eosinophil counts was observed 3 h after challenge in atopic subjects, but not in nonatopic subjects. PAF insufflation caused a significant release of ECP in nasal lavage fluids 30 min and 3h after challenge in atopic subjects, and 3 h after challenge in nonatopic subjects. ECP levels in the nasal lavages collected 30 min and 3 h after challenge with PAF were higher in atopic than in nonatopic subjects. Eosinophil counts correlated with ECP levels in the nasal lavages collected 30 min after PAF challenge in atopic subjects. Nasal challenge with lyso-PAF did not provoke any release of ECP. No significant increase of histamine and $iLTC_4$ levels in nasal lavages was found after challenge with either PAF or lyso-PAF.

These results indicate that PAF-induced nasal eosinophilia is accompanied by ECP release, which appears earlier and is more marked in atopic than in nonatopic subjects.
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0The lipid mediator platelet-activating factor (PAF)-acether has a broad range of biological activities, which may be important in inflammatory and allergic reactions [1]. We have investigated the possible involvement of PAF in allergic rhinitis, and have found that PAF can be released, along with its precursor/metabolite lyso-PAF, in nasal lavage fluids during the early antigen-induced reaction in patients with respiratory allergy [2]. Nasal challenge with PAF provokes nasal obstruction with an increase in nasal airway resistances [3], and nasal hyperreactivity [4, 5]. Furthermore, nasal neutrophilia and eosinophilia have been observed after challenge with PAF, with a more rapid and more marked response in atopic than in normal subjects [6]. PAF is recognized as a potent bronchoconstrictor in humans [7], but some of its effects *in vivo* may be mediated indirectly by the release of secondary mediators [8–11]. Cyclo-oxygenase inhibitors and thromboxane or leukotriene (LT) antagonists can modulate PAF-induced bronchoconstriction, suggesting that these substances could mediate some PAF-induced effects on respiratory airways [8, 10, 11]. Generation of leukotrienes in response to PAF stimulation has been described from perfused rabbit lung [12], perfused guinea-pig lung [13], and human neutrophils [14], and eosinophils [15]. PAF can also induce histamine release from rat kidney mast cells [16], and human basophils [17].

The aim of this study was to evaluate whether the effects of PAF on the nose are direct, or mediated by the release of secondary mediators. We have performed nasal challenge with PAF in 10 allergic subjects and 10 normal subjects. In addition, we have evaluated accompanying cytological changes and mediator release (histamine, LTC_4, eosinophil cationic protein) in nasal lavage fluids.

Subjects and methods

Subjects and study design

Ten patients with allergic rhinitis (6 men and 4 women, aged 19–37 yrs) and 10 normal subjects (5 men and 5 women, aged 18–34 yrs) were selected for this study. Allergic rhinitis was diagnosed by clinical history and skin-prick tests. The study was performed in the winter,

when the patients were symptom free and were not taking any medication. Informed consent was obtained from each subject prior to study. Each subject underwent nasal stimulation with PAF, lyso-PAF and saline solution, which were instilled in a blinded fashion at intervals of at least one month. Nasal lavages were performed under basal conditions and at different postchallenge times (30 min, 1, 3 and 24 h), to evaluate mediator release and changes in nasal cytology. The results obtained after nasal insufflation of saline solution were used as controls.

Nasal challenge and nasal lavage procedure

PAF (1-0-hexadecyl-2-acetyl-sn-glycero-3-phosphorylcholine; Bachem, Bubendorf, Switzerland) and lyso-PAF (1-0-hexadecyl-sn-glycero-3-phosphorylcholine; Bachem, Bubendorf, Switzerland) were dissolved in 100% ethanol (final concentration 1%) and diluted in 0.9% w/v NaCl solution containing 0.25% w/v serum albumin (Institut Mérieux, Lyon, France). These solutions were divided into small aliquots and frozen at -20°C. The solution employed for challenge was thawed just before use. PAF, lyso-PAF or saline solution were nebulized into the nose by means of a disposable metered-dose nebulizer calibrated to deliver 100±10 µl per puff. The dose of 500 nmol of PAF was chosen because we have previously observed that this could provoke nasal symptoms and changes in nasal cytology in most subjects [3, 6].

