Background: Persulfate salts have been identified as a cause of occupational asthma (OA). The aim of the present study was to describe the clinical characteristics, diagnostic testing results, and follow-up of eight patients with OA that was triggered by these chemical compounds.

Methods: Eight patients with OA due to exposure to persulfate salts were studied. Immunologic, lung function, and specific bronchial challenge tests (SBCTs) were performed in all patients. Once their condition had been diagnosed, the patients were seen every 1, 3, and 6 months for a mean duration of 18 months.

Results: The mean time of exposure to persulfate salts up to diagnosis was 15 years (range, 3 to 27 years), and mean time that had elapsed between symptom onset and diagnosis was 38 months (range, 3 to 120 months). Three patients were smokers, six patients presented with rhinitis prior to asthma in relation to persulfate exposure, and three presented with dermatitis. The results of total IgE tests were positive in six patients, and the results of skin-prick tests for detection of persulfate salts were positive in five of these patients. The results of a SBCT was positive in the seven patients in whom it was performed. Symptoms persisted in all but one patient and required medical treatment.

Conclusions: The results suggest that the reliable diagnosis of OA due to persulfate salts must be based on the specific challenge test until further experience has been acquired. Despite avoiding exposure, patients continued with symptoms and required treatment for the control of symptoms. Finally, a dependent IgE mechanism appears to be implicated in the pathogenesis of OA due to exposure to persulfate salts.

Key words: bronchial challenge test; occupational asthma; persulfate salts

Abbreviations: OA = occupational asthma; PBS = phosphate-buffered saline; PC20 = provocative concentration of a substance causing a 20% fall in FEV1; PEF = peak expiratory flow; SBCT = specific bronchial challenge test

Persulfate salts are highly reactive, low-molecular-weight, chemical compounds that are widely used in different manufacturing processes in the chemical, pharmaceutical, metallurgic, textile, photographic, food, and, particularly, cosmetic industries. Although the first cases of occupational asthma (OA) due to persulfate salts were described in hairdressers and persulfate production workers in the chemical industry 30 years ago, the prevalence of the disease remains unknown. Blainey et al. in a cross-sectional study of employees in a hairdressing salon found that 4 of 23 had OA due to exposure to persulfate salts, and Leino et al. reported an 0.8% prevalence in Finnish hairdressers. Discrepancies as to incidence also were observed. In this respect, based on the English Registry of Surveillance of Work-related and Occupational Respiratory Disease, Cullinan and Newman Taylor estimated the incidence of OA in hairdressers to be around 81 cases.
per million persons exposed per year, whereas Albin et al. found an incidence of 3.9 per 1,000 persons exposed per year in female Swedish hairdressers.

Thus, although persulfate-induced asthma may represent up to 4% of all OA cases, the mechanism by which persulfate salts induce asthma, the risk factors for its development, the value of diagnostic tests, and the evolution of these patients remain unknown. This may be due to the small number of cases studied systematically. Although several case reports have been published to date, only two series, using four and five patients, respectively, have been studied to date. For these very same reasons, the follow-up of these patients is also unknown.

The present report describes the clinical features of, the diagnostic tests conducted in, and the follow-up of the largest series of patients with OA due to this chemical compound that have been published to date.

**Materials and Methods**

**Study Population**

Eight women (mean age: 35 years; range: 23 to 46 years), the total number of patients in whom asthma due to persulfate salts had been diagnosed at our occupational respiratory disease unit between 1997 and 2001, were prospectively studied. Three patients were employed in a cosmetic product factory where they mixed persulfate salts with other chemical agents to produce hair bleaches. Five patients worked with dyes in hairdressing salons. In the latter cases, the hair bleaches containing persulfate salts were supplied to the patient in powder form and the workers mixed them with hydrogen peroxide to form a paste, which then was applied to the hair.

At the time of diagnosis, a clinical history including exhaustive occupational history was taken, and lung function, immunologic, and specific bronchial challenge tests (SBCTs) were performed in all patients.

