Occupational Asthma and Occupational Rhinitis in Hairdressers*

Gianna Moscato, MD; Patrizia Pignatti, PhD; Mona-Rita Yacoub, MD; Canzio Romano, MD; Sandro Spezia; and Luca Perfetti, MD

Background: Hairdressers are at risk for occupational respiratory diseases, but the risk factors, causal agents, and underlying mechanisms are not completely defined.

Aim: To describe the features of a large group of hairdressers consecutively referred to our center for suspected occupational asthma (OA) over an 8-year period, the type of occupational respiratory diseases, the etiologic agents, and the diagnostic tests.

Results: Forty-seven hairdressers (mean age, 25 years; range, 17 to 52 years) were studied. On the basis of the response to the specific inhalation challenge (SIC), 24 patients received a diagnosis of OA (51.1%), which was due to persulfate salts in 21 patients (87.5%), permanent hair dyes in 2 patients (8.3%), and latex in 1 patient (4.2%). Thirteen of these 24 patients (54.2%) also received a diagnosis of occupational rhinitis, which was due to persulfate salts in 11 patients (84.6%) and to paraphenylenediamine in two patients (15.4%). Patients with persulfate asthma had a long period of exposure to bleaching agents, a long latent period between the start of exposure and the onset of symptoms, and a prevalent eosinophilic airway inflammation in induced sputum. The skin-prick test with ammonium persulfate performed in a subset of patients gave negative results.

Conclusions: In the present study, we confirmed that persulfate salts are the major agents involved in OA and occupational rhinitis in hairdressers. The positive response to the SIC in only a part of the population of symptomatic exposed workers, the period between the start of exposure and the onset of symptoms, the type of response to the SIC, and the high frequency of association of asthma with other diseases such as dermatitis and rhinitis suggest an immunologic mechanism that remains to be elucidated. (CHEST 2005; 128:3590–3598)

Key words: hairdressers; occupational asthma; occupational rhinitis; persulfate

Abbreviations: BSA = bovine serum albumin; LMW = low molecular weight; OA = occupational asthma; PD_{20} = provocative dose of methacholine causing a 20% fall in FEV1; SIC = specific inhalation challenge; SPT = skin-prick test; TLV = threshold limit value; TWA = time-weighted average

Hairdressers are exposed to several reactive agents with potentially irritant and sensitizing effects on the airways and on the skin. Several data from population1–5 and clinical studies6–19 show that these workers are at high risk for occupational asthma (OA). In France, according to the Observatoire National des Asthmes Professionnels data in 1996 to 1999, hairdressing represents, among patients with OA, the fourth most frequent occupation (both sexes), and the second most frequent occupation in women, accounting for 6.8% of cases.1

Bleaching agents and particularly persulfate salts are considered the major cause of respiratory symptoms1–3,6–19 although the mechanism in inducing asthma is not understood. The risk factors for sensitization and development of OA in exposed workers are not known, and the diagnostic workup is not defined.

Clinical studies6–19 on airway symptoms in hairdressers are all based on a few exposed cases or on small numbers of hospital patients. In the present article, we describe the clinical features of a large group of hairdressers observed in our institute between 1996 and June 2004, the type of occupational respiratory diseases, the etiologic agents, and the diagnostic tests. To our knowledge, this is the largest group of hairdressers observed in a clinical unit to date.
was diagnosed by the following criteria 21–22: clinical history slow-release theophylline or inhaled steroids for at least 48 h bronchodilator or sodium cromoglycate for at least 24 h, and infection symptoms and had not received oral steroids or anti-history of atopy and smoking habits was also obtained. At the time specific tasks and/or specific agents; date of the last symptoms; work (stop/resume test); relationship between symptoms and periods at and away from (bronchial, nasal, cutaneous); duration of exposure before onset (following information was obtained: description of the current range, 17 to 52 years) consecutively referred to our allergy unit inflammation before the SIC.