To evaluate changes in nasal cytology and mediator levels, nasal lavage fluids were collected using a technique described previously [2, 18]. Briefly, 5 ml of 0.9% w/v NaCl were instilled into each nostril. After 10 s, the subject expelled the mixture of saline solution and mucus, which was collected in conical polypropylene tubes (Falcon, Becton Dickinson Labware, Oxnard, CA, USA). Recovery of nasal lavage fluid ranged 50–80% of the starting volume (10 ml for each washing). Nasal lavages were performed before and 30 min, 1, 3 and 24 h after nasal stimulation. Nasal lavage fluids were shaken to disperse mucus, and aliquots were collected for total cell counts, which were performed in duplicate in a Fuchs Rosenthal chamber (Firma Walter Schrenck Gmbh, Hofheim am Taunus, Germany) after staining with Turk liquid (50 µl sample and 450 µl Turk liquid, prepared by Farmacia Ospedale Policlinico, Milan, Italy). Eosinophil count was performed by Randolph staining (solutions provided by Farmacia Ospedale Policlinico, Milan, Italy) [19]. The lavage samples were then centrifuged at 1,000×g for 10 min at 4°C. The supernatant of each sample was aspirated and the cell pellet was resuspended in 1 ml of 0.9% NaCl with 0.1% human serum albumin (HSA). Two cytospin slides for each sample were prepared (100 µl with 2–4×10^4 cells per slide; centrifugation at 500 rpm for 10 min in a Shandon cytocentrifuge; Shandon Southern Ltd, Runcorn, Cheshire, UK). Cytocentrifuge slides were stained by May-Grünwald Giemsa (staining solutions provided by Farmacia Ospedale Policlinico, Milan, Italy) and examined by light microscope under oil immersion. At least 200–300 cells were examined in each slide. The cells were classified as epithelial cells, neutrophils, eosinophils and mononuclear cells of unclear origin, a category that included lymphocytes and monocytes. The reader was blinded as to whether the subject had received PAF, lyso-PAF or saline solution.

Mediator assays

Histamine. Aliquots of the supernatants from nasal lavage fluids were diluted 1/2 with 4% v/v perchloric acid, centrifuged at 2,000×g for 15 min at 4°C, and assayed in duplicate for histamine concentration by an automated fluorometric technique [20]. The sensitivity of this method is 1 ng·ml^{-1}.

LTC_4. Aliquots of the supernatants for the leukotriene assay were aspirated, decanted and extracted following the method of ANDERSON *et al*. [21]. The lavage supernatants were mixed with four volumes of absolute ethanol (Carlo Erba, Milan, Italy) and left at 2–8°C for 30 min. The protein-rich precipitate was removed by centrifugation at 3,000×g for 30 min at 4°C; the ethanol supernatant was collected, decanted and then removed by rotary evaporation under vacuum. The samples were stored at -20°C and then redissolved in distilled water for radioimmunoassay.

The determination of immunoreactive leukotriene C_4 ($iLTC_4$) was made by radioimmunoassay, using commercially available kits (Amersham, Littlechalfont, UK), performed according to the method of HAMMOND *et al*. [22]. The anti-LTC_4 antibody utilized in the assay cross-reacts with LTD_4 (64%) and LTE_4 (64%). The sensitivity of the assay is 0.125 ng·ml^{-1} and the intra-assay and interassay variations do not exceed 10%. Every sample was assayed in duplicate and the results were expressed as ng·ml^{-1} lavage fluid. The results of the radioimmunological assay for $iLTC_4$ in nasal lavage fluids were previously validated by high performance liquid chromatography analysis [2, 18], performed according to the technique of SAUTEBIN *et al*. [23].

