

T cell involvement in persulfate triggered occupational contact dermatitis and asthma

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Background: Ammonium and potassium persulfates may induce a variety of cutaneous and respiratory diseases. The precise underlying mechanisms, however, are unclear.

Objective: To describe a hairdresser, who developed contact dermatitis, rhinoconjunctivitis, and bronchial asthma of delayed onset after occupational exposure to hair bleaches containing persulfate salts and to provide evidence for a common T-cell mediated mechanism responsible for the clinical manifestations.

Methods: We performed skin testing, routine histologic and immunohistochemical examination of the skin reaction after prick testing, lymphocyte proliferation analysis, nasal challenge test, and pulmonary function testing.

Results: The causative role of bleaching powder and ammonium persulfate was demonstrated by case history, skin tests, and a nasal challenge test. Patch tests produced a delayed cutaneous reaction to ammonium persulfate confirming contact sensitization. Prick tests with bleaching powder and ammonium persulfate were negative at 15 minutes but revealed a late skin reaction with a papule at the prick sites after 24 hours. Histologic examination of this late reaction demonstrated a perivascular infiltration comprising predominantly T lymphocytes. Further, a significant proliferation of T cells to bleaching powder was reproducibly found by a lymphocyte proliferation analysis. Nasal challenge test with bleaching powder showed a significant reduction of air flow after 24 hours.

Conclusion: Our findings suggest that immunologic mechanism with direct involvement of T cells may not only play an important role in the pathogenesis of the cutaneous but also in the respiratory and rhinoconjunctival reactions.

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INTRODUCTION

Ammonium and potassium persulfates are powerful oxidizing agents, widely used in the production of metals, textiles, photographs, rubber, foods, soaps, detergents, and hair bleaches. A variety of cutaneous and respiratory diseases induced by persulfates have been reported in hairdressers and their customers.^{1–11} Although irritant as well as immediate and delayed-type allergic reactions have been implicated, the precise underlying pathomechanisms

have remained partly unclear.^{1–11} We report the case of a female hairdresser, who developed contact dermatitis, rhinoconjunctivitis and bronchial asthma of delayed onset after occupational exposure to hair bleaches containing persulfate salts. Our data suggest a common T-cell mediated mechanism behind her broad spectrum of clinical manifestations.

CASE REPORT

After an apprenticeship of 3 years, a 24-year-old female hairdresser, with no history of atopy, initially noticed nasal and ocular itching, sneezing, and rhinorrhea whenever working with bleaching powder. Subsequently, she experienced episodes of dyspnea and dry cough, which usually started 1 to 2 hours after exposure to bleaching pow-

der and aggravated especially during the night. In addition, eczematous lesions on both sides of her hands and forearms developed. Initially she was free of symptoms on weekends or holidays. After being off work for 4 months, she showed marked improvement of her cutaneous and respiratory symptoms, although dry cough awakened her occasionally at night.

Her physical examination at this time and laboratory results were normal, particularly no blood eosinophilia was detected. Total IgE was 159 kU/L. Patch tests revealed delayed skin reactions to ammonium persulfate (2.5% in petrolatum) and nickel sulfate (5% in petrolatum) after 48 and 72 hours. Skin prick tests performed with common aeroallergens were negative. Prick and scratch tests with bleaching powder (0.01 to 100 mg/mL) and freshly prepared ammonium persulfate (1% and 5%) were negative at 15 minutes. A papule, however, reproducibly developed at the prick sites after 24 hours in a dose-dependent manner (with concentrations from 1 to 100 mg/mL for bleaching powder and 1% to 5% for ammonium persulfate) and gradually healed within 48 to 72 hours. No immediate or late skin test reactions were observed in 15 controls.