Forty-seven hairdressers (43 women; mean age, 25 years; range, 17 to 52 years) consecutively referred to our allergy unit from 1996 to 2004 for suspected OA were studied. A detailed occupational history was obtained from the patients, and the following information was obtained: description of the current and previous job; specific tasks; products used in the workplace; modality of exposure (cutaneous, respiratory); type of symptoms (bronchial, nasal, cutaneous); duration of exposure before onset of symptoms; duration of symptoms from onset to diagnosis; relationship between symptoms and periods at and away from work (stop/resume test); relationship between symptoms and specific tasks and/or specific agents; date of the last symptoms; and date of last exposure. Information on personal and family history of atopy and smoking habits was also obtained. At the time of diagnosis (baseline), the patients did not have any respiratory infection symptoms and had not received oral steroids or anti-histamines for at least 2 weeks, anticholinergic or adrenergic bronchodilator or sodium cromoglycate for at least 24 h, and slow-release theophylline or inhaled steroids for at least 48 h before the challenge.

Asthma was diagnosed according to international National Institutes of Health/World Health Organization guidelines.20 OA was diagnosed by the following criteria21–22: clinical history suggesting work-related asthma, diagnosis of asthma, and positive response to SIC.23

Immunologic Tests

SPTs for common inhalant allergens24 and for latex were performed with commercial extracts (Lofarma Allergeni; Milan, Italy). To better evaluate the underlying mechanism of ammmonium persulfate in inducing asthma, 14 of 21 patients with a positive response to the SIC with this compound (see below) were also submitted to SPTs with ammonium persulfate; 7 of 21 patients refused to undergo the test. The test was performed only in patients with a positive SIC response to ammonium persulfate due to ethical reasons (possible risk of sensitization by SPT to an agent the patient is occupationally exposed to). The test was carried out using freshly prepared ammonium persulfate solutions at a concentration of 1% and 5% weight/volume in saline solution.18 Histamine was used as a positive control, and saline solution was used as a negative control. Each test was read after 20 min. SPTs with ammonium persulfate were also read at 2 to 4 h and at 24 h. A positive reaction was defined as a wheal diameter ≥ 3 mm in the absence of a reaction to the control diluent and in the presence of a positive reaction to histamine.25

Atopy was defined by at least one positive SPT response to common allergens. Patch tests were performed by application of agents (FIRMA; Florence, Italy) on the back with readings at 48 h and 72 h.26 Diagnosis of allergic occupational dermatitis was made in presence of dermatitis, positive patch result to a occupational agent, exposure to the agent, and positive stop/resume test result. Total and specific IgE for common inhalant allergens and for latex were also measured (UniCAP System; Pharmacia AB; Uppsala, Sweden).

Lung Function Tests

Spirometry was performed according to European Respiratory Society guidelines27 by means of a computerized water-sealed spirometer (BIOMEDIN; Padova, Italy). Bronchial challenge with methacholine was performed by means of a nebulizer (MEFAR; Brescia, Italy) connected to a dosimeter as previously reported.28 The provocative dose of methacholine causing a 20% fall in FEV1 (PD20) was expressed in micrograms and was considered to be positive if the PD20 was < 1,000 µg. The reversibility test was performed with the nebulization of salbutamol (100 µg followed after 5 min by another 100 µg) and the result was considered positive if there was an increase in FEV1 > 12% (in addition to an absolute increase of 200 mL).29

SIC

Each patient signed an informed consent approved by the ethical committee of our institute for the SIC. SICs were performed as described by Pepys and Hutchinson23 and Vandenplas and Malo.30 Each patient underwent the challenge with any suspected sensitizing agent and/or product present at the workplace. SICs with single agents/products were performed following the criterion of increasing likelihood of a positive response (eg, the more suspect the agent from the history, the later the SIC). Tested agents were ammonium persulfate (n = 44), paraphenylenediamine (n = 36), latex (n = 24), hair-waving solutions (n = 6), and permanent hair dyes (n = 4).

The challenges were performed in an inhalation chamber (7.46 m3) as follows: as a control, and on the first day the patient was exposed to ethanol for 30 min (cumulative exposure). If no significant change (variation of FEV1 ≥ 10%) in FEV1 occurred within 7 h in the following days, the patient was exposed to the suspected agents/products.

SIC with ammonium persulfate was performed by a 30-min nebulization of a solution of 8 mg of ammonium persulfate in 3 mL of distilled water. The concentration of ammonium persulfate in the inhalation chamber was evaluated, during two different challenges on separate days, by air sampling at 10', 20', and 30' after starting exposure using an air pump with a constant flow of 3 L/min. The analysis was performed by means of mobile-phase ion chromatography. A mean concentration of 1.01 ± 0.11 mg/L over the 30-min exposure was measured.