Eosinophil cationic protein. The concentration of the eosinophil cationic protein (ECP) was measured by radioimmunoassay, using a commercially available kit (Pharmacia, Uppsala, Sweden), which followed the method of VENGE *et al*. [24]. The sensitivity of the assay is 2 ng·ml^{-1} and cross-reactivity of the anti-ECP rabbit antiserum is less than 0.06% with eosinophil peroxidase.

Statistical analysis

Results were expressed as mean±SEM. The two-tailed Student's t-test for paired data was used to analyse the changes in cell populations and mediator levels in the nasal lavages (prechallenge values were compared with postchallenge values obtained at different times; moreover, the values obtained after PAF or lyso-PAF challenge were compared with the values obtained after insufflation of saline solution). Pearson's correlation coefficient was used to analyse the correlation between cells and mediator levels. P-values lower than 0.05 were considered significant.

Results

Cytological changes in nasal lavage fluids after stimulation with PAF, lyso-PAF or saline solution

Total cells counts (mean±SEM) in prechallenge nasal lavages were 208.9±58.1×10³ (range 50–675×10³) in atopic subjects and 184.2±45.9×10³, (range 34–422×10³) in normal subjects, although the difference was not significant. Nasal stimulation with PAF provoked an increase in total cell counts in the nasal lavages collected 3 h after stimulation in both groups (atopic subjects 385.8±51.7×10³; p<0.006, (range 91–1,040 ×10³); nonatopic subjects 410.4±106.5 ×10³; p<0.05 (range 100–600 ×10³)). In contrast, no significant increase in total cell counts was observed after lyso-PAF or saline insufflation. Both groups showed higher total cell counts after PAF challenge than after saline insufflation (atopic subjects p<0.05 at 1 h, and p<0.02 at 3 h; nonatopic subjects p<0.05 at 1 h, and p<0.02 at 3 h).

Epithelial cells, neutrophils and eosinophils were identified as the three main types of cells in nasal lavage fluids, and represented almost the total cell counts. Challenge with PAF induced nasal neutrophilia, which appeared after 30 min in atopic subjects and after 1 h in nonatopic subjects and peaked after 3 h in both groups. Milder neutrophilia was found 3 h after lyso-PAF challenge in both groups (fig. 1). PAF challenge also provoked eosinophilia, which was evident after 30 min in atopic subjects and after 3 h in nonatopic subjects. Increased eosinophil counts were found 3 h after lyso-PAF challenge in atopic subjects, but not in nonatopic subjects (fig. 2).