**Lung Function Tests**

Spirometry was performed (Datospir 200; Sibel; Barcelona, Spain) according to European Respiratory Society guidelines. The reference values used were those proposed by Roca et al. for the Mediterranean population. Bronchial challenge with methacholine was undertaken using the method described by Chai et al. Briefly, a dosimeter (Mefar MB3; Ele H2O; Medicalli; Brescia, Italy) was used, and increasing doses of methacholine (range: 0.003 to 16 mg/mL) were inhaled at 3-min intervals until FEV1 had fallen by 20% of its baseline value or the subject had inhaled the maximum concentration of methacholine. The provocative concentration of a substance (methacholine) causing a 20% fall in FEV1 (PC20) was expressed in milligrams per millilitre. The result of the methacholine challenge was considered to be negative if the PC20 was > 8 mg/mL, according to European Respiratory Society guidelines.

Subjects were provided with portable peak flow recorders (mini Wright; Clement Clarke International; Harlow, Essex, UK) and diary cards, and were instructed in their use following the indications of Moscato et al. They were requested to record peak expiratory flow (PEF) rates at least four times per day for 2 weeks at work and 2 weeks off work. The recording was considered to be positive when the qualitative assessment made by one of the authors, an expert in this type of reading, revealed evident changes between the exposure periods.

**Immunologic Test**

Skin-prick tests to detect common inhalant allergens were performed according to the method described by Pepys. A skin-prick test with potassium and ammonium persulfate (Sigma-Aldrich Corporation; St. Louis, MO) also was performed in all subjects. This test was carried out using freshly produced 5% (weight/volume) ammonium and potassium persulfate solutions. A phosphate-buffered saline (PBS) solution was used as a solvent owing to the acidity of the aqueous solutions. Histamine served as a positive control, and a PBS solution served as a negative control. The results of the test were read at 15 min, and were considered to be positive when the largest and smallest diameter of the wheal divided by 2 was ≥ 3 mm greater than that obtained with the negative control (ie, PBS solution). The histamine positive control was > 3 mm in all patients.

The total IgE level also was measured (UniCAP System; Pharmacia AB; Uppsala, Sweden), and a level > 150 IU/mL was considered to be high.

**SBCT**

SBCTs with potassium persulfate were performed following the method proposed by Pepys and Hutchcroft for chemical agents and the European Respiratory Society guidelines. Subjects were admitted to the hospital for the duration of the test. On the first day, 5 g potassium persulfate were mixed with 150 g lactose and were tipped from one tray into another 30 cm away in a challenge room with independent air extraction. On successive days, if the test proved negative, then 10, 15, and 30 g potassium persulfate mixed with 150 g lactose were tested. All subjects were challenged for 10 min, unless respiratory symptoms developed before that time, in which case the challenge was stopped. Changes in pulmonary function were followed in all patients by measuring FEV1 and FVC at 15 min intervals for the first hour and at hourly intervals thereafter. A response was considered to be positive when FEV1 fell by > 20% of its baseline value in the absence of any change in response to a control challenge of lactose powder alone that was conducted on a separate day.

**Follow-up**

All patients were advised to avoid exposure to persulfate salts. Medical appointments with forced spirometry were held at 1 month, 3 months, and, later, every 6 months postdiagnosis.

Inhaled bronchodilators and/or corticosteroids (depending on the patient’s symptoms, physical examination, and spirometry results) were administered according to the criteria proposed by the Global Initiative for Asthma.

**Results**

**Clinical Characteristics**

Clinical characteristics of the patients are shown in Table 1. The mean time of contact with persulfate salts prior to diagnosis was 15 years (range, 3 to 27 years), and the mean time elapsed between
symptom onset and diagnosis was 38 months (range, 3 to 120 months). All patients developed cough, chest tightness, and wheezing, and initially presented symptoms after work and at night, except patient 7 whose symptoms had occurred during work from the beginning of onset. Symptoms later worsened, appearing also during the day and with no improvement in exposure-free periods, except in patient 6. Three patients (2, 4, and 5) had to attend the emergency department on some occasion, although only patient 2 required hospital admission. Three patients were smokers. Six patients presented with rhinitis prior to their asthma that was related to contact with persulfate salts, and three patients presented with dermatitis. No patient had experienced asthma, rhinitis, or dermatitis prior to initiating contact with persulfate salts.