SIC with paraphenylenediamine was performed by a 30-min nebulization of a solution of 12.5 mg of paraphenylenediamine in 3 mL of ethanol 65% in water. SIC with latex was performed as previously described.31 SIC with hair-waving solutions (n = 6) and hair permanent dyes (n = 4) were performed with the occupational method.7 Each patient was consecutively exposed for 2, 4, 8, and 16 min, resulting in a total exposure time of 30 min.

Spirometry and peak expiratory flow were measured after each exposure. Spirometry and peak expiratory flow were monitored also at 5, 15, 30, and 60 min after the end of exposure and then every hour for 7 h and after 24 h. The test result was considered positive in case of FEV1 fall ≥ 20% compared to baseline. The responses were classified into three patterns: early if they occurred within 1 h after the end of exposure, late if they occurred after > 1 h, or dual, characterized by both an early and a late response.30

www.chestjournal.org

CHEST / 128/5 / NOVEMBER, 2005 3591
A diagnosis of occupational rhinitis was made in case of a positive nasal response. In the absence of international guidelines for the diagnosis of occupational rhinitis, the diagnosis was made in the presence of a positive symptom score after the SIC as described below. In order to evaluate nasal response to suspected occupational agents, symptoms were assessed and rhinoscopy was performed at 5, 15, 30, and 60 min after the end of exposure (on the control day and during SIC) and then every hour for 7 h and at 24 h. At each time point, the following symptoms and signs were assessed and recorded: nasal itching, sneezing, nasal obstruction, rhinorrhea, and mucosal edema. Each parameter was scored from 0 to 3. If the total score at each time point was ≥ 6, without any change on the control day, a positive nasal response was recorded and occupational rhinitis to that agent was diagnosed.

**Sputum Induction and Processing**

Sputum was induced and processed as previously described in 10 patients with positive SIC findings to ammonium persulfate and in 11 SIC-negative patients. The test was performed before the specific challenge, and in only the patients observed after 1999, when it was introduced into the practice of our laboratory.

Briefly, FEV₁ was measured before and 10 min after inhalation of salbutamol (200 µg). Ultrasonically nebulized (De Vilbiss 65; De Vilbiss; Somerset, PA) hypertonic (4.5%) saline solution was inhaled for 1, 2, 4, 6, and 16 min. FEV₁ was measured 1 min after each inhalation period. Patients were instructed to rinse their mouth with water and to cough and produce sputum after each inhalation period

Induced sputum was conserved at 4°C before starting the processing within 2 h. Sputum plugs were selected from saliva, weighed, and treated for 15 min with a volume (in microliters) of 0.1% dithiothreitol (Sputolysin 10%; Calbiochem; La Jolla, CA) diluted in 3% bovine serum albumin (BSA), equal to four times (in microliters) the weight (in milligrams) of sputum plugs. Then, an equal volume of BSA (phosphate-buffered solution) was added to the mixture and filtered with a 70 µmol/L cell strainer (Falcon; Becton Dickinson; Franklin Lakes, NJ). Cells were separated from supernatant by centrifugation at 300 g for 5 min and diluted in a volume of 1% BSA in phosphate-buffered saline solution equal to the volume of dithiothreitol added at first. Cell count and viability by Trypan blue exclusion were determined with optical microscopy. Cytospins were stained (Diff-Quick; Dade Diagnostika GmbH; Unterscheiheim, Germany) and analyzed for differential cell count. Sputum samples with < 30% of squamous cells were considered acceptable. Significant eosinophilic airway inflammation was defined when sputum eosinophils were > 3%.

**Statistical Analysis**

Age was expressed as mean (range); other variables were expressed as median (first to third quartiles). When range was used, it was indicated. Data were analyzed by means of Mann-Whitney U test, χ² test, and Spearman rank test; p values < 0.05 were considered significant. Analysis was performed using statistical software (Statistica for Windows, release 4.5; StatSoft; Tulsa, OK).