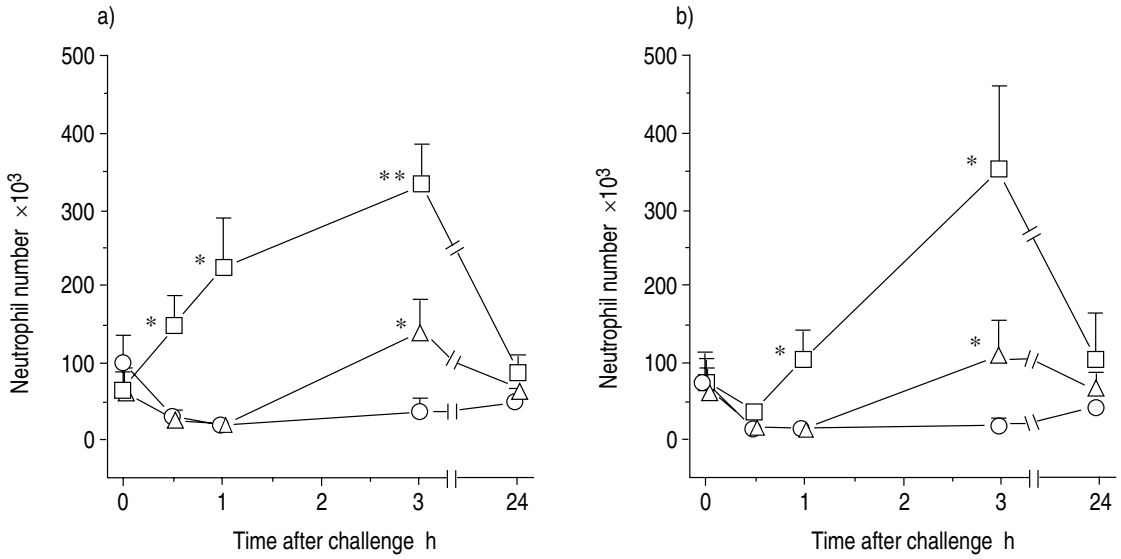

Fig. 1. – Time course of neutrophil counts in nasal lavage fluids collected after PAF (❑ , 500 nmol), lyso-PAF (Δ, 500 nmol), or saline solution (○, 0.9% w/v NaCl solution) challenge: a) in 10 atopic subjects; and b) in 10 normal subjects. Results are expressed as mean±SEM. *,**: significantly different from control value after insufflation of saline solution at p<0.05, <0.01. PAF: platelet-activating factor.

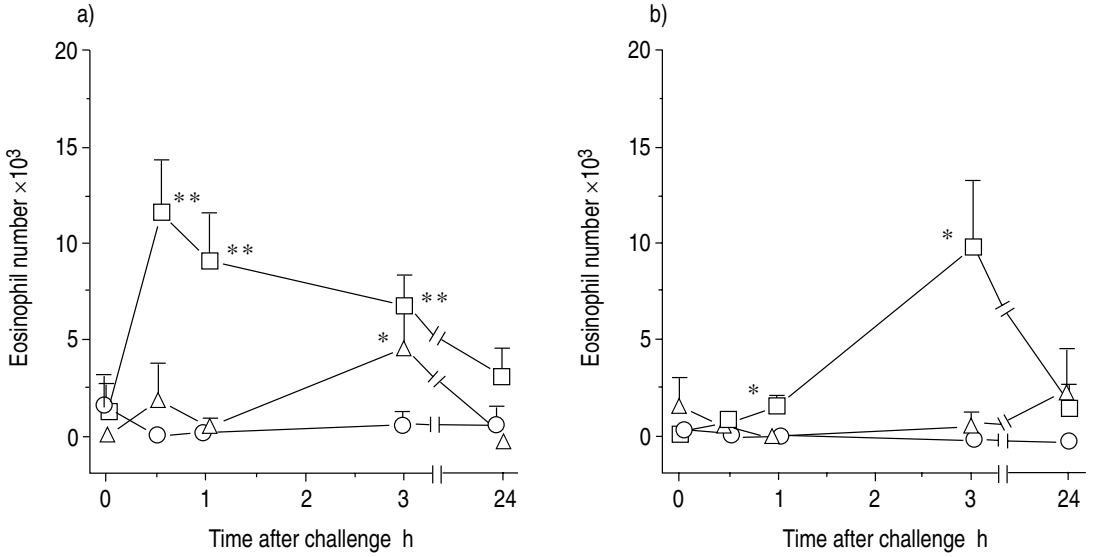

Fig. 2. – Time course of eosinophil counts in nasal lavage fluids collected after PAF (❑, 500 nmol), lyso-PAF (Δ, 500 nmol), or saline solution challenge (○): a) in 10 atopic subjects; and b) in 10 normal subjects. Results are expressed as mean±SEM. *,**: significantly different from control value after insufflation of saline solution at p<0.05, <0.01. PAF: platelet-activating factor.