**Lung Function Tests**

The results of spirometry and methacholine tests are detailed in Table 2. All patients had normal spirometry findings at the time of diagnosis. The methacholine test was positive in all patients except one (patient 4).

PEF monitoring was consistent with OA in all cases in which it was performed, with the exception of patient 8. This study was not conducted in patients 1 and 4 as they had left their work during the diagnostic study period.

**Immunologic Test**

A skin-prick test to detect exposure to persulfate salts was positive in five patients, as shown in Table 2. Patient 6 presented with an anaphylactic reaction when the prick test to persulfates was performed, with severe bronchospasm that resolved with the administration of topical bronchodilators, subcutaneous adrenaline, and systemic corticosteroids.

Skin-prick tests against potassium and ammonium persulfate also were performed in three healthy subjects and three nonexposed asthmatic patients who served as control subjects. The tests were negative in all of these patients. Total IgE values proved to be high in six patients.

**SBCT**

SBCT was positive in the seven patients in whom it was performed, eliciting an early response in one patient, a late response in five patients, and a dual response in one patient (Fig 1 and Table 2).

Patient 6 did not undergo the SBCT since, as

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**Table 1—Clinical Characteristics of Patients Studied**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, yr</th>
<th>Duration of Exposure, yr</th>
<th>Latency Period, mo</th>
<th>Smoking History</th>
<th>Rhinitis*</th>
<th>Dermatitis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46</td>
<td>10</td>
<td>18</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>43</td>
<td>25</td>
<td>28</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>7</td>
<td>12</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>44</td>
<td>20</td>
<td>120</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>24</td>
<td>3</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>27</td>
<td>32</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>15</td>
<td>18</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>25</td>
<td>10</td>
<td>72</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*In relation to contact with persulfate salts.

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**Table 2—Results of Diagnostic Tests Performed in the Patients Studied**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Total IgE, kU/L</th>
<th>Skin-Prick Test to Inhalant Allergens</th>
<th>Prick Test to Persulfates</th>
<th>Methacholine PC20, mg/mL</th>
<th>PEF Study</th>
<th>Response to SBCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>182</td>
<td>+</td>
<td>–/-</td>
<td>0.36</td>
<td>ND</td>
<td>+ (late)</td>
</tr>
<tr>
<td>2</td>
<td>203</td>
<td>–</td>
<td>–/-</td>
<td>0.06</td>
<td>+</td>
<td>+ (biphasic)</td>
</tr>
<tr>
<td>3</td>
<td>1,295</td>
<td>–</td>
<td>–/-</td>
<td>0.18</td>
<td>+</td>
<td>+ (late)</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>+/+</td>
<td>&gt; 8</td>
<td>ND</td>
<td>+</td>
<td>+ (late)</td>
</tr>
<tr>
<td>5</td>
<td>509</td>
<td>–</td>
<td>+/+</td>
<td>0.06</td>
<td>+</td>
<td>+ (late)</td>
</tr>
<tr>
<td>6</td>
<td>32</td>
<td>+/+</td>
<td>1.50</td>
<td>ND</td>
<td>+</td>
<td>+ (late)</td>
</tr>
<tr>
<td>7</td>
<td>342</td>
<td>+/+</td>
<td>1.89</td>
<td>+</td>
<td>+ (late)</td>
<td>+ (immediate)</td>
</tr>
<tr>
<td>8</td>
<td>541</td>
<td>+/+</td>
<td>6.50</td>
<td>–</td>
<td>+ (late)</td>
<td></td>
</tr>
</tbody>
</table>

*+: positive; –: negative; ND: not done.
†Ammonium/potassium.
‡Severe bronchospasm after skin-prick test with persulfates.
mentioned previously, she presented with severe bronchospasm when the skin-prick test for detecting exposure persulfate salts was performed. The test also was performed in three healthy subjects and three asthmatic subjects, and the findings were negative in all.