**RESULTS**

From 1996 to 2004, 47 hairdressers were referred to our center for suspected OA. All were enrolled in the study. The characteristics of the patients are shown in Table 1. SICs induced a bronchial response in 24 patients (51.1%), who received a diagnosis of OA. The responsible agents were ammonium persulfate in 21 cases (87.5%), permanent hair dyes in 2 cases (8.3%), and latex in 1 case (4.2%). In 13 of these 24 patients (54.2%), a nasal response was also induced by the SIC. These patients also received a diagnosis of OA. The responsible agents were ammonium persulfate in 11 cases (84.6%) and paraphenylenediamine in 2 cases (15.4%). In the remaining 23 patients (patients without OA), SIC induced a nasal response in 2 patients, resulting in a diagnosis of OA to persulfate in 1 patient and to latex in the

**Table 1—Characteristics of the Patients Enrolled**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total Population (n = 47)</th>
<th>SIC-Positive, Ammonium Persulfate (n = 21)</th>
<th>SIC-Negative, Ammonium Persulfate (n = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male gender</td>
<td>43/4</td>
<td>17/4</td>
<td>22/1</td>
</tr>
<tr>
<td>Age, yr</td>
<td>25 ± 8.2</td>
<td>25.7 ± 8.7</td>
<td>24.3 ± 7.3</td>
</tr>
<tr>
<td>Atopy, yes/no</td>
<td>21/26</td>
<td>10/11</td>
<td>11/12</td>
</tr>
<tr>
<td>Current smoker/nonsmoker</td>
<td>16/31</td>
<td>8/13</td>
<td>7/16</td>
</tr>
<tr>
<td>Stop/resume test, yes/no</td>
<td>37/10</td>
<td>21/10</td>
<td>13/10</td>
</tr>
<tr>
<td>Overall duration of exposure, yr</td>
<td>6 (3–11.5)</td>
<td>7 (3–11)</td>
<td>5 (3–11.5)</td>
</tr>
<tr>
<td>Duration of exposure before symptoms, yr</td>
<td>5 (2–10)</td>
<td>5.3 (2–9)</td>
<td>3 (1.5–9.4)</td>
</tr>
<tr>
<td>Duration of symptoms before diagnosis, yr</td>
<td>1.5 (0.7–2)</td>
<td>1 (0.5–2)</td>
<td>1 (0.8–3)</td>
</tr>
<tr>
<td>FEV₁ percentage of predicted</td>
<td>106 (98–111)</td>
<td>101 (95–110)</td>
<td>110 (98–111)</td>
</tr>
<tr>
<td>Methacholine test result, positive/negative</td>
<td>14/33</td>
<td>12/91</td>
<td>1/221</td>
</tr>
<tr>
<td>PD_{max}, µg</td>
<td>2,083 (909–2,222)</td>
<td>908 (473–1,417)</td>
<td>2,200 (2,083–2,317)</td>
</tr>
<tr>
<td>Bronchodilator test result, positive/negative</td>
<td>6/41</td>
<td>6/15</td>
<td>0/23</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SD, No., or median (first to third quartiles).

†χ² test, p = 0.0006, SIC positive vs SIC negative.

‡χ² test, p = 0.0001 SIC positive vs SIC negative.

§χ² test, p = 0.0082, SIC positive vs SIC negative.
other patient (both patients also had non-OA). In addition, in the same group, three patients received a diagnosis of non-OA plus nonoccupational rhinitis and one patient had nonoccupational rhinitis. In the overall group (n = 47), 17 patients received a diagnosis of allergic occupational dermatitis, 7 patients in the group with OA, and 10 patients in the group without OA.

Since the number of patients with OA due to substances other than persulfate salts was small, a comparison was made only between the two groups of patients, respectively, with OA due to persulfate and to other substances used at the workplace, (patients with a positive SIC response to ammonium persulfate, n = 21) and patients without OA due to persulfate (patients with a negative SIC response to ammonium persulfate, n = 23).