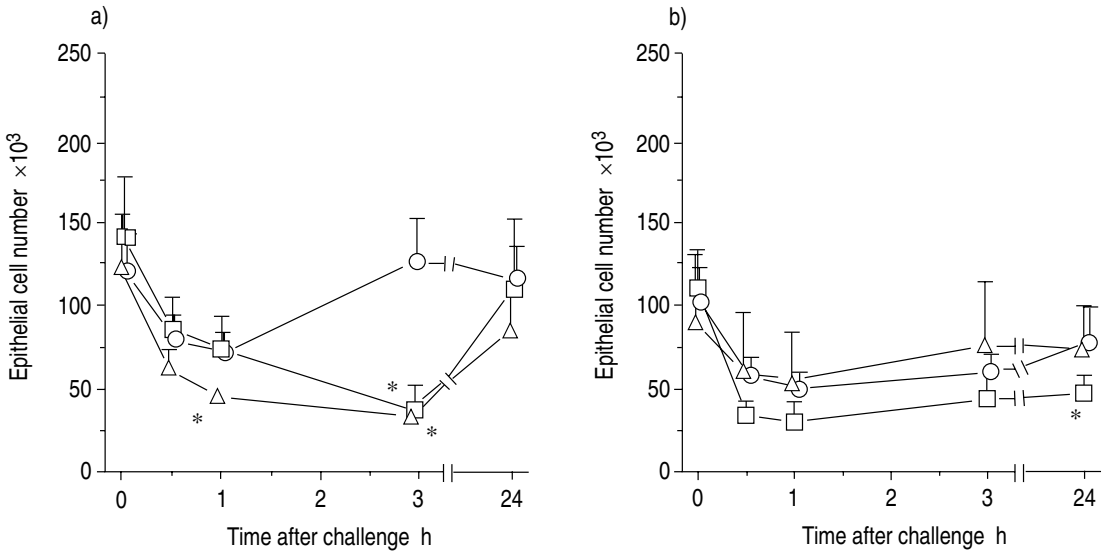

Fig. 3. – Time course of epithelial cell counts in nasal lavage fluids collected after PAF (❑, 500 nmol), lyso-PAF (Δ, 500 nmol), or saline solution challenge (○); a) in 10 atopic subjects; and b) in 10 normal subjects. Results are expressed as mean±SEM. *: significantly different from control value after insufflation of saline solution at $p<0.05$. PAF: platelet-activating factor.

The time course of epithelial cell counts was inverse to that of neutrophils, with reduced counts in the first three hours following PAF challenge. Epithelial cell counts were also decreased 3 h after lyso-PAF challenge in atopic subjects (fig. 3).

Saline insufflation was devoid of any significant effect on cellular composition of nasal lavage fluids.

Mediator levels in nasal lavage fluids

Histamine. Histamine concentration (mean±SEM) in prechallenge lavages was 15.3±4.5 ng·ml^{-1} (range 2–50 ng·ml^{-1}) in atopic subjects, and 15.4±6.1 ng·ml^{-1} (range 2–66 ng·ml^{-1}) in nonatopic subjects, without any significant difference between the two populations. As observed previously [2, 18], the histamine found in prechallenge conditions was not associated with any clinical symptoms. No significant changes in histamine concentration were found after PAF challenge, though a trend towards a reduction was observed in the nasal lavages collected up to 3 h after challenge. The time course of histamine concentration was similar after PAF, lyso-PAF or saline insufflation (table 1). Furthermore, the response was similar in both groups.

LTC_4. Low levels of $iLTC_4$ were found in the nasal lavages collected under basal conditions (mean±SEM 0.40±0.11 ng·ml^{-1}, range 0.12–1.0 ng·ml^{-1}, in atopic subjects; and 0.37±0.10 ng·ml^{-1}, range 0.12–1.2 ng·ml^{-1} in nonatopic subjects). A trend towards a reduction in $iLTC_4$ concentration was found in the nasal lavages collected up to 3 h after PAF challenge, with a modest increase at 24 h. The time course of LTC_4 concentration was similar after PAF, lyso-PAF or saline insufflation (table 2).