**Follow-up**

The mean duration of follow-up was 18 months (range, 6 to 36 months). The clinical evolution and \( \text{FEV}_1 \) of each patient are detailed in Table 3. Five patients avoided exposure to persulfate salts, and three patients adopted protective measures following diagnosis. Except for one patient (patient 3), all continued with asthma symptoms and required medical treatment for control of those symptoms. Furthermore, a deterioration in \( \text{FEV}_1 \) was observed in five patients despite the medical treatment.

**Discussion**

From the small proportion of exposed workers who develop OA due to persulfate salts,\(^6\)–\(^8\) the latent

![Figure 1. Bronchial response to SBCT with potassium persulfate in the study population.](image-url)

**Table 3**—Follow-up Details Obtained in Eight Patients*

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Mean Follow-up Time, mo</th>
<th>Exposure Postdiagnosis</th>
<th>Symptom Persistence†</th>
<th>Treatment Required</th>
<th>( \text{FEV}_1 ) at Diagnosis, L (%)</th>
<th>( \text{FEV}_1 ) at Latest Control, L</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>36</td>
<td>No</td>
<td>Yes (2)</td>
<td>Yes</td>
<td>2.68 (99)</td>
<td>2.25</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>No</td>
<td>Yes (2)</td>
<td>Yes</td>
<td>1.87 (79)</td>
<td>1.37</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>3.02 (92)</td>
<td>2.96</td>
</tr>
<tr>
<td>4</td>
<td>24</td>
<td>No</td>
<td>Yes (1)</td>
<td>Yes</td>
<td>2.62 (98)</td>
<td>2.63</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>No</td>
<td>Yes (1)</td>
<td>Yes</td>
<td>3.45 (105)</td>
<td>3.57</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>Yes</td>
<td>Yes (2)</td>
<td>Yes</td>
<td>2.70 (107)</td>
<td>2.30</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>Yes</td>
<td>Yes (2)</td>
<td>Yes</td>
<td>3.47 (108)</td>
<td>3.09</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>Yes</td>
<td>Yes (1)</td>
<td>Yes</td>
<td>3.85 (106)</td>
<td>3.61</td>
</tr>
</tbody>
</table>

*Latest control-\( \text{FEV}_1 \) data obtained at the last appointment of the patients with the physician in the outpatients' department, prior to the writing of the manuscript.
†Values in parentheses refer to the classification of patients according to the Global Initiative for Asthma.
period between onset of exposure and the onset of symptoms, and the type of response observed in the challenge test suggest that persulfate-induced OA is mediated by an immunologic mechanism. The results obtained in the present study suggest that this immunologic mechanism might be mediated by IgE, since a skin-prick test that is positive for persulfate salts had been obtained in five patients (62%), as also has been observed in approximately 50% of the cases that have been published to date.\(^1\) Furthermore, elevated serum total IgE levels were observed in six patients, and one patient experienced an anaphylactic reaction. Both events also have been described by other authors.\(^1,3,12,14\) However, other mechanisms also may be involved. Blainey et al\(^6\) suggested that mast cells may play a role in the pathogenesis of the late asthmatic reactions following the inhalation of persulfate salts, since they found a significant rise in serum neutrophil chemotactic activity paralleling airflow obstruction. Finally, Yawalkar et al\(^1\) suggested that T cells may play a role in the pathogenesis of OA due to persulfate salts after reporting a case in which skin-prick test positivity was observed after 24 h and histologic examination of the patient’s late reaction demonstrated a perivascular infiltration predominantly comprising T lymphocytes. This late response to the skin test was not observed in any of our patients.