Histologic examination of the papule at the prick site was consistent with a superficial dermatitis and showed a predominantly dermal, perivascular lymphocyte infiltration (Fig 1a). As revealed by immunohistochemical studies, lymphocyte infiltration consisted of approximately two-thirds of CD4+, CD45RO, HLA-DR+ (Fig 1b), and one-third of CD8+, CD45RO, HLA-DR+ cells (Fig 1c). Interestingly, CD8+ cells were predominantly seen in or nearer to the epidermis, whereas

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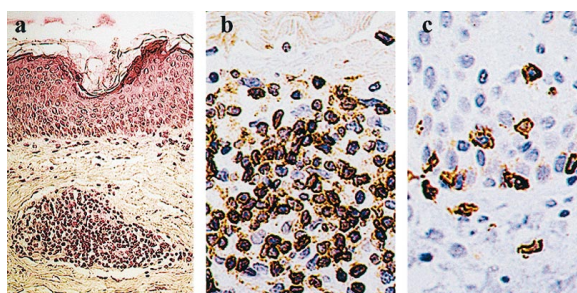


Figure 1. Histologic examination of the skin reaction to 5% ammonium persulfate 24 hours after prick testing, showing a superficial dermatitis with a predominantly dermal, perivascular lymphocyte infiltration. (a) Immunohistochemical analysis revealed a predominantly CD4+, perivascular T-cell infiltration. (b) In contrast, CD8+ cells were mainly located in or near the epidermis (c). Haematoxylin and eosin, original magnification $\times 250$ (a), immunoperoxidase staining, original magnification $\times 400$ (b,c).

Table 1. Results of Nasal Challenge and Spirometry Test with Bleaching Powder (0.1 mg/mL)

	Baseline mL (% norm)	0.5 Hour After Challenge mL (% norm)	2 Hour After Challenge mL (% norm)	24 Hour After Challenge mL (% norm)
Nasal air flow (left side at 150 Pa)	589	566	524	250
FVC	3460 (95%)	3450 (95%)	3370 (92%)	1930 (53%)
FEV ₁	2730 (86%)	2660 (84%)	2630 (82%)	1660 (52%)

CD4+ cells were mainly located in the perivascular dermis (Fig 1c).

Three lymphocyte transformation analysis (LTT) performed from heparinized blood of the patient as described previously¹² reproducibly demonstrated a significant, dose-dependent proliferation (³H-thymidin-incorporation) of T cells to bleaching powder (with 1 μ g bleaching powder: 3881 cpm $\pm$ 780 SD, with 10 μ g: 4075 cpm $\pm$ 812 SD, with 50 μ g: 4861 cpm $\pm$ 1525 SD, negative control: 1133 cpm $\pm$ 693 SD).

Spirometry was normal at the time of referral. Methacholine bronchial challenge showed a low degree of bronchial hyperreactivity (PD₂₀ = 1250 μ g). Nasal challenge test (active anterior rhinomanometry) with bleaching powder (0.1 mg/mL) produced nasal itching and a feeling of obstruction within 30 minutes after application, which gradually worsened during the next 24 hours. In addition, the patient complained of dry cough and dyspnea during the night following the nasal challenge. Active anterior rhinomanometry showed no significant reduc-

tion of nasal air flow at 150 Pascal after 0.5 and 2, but was positive after 24 hours (57.5%). A spirometry performed in parallel with rhinomanometry demonstrated a significant airway obstruction only 24 hours after the nasal challenge test (Table 1), which subsequently improved (>20%) after two puffs of salbutamol (0.2 mg), confirming reversible airway obstruction. A control spirometry performed 14 days later again showed baseline values. No subjective or objective reactions in the nasal challenge including spirometry and LTT were observed in four controls. On follow-up examination, 9 months after she had quit her profession and the patient was free of symptoms.

DISCUSSION

Clinical history and the results of our investigation are consistent with an occupational contact dermatitis, rhinoconjunctivitis and asthma in our patient by exposure to bleaching powder containing ammonium persulfate. As a low molecular weight compound, persulfates are thought to act as haptens,