Table 1. – Histamine levels in the nasal lavage fluids collected from 10 atopic subjects and 10 normal subjects after nasal challenge with 500 nmol platelet-activating factor (PAF) or lyso-PAF, or saline solution

	Histamine level ng·ml^{-1}				
	Baseline	30 min	1 h	3 h	24 h
Atopic subjects					
PAF	15.3±4.5 (2–50)	11.8±2.6 (2–30)	9.8±1.9 (2–18)	11.7±3.1 (2–31)	13.7±3.0 (2–28)
Lyso-PAF	18.5±7.4 (2–80)	16.4±6.3 (2–60)	14.1±6.4 (2–68)	15.6±7.2 (2–76)	18.7±8.2 (2–78)
Saline	17.2±7.2 (1–70)	13.6±6.5 (2–70)	12.4±4.1 (2–44)	14.6±5.6 (2–60)	17.1±6.6 (2–68)
Normal subjects					
PAF	15.4±6.1 (2–66)	13.3±5.8 (2–65)	12.8±5.5 (2–60)	11.9±4.2 (2–48)	12.9±4.2 (2–48)
Lyso-PAF	10.9±3.8 (2–42)	7.5±1.5 (2–17)	6.2±1.2 (2–14)	7.4±1.8 (2–19)	8.7±2.1 (2–20)
Saline	11.5±3.8 (2–36)	6.1±1.5 (2–15)	4.8±1.1 (2–12)	5.5±1.3 (1–14)	9.7±2.5 (2–28)

Data are presented as mean±SEM and range in parentheses.

Table 2. – $iLTC_4$ levels in the nasal lavage fluids collected from 10 atopic subjects and 10 normal subjects after nasal challenge with 500 nmol platelet-activating factor (PAF) or lyso-PAF, or saline solution

	$iLTC_4$ levels ng·ml^{-1}				
	Baseline	30 min	1 h	3 h	24 h
Atopic subjects					
PAF	0.40±0.11	0.12±0.0	0.17±0.04	0.13±0.01	0.18±0.02
	(0.12–1.00)		(0.12–0.52)	(0.12–0.25)	(0.12–0.32)
Lyso-PAF	0.27±0.06	0.21±0.07	0.19±0.04	0.21±0.05	0.18±0.04
	(0.12–0.69)	(0.12–0.88)	(0.12–0.58)	(0.12–0.65)	(0.12–0.52)
Saline	0.20±0.04	0.16±0.03	0.14±0.01	0.15±0.01	0.15±0.02
	(0.12–0.54)	(0.12–0.42)	(0.12–0.28)	(0.12–0.30)	(0.12–0.33)
Normal subjects					
PAF	0.37±0.10	0.25±0.09	0.12±0.0	0.14±0.01	0.21±0.006
	(0.12–1.20)	(0.12–1.05)	(0.12–0.12)	(0.12–0.23)	(0.12–0.80)
Lyso-PAF	0.16±0.02	0.17±0.05	0.12±0.0	0.12±0.0	0.19±0.02
	(0.12–0.36)	(0.12–0.64)	(0.12–0.12)	(0.12–0.12)	(0.12–0.40)
Saline	0.22±0.05	0.12±0.0	0.12±0.0	0.13±0.005	0.26±0.06
	(0.12–0.64)	(0.12–0.12)	(0.12–0.12)	(0.12–0.16)	(0.12–0.80)

Table 3. – ECP levels in the nasal lavage fluids collected from 10 atopic subjects and 10 normal subjects after nasal challenge with 500 nmol platelet-activating factor (PAF) or lyso-PAF, or saline solution