Patients With a Positive SIC Response to Ammonium Persulfate

The patients of this group were young (mean age, 25.6 ± 8.7 years) and mostly women (81%). Only a minority were current smokers (38.1%). The average overall duration of exposure was 7 years (range, 3 to 11 years), and the time elapsed between the beginning of exposure and the onset of symptoms (latency period) was 5.3 years (range, 1.8 to 9 years). Seven patients (33.3%) presented a family history of allergic disease. None of the patients reported previous occupations with possible risk factors for asthma, or symptoms of asthma, rhinitis, or dermatitis prior to the beginning of working as hairdressers. All 21 patients reported bronchial and/or nasal symptoms related to the workplace (positive stop/resume test result): 18 patients referred an association between bleaching and symptoms onset, while the remaining 3 patients were not able to relate symptoms to bleaching. In 11 patients, symptoms appeared almost 60 min after starting work, whereas in the other 10 patients the onset of symptoms varied from day to day. The time elapsed from the onset of respiratory symptoms and diagnosis was 1.5 years (range, 0.6 to 2 years). In addition to the diagnosis of OA, 8 patients (38.1%) also received a diagnosis of occupational dermatitis and 11 patients (52.4%) received a diagnosis of occupational rhinitis. Among hairdressers with both asthma and occupational rhinitis, seven patients reported a simultaneous onset of nasal and bronchial symptoms, whereas in the other four patients rhinitic symptoms had preceded the onset of bronchial symptoms. Eleven patients (52.4%) also reported skin symptoms (dermatitis or urticaria).

Immunologic Tests

SPTs results for common inhalant allergens were positive in 10 patients (47.6%), who were considered atopics. SPT results with ammonium persulfate were negative in all patients tested (n = 14). Patch test results with ammonium persulfate were positive in six patients; five of which were also positive to other substances used at the workplace; in three patients, patch test results were positive only for other substances used at the workplace. In the nine patients with a positive patch test result to ammonium persulfate or to other substances used at the workplace, a diagnosis of occupational dermatitis was made in addition to the diagnosis of OA. Sixteen patients (76.2%) had high total IgE levels (> 120 kilounits per liter); 11 patients (52.4%) had specific IgE for common inhalant allergens as well as 2 patients (9.5%) for latex.

Lung Function Tests

The results of spirometry, methacholine tests, and bronchodilator tests are shown in Table 1. All patients had normal spirometry findings at the time of diagnosis. The methacholine test result was positive in 12 patients (57.2%). The average time between last exposure and methacholine challenge was 4 days (range, 1.5 to 8 days). The bronchodilator test result was positive in only a third of patients (28.5%).

SIC

SIC with ammonium persulfate induced an early bronchial response in 4 patients (19.0%), an isolated late response in 14 patients (66.7%), and a dual response in 3 patients (14.3%). The details of the specific challenge tests are described in Table 2 and in Figure 1. The time onset of the late phase in late or dual responses negatively correlated with the overall duration of work exposure (r = -0.69, p = 0.002). Eleven patients also had a positive nasal response to the SIC, as shown by symptom score, and a diagnosis of occupational rhinitis was made. The nasal response preceded the late bronchial response in all cases.

Induced Sputum

The induced sputum cell count of patients with SIC positive to ammonium persulfate is reported in

Table 2—Characteristics of the SIC With Ammonium Persulfate in the Patients SIC Positive to this Agent (n = 21)*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SIC Positive, Ammonium Persulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern of bronchial response, early/late/dual</td>
<td>4/14/3</td>
</tr>
<tr>
<td>Time of the onset of the late reaction, min</td>
<td>150 (115–240)</td>
</tr>
<tr>
<td>Maximum fall in FEV1 during SIC, %</td>
<td>29 (24–34)</td>
</tr>
</tbody>
</table>

*Data are expressed as No. or median (first to third quartiles).
Table 3. Seven of 10 of these patients (70.0%) in this group had eosinophilic airway inflammation. The frequency of patients with eosinophilic airway inflammation tended to be higher in the SIC-positive patients compared to SIC-negative patients (3 of 11 SIC-negative patients, 27.3%) \( p < 0.05 \). The total amount of neutrophils was low in both groups; nevertheless, SIC-positive hairdressers had a significantly lower amount of sputum neutrophils compared to SIC-negative patients. The average time elapsed between the last work exposure and the sputum induction was comparable in the two groups of patients (SIC-positive hairdressers, 4.5 days; range, 3 to 21 days; SIC-negative hairdressers, 4.0 days; range, 0 to 60 days). No correlation between sputum eosinophils and the last work exposure, PD\(_{20}\) values, disease duration, IgE levels, and FEV\(_1\) maximal fall after SIC was found.

**Patients With Negative SIC Results to Ammonium Persulfate**

The general characteristics of these patients are described in Table 1. No significant difference was found between the two groups in age, sex, atopy, IgE levels, smoking habits, overall duration of exposure, latent period before onset of symptoms, duration of symptoms before diagnosis, and baseline FEV\(_1\) percentage. A significantly lower number of positive responses to the methacholine test was found in this group of patients \( p = 0.0001 \), compared with patients with positive SIC responses to ammonium persulfate. Positive stop/resume test results were significantly more frequent in the SIC-positive group vs the SIC-negative group (Table 1).