inducing contact dermatitis through a T cell-mediated hypersensitivity reaction. In this context, recent reports indicate that contact hypersensitivity is associated with activation of a complex set of hapten-specific T cells, leading to generation of both CD4+ and CD8+ T-cells.¹³ Furthermore, a network of type 1 and type 2 cytokines such as INF- γ and IL-4/IL-10, respectively, are involved in initiating and promoting contact hypersensitivity reactions.^{14–16} Interestingly, CD4+ and in particular CD8+ cells, producing INF- γ , have been suggested to play a critical role as effector cells, while CD4+ cells, mainly producing IL-4 and IL-10 were important as regulators of contact hypersensitivity.^{16–18} In persulfate-mediated asthma or rhinoconjunctivitis, however, the underlying pathomechanism has not been elucidated so far. Previous reports have postulated a nonallergic mechanism such as damage of mucus membranes through chemical irritation¹⁰ or pseudoallergic mechanisms through the release of histamine by direct action on mast cells.^{1,9} In contrast, other reports have suggested an allergic pathomechanism based on positive prick and scratch tests with persulfate salts in some patients.^{2–7,11} To our knowledge, elevated serum-specific IgE antibodies have not been detected in any of the patients reported so far. Serum-specific IgE antibodies were not determined in our case, since the delayed onset of symptoms after exposure to persulfates as well as negative prick tests did not suggest an IgE-mediated reaction. In contrast, clinical history, namely the time course of several months between first exposure and onset of symptoms, the delayed onset of respiratory symptoms following nasal challenge test, late skin reactions and positive LTT results in our patient strongly suggest a T cell-mediated mechanism for both skin and respiratory symptoms. Previous reports have also indicated that persulfates may elicit irritant reactions.¹⁰ In this case, however, a latent period between first exposure and onset of respiratory symptoms at work strongly suggest a

sensitization phase and not a direct irritant reaction to persulfates. Furthermore, our patient only had a low degree of bronchial hyperreactivity and did not show signs of bronchial obstruction after unspecific stimuli such as inhalation of physiologic saline or after strenuous physical activity. In addition, no positive reactions after nasal challenge test were observed in four controls even though one of these individuals also had a low degree of bronchial hyperreactivity. An immunologic and irritant mechanism to persulfates may not be mutually exclusive and it is possible that an additional irritant reaction partly contributed to the induction of the respiratory symptoms in our patient.

Previously, asthmatic reactions to other low molecular compounds such as isocyanate, anhydride, acrylate, formaldehyde, wood dust, and metal salts have also been reported.¹⁹ In most subjects with occupational asthma to such low molecular weight compounds, the mechanism is generally not IgE-mediated. The pathogenesis of these reactions are unknown and in particular, the role of T cells in inducing respiratory symptoms is poorly understood so far.^{19–21} Increasing evidence suggests that activated T cells are capable of directly initiating and promoting inflammation in the airways.^{20,21} Distinct alterations in T cell subsets have been found in bronchoalveolar lavage (BAL) or in peripheral blood in allergic and intrinsic asthmatic subjects.²² Whereas the majority of T cell clones derived from atopic patients with allergic asthma have been shown to be CD4+,²³ T cell clones derived from patients with toluene diisocyanate-induced asthma mainly belong to the CD8+ phenotype.²⁴ In addition, distinct patterns of T cell-derived cytokines and chemokines are thought to play a central role in orchestrating the inflammatory response in the airways.^{20,22,24} Interestingly, immunohistochemical analysis of the positive skin reaction to ammonium persulfate (Fig 1) also revealed an infiltration of both CD4+ and CD8+ T cells with an accumulation of the later near or in the epi-

dermis. Similarly, it is possible that an infiltration of these cells in the bronchial mucosa may initiate an immune-mediated mechanism, finally leading to development of airflow obstruction. Taken together, our data provide evidence that T lymphocytes specific for low molecular compounds like persulfates may be directly involved in mediating inflammatory processes in the airways, rather than only acting through induction of IgE synthesis in persulfate triggered occupational asthma. Further studies are necessary to elucidate the precise pathomechanisms leading to persulfate-triggered asthma.

Since ammonium persulfate contained in bleaching powder is known to be one of the most important contact allergens in the hairdressing profession, physicians should be aware of the potential risk of these agents inducing occupational asthma as well. Patients remaining in the same job generally worsen with time and may even suffer from continued asthma despite cessation of exposure. Patients with contact dermatitis should also be carefully monitored with regard to respiratory symptoms, since early diagnosis and removal from exposure are important for improving the long-term outcome in these patients.

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