	ECP levels ng·ml^{-1}				
	Baseline	30 min	1 h	3 h	24 h
Atopic subjects					
PAF	19.7±7.0	23.1±7.8*†	14.9±4.3	24.9±6.1*†	19.8±5.5
	(2–57)	(2.6–64.9)	(2–31.8)	(2–50)	(2–47.1)
Lyso-PAF	17.3±5.6	6.1±1.9	8.9±3.8	8.5±1.9	9.8±3.8
	(2–49)	(2–20.8)	(2–33.7)	(2–19.5)	(2–40.5)
Saline	19.8±7.3	6.3±2.2	6.7±2.8	9.7±3.8	17.2±6.8
	(2–52.3)	(2–19.9)	(2–28.1)	(2–39.9)	(2–49.8)
Normal subjects					
PAF	16.9±6.5	4.8±1.2	5.8±2.0	9.0±1.6*	12.2±2.8
	(2.3–52.9)	(2–14.9)	(2–23.1)	(4.6–23)	(2.9–32.1)
Lyso-PAF	14.5±4.1	5.2±0.9	4.3±1.0	6.3±1.0	10.7±3.1
	(2–40.7)	(2–10.4)	(2–12.4)	(2.7–13.2)	(2–33)
Saline	13.9±3.6	6.9±1.6	4.0±0.7	5.6±1.1	12.1±3.6
	(2–31.6)	(2–13.8)	(2–8.7)	(2–12.7)	(2–37.1)

Data are presented as mean±SEM and range in parentheses. *: significantly different from control value after insufflation of saline solution at $p<0.05$. †: significantly different from normal (nonatopic) subjects at $p<0.05$. ECP: eosinophil-derived cationic protein.

ECP. ECP was found in prechallenge nasal lavages in both groups (mean±SEM 19.7±7.1 ng·ml^{-1}, range 2–57 ng·ml^{-1}, in atopic subjects, and 16.9±6.5 ng·ml^{-1}, range 2.3–52.9 ng·ml^{-1}, in nonatopic subjects, without any significant difference between the two populations). A trend towards an increase in ECP levels, when compared to basal values, was found after PAF challenge in atopic subjects, but not in nonatopic subjects (in particular, 30 min and 3 h after challenge). When ECP levels after PAF challenge and after saline insufflation were compared, significantly higher values were observed 30 min and 3 h following PAF challenge in atopic subjects and 3 h after PAF challenge in nonatopic subjects (table 3). Furthermore, ECP levels in the nasal lavages collected 30 min and 3 h after challenge with PAF were higher in atopic than in nonatopic subjects ($p<0.05$). No difference was found between the ECP concentrations following lyso-PAF challenge and saline insufflation.

A significant correlation was observed between eosinophil counts and ECP concentrations in the nasal lavages collected 30 min after challenge with PAF in atopic subjects ($r=+0.6$; $p<0.05$).

Discussion

These results indicate that nasal eosinophilia induced by challenge with PAF is accompanied by the release of

ECP. This release is more rapid and more marked in atopic than in nonatopic subjects. PAF is a potent chemoattractant for eosinophils and neutrophils both *in vivo* and *in vitro* [6, 25]. A preferential accumulation of eosinophils after intradermal injection of PAF in atopic subjects was demonstrated by HENOCQ and VARGAFTIG [26]. We have found, not only a more marked nasal eosinophilia in atopic than in nonatopic subjects following challenge with PAF, but also a more rapid response in the former than in the latter, indicating that the two populations have a different capacity to recruit inflammatory cells. *In vitro* PAF has the capacity to stimulate eosinophil adhesion to endothelial cells [27] and eosinophil degranulation [28], with subsequent release of preformed mediators, such as ECP and major basic protein (MBP). Our data indicate that PAF maintains the capacity to induce the release of ECP *in vivo* when insufflated in the nose. ECP was also found in measurable amounts in prechallenge lavages, in the absence of any clinical symptoms; these levels probably reflect the basal rate of eosinophil migration and spontaneous release of mediators. Similarly, high histamine levels have been found in nasal lavage fluid, without any relation to clinical symptoms [18].