The diagnosis of OA is usually suggested by clinical history; however, it is often not sufficient to reach a definitive diagnosis\(^29\) and should be complemented by serial measurements of PEF, immunologic testing, and/or bronchial challenge testing. Immunologic tests are of little use for the diagnosis of persulfate-induced OA since the sensitivity and specificity of the skin-prick test, which in our series was positive in five of eight patients, remain unknown. In this respect, a 1995 study\(^13\) showed that 8 of 52 subjects who had been exposed to persulfate salts had positive skin-prick tests, regardless of whether they had experienced respiratory symptoms or not. On the other hand, in the different works published in which a specific IgE to persulfate salts was studied, no positive values could be found. In our experience, the PEF study proved useful since a response that was consistent with OA was elicited in all but one of the patients in whom it could be performed. Conversely, in the series of Blainey et al\(^6\), only one of four patients showed a consistent response, and Anconetani et al\(^11\) published a case in which the PEF study was also negative.

Bearing in mind that the main exposure to persulfate salts occurs in hairdressers, who also may be exposed to other agents (such as hemm\(^30\) or paraphenylenediamine\(^31\)) that also can cause OA, or to different nonspecific irritants that are capable of triggering bronchospasms in individuals with or without asthma,\(^32\) the performance of specific challenge tests for persulfate salts may be indicated in many patients. Different methods of performing this test have been used. Some authors have carried out the test by attempting to reproduce the conditions in the workplace,\(^4,5\) others by aerosolizing a potassium persulfate nondialyzed extract by a nebulizer.\(^11\) Finally, Blainey et al\(^6\) performed the test by mixing 30 g bleach powder with 50 g lactose and tipping it from one tray to another 30 cm away in a challenge chamber with independent air extraction. In the latter study, three patients also were challenged with persulfate salts; however, the authors did not detail the characteristics of the mixture. In the present study, the test was performed on consecutive days with the quantity of potassium persulfate increased and mixed with lactose with the following two objectives: to avoid overexposure in potentially sensitive patients; and to attempt to show a possible dose-response relationship, which was observed in patients 1, 2, and 4 of our series (Fig 1). Late response was the most frequently observed form both in our patients and in those in the literature,\(^4,6,11,12\) although three cases of early responses\(^4,15,17\) and one of dual response\(^16\) also have been reported.

With regard to the evolution of patients in whom asthma due to persulfate salts has been diagnosed and in contrast to the cases described by Macchioni et al,\(^18\) we observed that seven of our patients had persistent asthma despite avoiding exposure. It is known that a significant number of patients with OA with latency do not recover, even after several years away from exposure.\(^33\) In the case of OA due to exposure to isocyanates, our group\(^34\) has shown that approximately 71% of patients continue with bronchial hyperreactivity despite avoiding exposure, a percentage that is similar to that already demonstrated by other authors.\(^35\) Similarly, in the case of patients with OA due to western red cedar, approximately 60% of patients who avoid exposure continue to have asthma and require treatment for its control.\(^36\) The duration of symptoms before removal from exposure is a prognostic indicator, irrespective of the agent. Early removal from exposure increases the likelihood of recovery.\(^33\) In the present series of patients, the latency time between the onset of symptoms and diagnosis was prolonged, ranging from 3 to 120 months, which could account for the unfavorable evolution observed later. Furthermore, worsening in FEV\(_1\) was found in two patients who failed to avoid exposure (patients 6 and 7). In this respect, a follow-up study of 280 patients with asthma due to western red cedar exposure showed the longitudinal decline in FEV\(_1\) to be significantly greater in those who were still exposed to red cedar compared to those who had been exposed but did not have asthma.\(^37\)
In conclusion, the results of the present study suggest that a dependent IgE mechanism is involved in persulfate-induced asthma. Furthermore, they support the theory that early diagnosis and prompt removal from exposure are essential for the treatment of these patients, as generally occurs in all patients with OA. Finally, until other tests provide more diagnostic precision, the diagnosis of OA due to persulfate salts must be based in many cases on the specific challenge test.

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