The time between the last exposure and methacholine challenge was 3 days (range, 1 to 45 days) without any significant difference with the other group. No significant response to the bronchodilator test was found in any patient of this group. The maximal percentage fall in FEV\(_1\) during the SIC with ammonium persulfate was 6% (range, 2 to 15%) [Fig 1].

**Conclusions**

In this study, we have described the largest group of hairdressers published to date referring to a clinical unit for suspected occupational asthma. We found that one half of these exposed workers had OA, which was caused by persulfate salts in most cases.

It is interesting to note that nearly half of the patients studied, although reporting symptoms at the work place, did not receive a diagnosis of asthma or OA. We hypothesize that their respiratory symptoms could be irritative and transitory, being related to the particular environment in hairdresser salons, where many irritating factors are often present (temperature, vapors, solvents, perfumes, and dust).

OA was associated with occupational rhinitis in 54.2% of cases, and in 52.4% of cases of persulfate asthma. These data confirm the association between

<table>
<thead>
<tr>
<th>Variables</th>
<th>SIC Positive, Ammonium Persulfate (n = 10)</th>
<th>SIC Negative, Ammonium Persulfate (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viability, %</td>
<td>77.4 (64.8–85.0)</td>
<td>79.2 (69.8–83.2)</td>
</tr>
<tr>
<td>Macrophages, %</td>
<td>67.4 (48.3–80.1)</td>
<td>45.6 (27.3–65.9)</td>
</tr>
<tr>
<td>Neutrophils, %</td>
<td>16.9 (5.2–21.5)</td>
<td>36.2 (19.4–41.5)</td>
</tr>
<tr>
<td>Eosinophils, %</td>
<td>6.1 (0.3–11.4)</td>
<td>1.0 (02–2.8)</td>
</tr>
<tr>
<td>Lymphocytes, %</td>
<td>1.5 (0.5–2.2)</td>
<td>2.2 (0.3–3.4)</td>
</tr>
<tr>
<td>Epithelial cells, %</td>
<td>4.1 (1.1–6.5)</td>
<td>2.0 (1.0–13.2)</td>
</tr>
<tr>
<td>Total cells/mg</td>
<td>1,800 (880–2,210)</td>
<td>3,280 (1,650–5,060)</td>
</tr>
<tr>
<td>Macrophages, cells/mg</td>
<td>1,372 (752–1,498)</td>
<td>1,405 (607–2,890)</td>
</tr>
<tr>
<td>Neutrophils, cells/mg</td>
<td>210 (78–3,009)</td>
<td>1,049 (378–1,488)</td>
</tr>
<tr>
<td>Eosinophils, cells/mg</td>
<td>67.2 (5.4–171.3)</td>
<td>28.9 (8.8–89.2)</td>
</tr>
<tr>
<td>Lymphocytes, cells/mg</td>
<td>12.5 (8.8–34.0)</td>
<td>70.6 (4.3–111.4)</td>
</tr>
<tr>
<td>Epithelial cells, cells/mg</td>
<td>54.7 (11.5–114.6)</td>
<td>147.8 (32.4–245.0)</td>
</tr>
</tbody>
</table>

*Data are expressed as median (first to third quartiles).

\( \dagger p = 0.02 \), SIC positive vs SIC negative.
asthma and rhinitis also in this occupational sector. In our cases of persulfate asthma, rhinitic symptoms preceded bronchial symptoms in a percentage of cases lower than that reported by Munoz et al. This percentage, however, recalls previous findings of our group in a wide group of patients with OA due to low-molecular-weight (LMW) agents in Italy (32.7%). In three of the present cases, one due to persulfate, an isolated rhinitis without asthma was found; since rhinitis is considered an early marker of asthma, it could be interesting to follow up these patients to evaluate the possible development of asthma. A percentage of 38.1 of persulfate asthma cases was associated with occupational dermatitis, confirming the high frequency of contact dermatitis in hairdressers.

The patients were young, mostly women, in agreement with previous observations. This reflects the general trend of this profession in most countries.

No difference was found between the patients with persulfate asthma and patients without concerning atopy and smoking habits. Similarly to previous studies, only half of patients with persulfate asthma were atopics, confirming that atopy is not an important risk factor in OA due to LMW agents.