We did not detect any significant increase in histamine levels in nasal lavage fluids after challenge with PAF. This could be due to the failure of PAF to stimulate nasal mast cells or to the release of only low amounts of histamine. Also, a slow release followed by metabolic inactivation could hamper the detection of histamine release in nasal lavage fluids. Although ALESSANDRI *et al*. [16] have shown that PAF can induce histamine release from rat kidney mast cells, other authors [29] have failed to find any significant histamine-releasing activity of PAF on human skin mast cells. The difference in responsiveness may be related to the heterogeneity of rat and human mast cells. Our results suggest that nasal challenge with PAF does not provoke any significant histamine release, and are in line with the failure to find any increase in plasma histamine following bronchial challenge with PAF in allergic asthmatics [30].

As far as $iLTC_4$ release is concerned, it has been demonstrated that PAF can induce peptide-leukotrienes release from purified eosinophils [15], and from perfused rabbit [12] or guinea-pig [13] lung. Moreover, increased urinary levels of peptide leukotrienes and thromboxane A_2 have been found by TAYLOR *et al*. [9] in subjects undergoing bronchial stimulation with PAF. Therefore, an increase in $iLTC_4$ levels in nasal lavage fluids could be expected, but we have not found any significant $iLTC_4$ release. Using the model of nasal challenge followed by nasal lavages, we could demonstrate $iLTC_4$ release during the early allergen-induced reaction in allergic patients [2, 18]. Therefore, if $iLTC_4$ is generated and released in the nose following PAF challenge, the amount should be lower than that released after antigen challenge. Other possible explanations of the failure to find $iLTC_4$ release may be a difference in responsiveness of bronchopulmonary cells and nasal cells to PAF stimulation, with the former generating and releasing higher amounts of $iLTC_4$ than the latter, and a slow release coupled with rapid metabolic degradation.

It is noteworthy that a significant increase in neutrophils was observed after insufflation of lyso-PAF both in atopic and nonatopic subjects, although the effects of this phospholipid were weaker and slower compared to PAF. Moreover, an increase in eosinophils was observed in the nasal lavages collected 3 h after challenge in atopic subjects, but not in nonatopic subjects. These results are in line with the findings of SAKAMOTO *et al*. [31] who have demonstrated that inhaled lyso-PAF can increase lung resistance and airway microvascular leakage in the guinea-pig, and that its effects are inhibited by a specific PAF receptor antagonist (WEB 2086). Lyso-PAF is generally considered to be biologically inactive *in vitro*; therefore, the changes in nasal cytology observed in the present study, as well as the effects on guinea-pig airways, could be the consequence of the acetylation and transformation of lyso-PAF into PAF *in vivo* in respiratory airways. In fact, it has been demonstrated that PAF can be produced by cultured bacteria supplemented with lyso-PAF [32], and PAF formation by eukariotic cells is strictly dependent on the concentration of lyso-PAF available [33]. The effects of lyso-PAF *in vivo*, however, are weaker than those of PAF, and, in fact, no significant release of ECP was observed after lyso-PAF administration either in atopic or in nonatopic subjects.

PAF and lyso-PAF are released during the early antigen-induced reaction in the nose of allergic patients [2, 34], and both lipids have the capacity to attract and activate neutrophils and eosinophils [6, 25–28]. Since the cytological picture of the late antigen-induced reaction in human nasal airways is characterized by local accumulation of eosinophils and neutrophils [35, 36], one could speculate that PAF contributes to the attraction of these cells and has a role in antigen-induced allergic inflammation in the nose. The results of this study indicate that PAF has the capacity to attract eosinophils and neutrophils and to provoke ECP release when insufflated in the human nose, and supports its possible implication in allergic rhinitis. However, further studies with PAF antagonists are needed to define the clinical relevance of PAF in allergic rhinitis more precisely.

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