Reactive airways dysfunction syndrome caused by bromochlorodifluoromethane from fire extinguishers

M Matrat, M F Laurence, Y Iwatsubo, C Hubert, N Joly, K Legrand-Cattan, J P L’Huillier, C Villemain, J C Pairon

Although the neurological and cardiovascular effects of Freons have been extensively described, the respiratory effects have been less well documented. We report four cases of occupational asthma following accidental exposure to bromochlorodifluoromethane (Halon 1211) due to release of the contents of a fire extinguisher. All subjects developed an irritative reaction of the upper airways and lower respiratory symptoms immediately after exposure. Non-specific bronchial hyperreactivity was present for at least two months in all subjects and was still present more than two years after exposure in one case. The diagnosis of reactive airways dysfunction syndrome can be adopted in at least three of these four cases.

Bromochlorodifluoromethane (CBrClF\textsubscript{2}, Halon 1211) is a colourless and almost odourless gas widely used in fire extinguishers. The use of Halons in fire extinguishers and other protective systems against fire ceased at the end of 2003. However, some rare exceptions exist to the general ban on ozone damaging agents, as the use of Halon 1211 will still be allowed after 2003 in the European Union in four circumstances: for use in aircraft extinguishers (portable fire extinguishers, fixed motor extinguishers, extinguishers for crew compartments, engine nacelles, cargo bays, and dry bays), extinguishers for safety of firefighters (initial extinction of fires), and military and police extinguishers for use on persons.\textsuperscript{1}

The acute toxicity of CBrClF\textsubscript{2} is usually considered to be related to central nervous system dysfunction\textsuperscript{2} and cardiac sensitisation to catecholamines with lowering of the threshold for arrhythmia.\textsuperscript{3}

Human exposure studies suggest that fluorocarbons can cause respiratory irritation.\textsuperscript{4,5} Some authors have reported respiratory irritant effects or reactive airways dysfunction syndrome (RADS) following accidental exposure to bromotrifluoromethane (Halon 1301)\textsuperscript{6,7} or thermal degradation products of Freons.\textsuperscript{8} We report four cases of occupational asthma following exposure to CBrClF\textsubscript{2}.

CASE REPORTS
The four cases occurred in two distinct episodes of accidental exposure to CBrClF\textsubscript{2} with fire extinguishers used in aeroplanes.

Incident A
Three subjects were involved in incident A, which occurred on 24 December 1998 during a flight. Accidental release of the contents of a portable fire extinguisher occurred during handling in the absence of a fire at the back part of the plane. Three crew members, two air hostesses, and a steward were exposed while transporting the defective fire extinguisher to a closed cabinet. Passengers were not concerned by the incident. The entire contents of the extinguisher were released. The estimated exposure time for the crew members was less than five minutes. Although the level of exposure could not be accurately determined, it was considered to be probably high.

Patient A1
Patient A1 was a 30 year old non-smoking air hostess with no medical history of respiratory or atopic disease. On medical examination immediately after arrival of the plane (about one hour later), she presented with signs of irritation of the upper respiratory tract. Chest auscultation and neurological examination were normal. During the days following the incident, she experienced asthma, dyspnoea on exertion, and cough at night. She stopped her sports activities because of respiratory symptoms. Spirometry performed on 5 February 1999 showed a slight decrease in FEV\textsubscript{1} (80% predicted) and FEF\textsubscript{25–75\%} (60% predicted), which were not improved by bronchodilators. Other spirometric measurements were normal. She consulted a hospital department of occupational medicine on 15 February 1999. Similar spirometric results were observed at this time. Bronchoscopy showed an inflammatory mucosa. Skin prick tests with the usual respiratory allergens (house dust mites, cockroaches, cat, dog, grass pollens and tree pollens (Betulaceae, Fagales, ash), mould (Alternaria, Aspergillus, Cladosporium, Penicilium) and latex) were negative. Inhaled steroids (budesonide) and a bronchodilator (formoterol) were prescribed. Fifteen months later (March 2000), a methacholine challenge was performed. At that time, patient A1 had stopped her treatment. A 24% decrease in FEV\textsubscript{1} was observed with a cumulative dose of 640 µg. Twenty eight months after the incident (April 2001), she still experienced cough at night and lung function parameters were unchanged.