In agreement with a previous study, our patients had been working as hairdressers for a long time before being referred to us for clinical investigation. The duration of exposure was not different between patients with or without persulfate asthma. Hairdressers are exposed to several risk factors, but we have no data on the levels of work exposure of our patients, particularly regarding the exposure to bleaching materials. Therefore, we cannot assume that similar duration of exposure means similar total dose of exposure.

Sensitization to LMW agents usually requires a shorter interval of time than sensitization to high-molecular-weight agents. In our patients with persulfate asthma, the latent period between the beginning of exposure and the onset of symptoms was longer than that reported in previous studies. This could be due to the fact that hairdressers, particularly at the beginning of their employment, carry out a variety of tasks and might not be continuously exposed to the same agent, thus requiring a longer time for sensitization.

The time elapsed between the onset of symptoms and diagnosis was relatively short. The patients were seen in an early phase of the disease, and this finding may probably explain the absence of impairment in respiratory function.

In patients with persulfate asthma, the clinical history was highly suggestive, and the stop/resume test result was positive in all patients with a specific association with the job of bleaching in most patients, confirming that history is a key point in the diagnostic workup of OA. Nevertheless, the finding of a positive stop/resume test result also in 13 patients of the group who had a negative response to the SIC underlines that clinical history should be confirmed by objective means. However, it is remarkable that negative stop/resume test results have been found only in the SIC-negative subgroup; this finding strongly suggest a role of this test in predicting a negative outcome of the SIC.

The skin-prick test result with ammonium persulfate performed in a subgroup of patients with persulfate asthma, as confirmed by a positive SIC finding, was negative in all patients. Positive SPT results to persulfate salts have been reported in a variable proportion of the cases that have been published to date, and also in exposed patients without symptoms. The method we used for SPTs is the same described by Wrbitzky et al in 1995, and similar to that reported by other authors, thus, our negative results may not be accounted for by a methodologic difference. Our findings cannot confirm the presence of an IgE mechanism in persulfate asthma, as suggested by previous authors.

Sputum analysis is a noninvasive tool for measuring airway inflammation in asthma and in OA. In the present study, 70% of patients with persulfate asthma who underwent this test had an eosinophilic inflammation. Neutrophils remained in the normal range, as defined by Spanevello et al in both groups of patients (SIC positive and SIC negative), although a lower percentage of sputum neutrophils were found in SIC-positive patients. To our knowledge, there is only another report in the literature on airway inflammation in five cases of occupational asthma due to persulfate salts, in which only one patient had an eosinophilic inflammation; however, three of the remaining four patients had undergone a corticosteroid treatment, possibly reducing airway inflammation. Whether exposure to LMW agents results in a prevalent eosinophilic or neutrophilic airway inflammation is still a question of debate. Anees et al reported that among the OA patients sensitized to LMW agents enrolled in their study, only 36.8% had sputum eosinophilia, and that sputum eosinophils did not relate to the causative agents, duration of exposure, or lack of treatment. Lemière et al found that sputum eosinophils were higher at baseline in patients with OA due to LMW agents compared to high-molecular-weight agents, suggesting that eosinophilic airway inflammation could be associated in these patients to the more frequent late asthmatic reaction. Otherwise, some authors reported a prev-
alent neutrophilic inflammation in patients with occupational asthma due to LMW agents both at baseline and after SIC.19–30

In previous studies, the challenge with persulfate salts has been carried out with different methods. In the article by Pepys et al7 and in more recent studies,2,9–10,13 the occupational method was used, attempting to reproduce in the laboratory the conditions at the workplace. Macchioni et al18 exposed the patients to bleaching dust containing potassium and ammonium persulfate through a mask. Munoz et al19,51 performed the test on consecutive days with increasing quantity of potassium persulfate mixed with lactose. The estimated concentration of this substance in the air was from 1 to 6 mg/μL.51 Other authors15 administered a solution of 1:50 weight/volume potassium persulfate extract through a nebulizer. In our study, we described a new method of exposure to ammonium persulfate, which consists of nebulizing a solution of ammonium persulfate in an inhalation chamber. The method was designed and standardized in order to overcome two major pitfalls in currently used methods, eg, lack of reproducibility, related to tipping substances from one shelf to the other by the patients themselves (occupational methods), and costly and prolonged investigations, related to progressively increasing exposure over several consecutive days.

Considering that the threshold limit value (TLV)/short time exposure limit for ammonium persulfate is not known, and that no data are available in the literature on the levels of exposure at the workplace, we took as a reference the TLV/time-weighted average (TWA). This is the value below which no health effect should be suffered by a normal worker exposed for 8 working h, 5 d/wk, over his/her lifetime. In order not to exceed the maximal total daily dose (calculated by TLV-TWA for 8 h), we considered that for an exposure of 30 min the maximal allowable concentration should be lower than 16 times the TLV-TWA (1.6 mg/μL). For safety reasons and in order to reduce as much as possible triggering of asthma through an irritative mechanism, we further reduced the concentration in the inhalation chamber to approximately 1 mg/μL. This method of exposure is simple and technically more reproducible than those employed up to now. It has proved effective in distinguishing responders and nonresponders with the cutoff of FEV1 fall of 20% (Fig 1). It has also proved devoid of any irritative effects in all patients (responders and nonresponders, with or without bronchial hyperreactivity). Finally, it has proved safe, being all bronchial responses, including the most severe, progressive in their onset and promptly reversed after inhaled bronchodilator.

Similarly to most previous studies,2,7,10–11,15,18–19 a late response was the most frequently observed, which was isolated in 14 of 21 cases and associated with an early component (dual response) in 3 other cases. These findings are in agreement with the clinical histories of our patients, who reported a late onset of symptoms, most frequently 1 h after the beginning of the working day. The degree of bronchial response to persulfate inhalation was moderate (maximal FEV1 fall of 29%), and in no case were medications needed to reverse the bronchoconstriction, showing the safety of the inhalation method we used. The finding that the time onset of the late component both in late and in dual responses negatively correlated with the overall duration of exposure suggests that patients with a longer duration of exposure have a higher degree of underlying airway inflammation.

Regarding the mechanisms involved in persulfate asthma, our findings of a positive response to the SIC in only a proportion of exposed workers, the presence of a latent period between first exposure and the onset of symptoms, the relatively low prevalence of atopy, and the high frequency of association of asthma with other diseases such as dermatitis and rhinitis suggest the involvement of an immunologic mechanism. However, the finding of negative responses to the SPT with ammonium persulfate and of an isolated late response in most cases31 tends to exclude an IgE-mediated mechanism. An underlying IgE mechanism in persulfate asthma has been suggested by other authors,16,19 and previous findings by our group52 of an anaphylactoid reaction to patch testing with ammonium persulfate also supported the hypothesis of the involvement of an IgE-mediated mechanism. Nevertheless, specific IgE has not been found in the serum of patients with respiratory diseases to persulfate salts, nor any other specific serum Ig.15 Other non-IgE mechanisms have been suggested. Blainey et al2 found a significant increase in neutrophil chemotactic activity after challenge with bleach powder, suggesting the involvement of mast cells. In the Italian study by Pisati et al,10 the bronchial response to the SIC with bleaching powder was inhibited by previous administration of disodium cromoglycate, also suggesting the involvement of mast cells in the bronchial response. The mechanism by which mast cells activation may occur in persulfate asthma is not understood. A study53 on animal mast cell preparation has shown that persulfate salts can release histamine directly, but this finding cannot explain why only some individuals are affected.5 Yawalkar et al54 suggested a role of T cells both in cutaneous and in respiratory and rhinoconjunctival reactions to persulfate salts. Nevertheless,
at present, the mechanism of asthma due to persulfate salts still remains unknown and requires further studies.

In conclusion, in the present study we have described the characteristics of the largest group of hairdressers with work-related respiratory symptoms published to date, finding that half of them had OA and rhinitis due to persulfate salts. The lack of difference in the duration of exposure to bleaching agents before the onset of symptoms in the two groups of patients (sensitized vs nonsensitized) suggests that sensitization to persulfate salts may be more related to an individual hypersusceptibility than to environmental factors, although evaluation of more accurate markers of exposure, ie, air concentrations, in the workplace are needed to confirm this hypothesis.

Although some observations suggest an underlying immunologic mechanism, we cannot confirm the involvement of an IgE-mediated mechanism for persulfate salt-induced asthma. Therefore, we confirm that the SIC is the “gold standard” for the diagnosis of persulfate asthma.

References