Patient A2
Patient A2 was a 29 year old non-smoking air hostess with no medical history of respiratory or atopic disease. Immediately after exposure, she presented with sore throat, nausea, and dizziness. Chest auscultation, neurological examination, standard parameters, and electrocardiogram on arrival of the flight were normal. During the days following the incident, she reported the presence of cough at night and dizziness. Spirometry and chest x ray examination were normal on day 5. During the following month, she suffered from palpitations and muscle pain during exercise. Four months after the incident, she still suffered from cough.

Abbreviations: FEF\textsubscript{25–75\%}, forced expiratory flow rate at 25–75\% of forced vital capacity; FEV\textsubscript{1}, forced expiratory volume in one second; FVC, forced vital capacity; RADS, reactive airways dysfunction syndrome
episodes of asthenia, dizziness, and a diagnosis of psychological post-traumatic syndrome was proposed. She had a slight decrease in FEV1 (91% predicted), while other spirometric parameters were normal. Methacholine challenge test revealed a 28% decrease in FEV1 with a dose of 160 μg. Diffusing capacity for CO was normal. Bronchoscopy showed inflammatory mucosa with abundant secretions. Inhaled steroid (beclomethasone) and bronchodilator (formoterol), and an anxiolytic (bromazepam) were prescribed. Ten months after the incident (October 1999) she still suffered from dizziness and cough at night. Baseline spirometric parameters were unchanged. Methacholine challenge test was negative (cumulative dose 1920 μg) at 21 months (September 2000) and the treatment with inhaled steroids was maintained. Twenty eight months after the accidental exposure (March 2001), she still complained of cough during exercise with no modification of baseline lung function values.

Patient A3
Patient A3 was a 39 year old steward with a medical history of allergic rhinitis; he was an ex-smoker with low cumulative smoking (less than 5 pack-years). He was the most severely exposed subject. Immediately after the incident, he experienced malaise, wheezing, and limb paraesthesia. Prednisone was prescribed for 10 days in the emergency unit, followed by complementary treatment including inhaled steroid (budesonide) and bronchodilator (terbutaline). In January 1999, baseline spirometric values were: FEV1, 90% predicted; FEV1/FVC ratio, 81%; and FEF25-75%, 105% predicted. FEV1 increased with bronchodilator (+15%). In February 1999, he presented with dyspnoea on exertion. Baseline spirometric parameters (during treatment with budesonide) were normal. Methacholine challenge test showed a 22% decrease in FEV1 with a cumulative dose of 1280 μg. Inhaled steroid (budesonide) and bronchodilator (bambuterol) treatment was maintained for at least six months and the patient was subsequently lost to follow up.

Incident B
Patient B1, involved in incident B occurring on 26 February 1999, was a 31 year old non-smoking air hostess, who tried to stop a passenger from manipulating a fire extinguisher, just before take-off. The passengers were not affected by the release of the contents of the extinguisher. The entire contents of the fire extinguisher were released and patient B1 reported that she was exposed for less than five minutes, as the door of the aeroplane was rapidly opened. Patient B1 had a medical history of childhood house dust mite induced asthma, but had not experienced any asthma attacks for 10 years. She experienced cough with dyspnoea, eye irritation,

### Table 1 Respiratory characteristics of the four patients according to Brooks and colleagues’ criteria

<table>
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<tbody>
<tr>
<td>Absence of previous respiratory complaints</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Childhood asthma with no asthma attack for past 10 years</td>
</tr>
<tr>
<td>Single exposure to high levels of CBrClF2</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Onset of asthma symptoms within 24 hours after exposure</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Symptoms lasting at least 3 months</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Baseline spirometry parameters (percentage of predictive value)</td>
<td>(February 1999)</td>
<td>(February 1999)</td>
<td>(February 1999)</td>
<td>(February 1999)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>3.14 (86%)</td>
<td>3.21 (90%)</td>
<td>4.81 (91%)</td>
<td>3.36 (95%)</td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>2.55 (80%)</td>
<td>2.82 (91%)</td>
<td>3.92 (90%)</td>
<td>2.92 (95%)</td>
</tr>
<tr>
<td>FEV1/FVC [%]</td>
<td>81%</td>
<td>88%</td>
<td>81%</td>
<td>87%</td>
</tr>
<tr>
<td>FEF25-75 (l/s)</td>
<td>2.41 (60%)</td>
<td>3.89 (98%)</td>
<td>4.85 (105%)</td>
<td>2.99 (77%)</td>
</tr>
<tr>
<td>Bronchial hyperresponsiveness</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Methacholine challenge</td>
<td>March 2000</td>
<td>April 2001</td>
<td>April 1999</td>
<td>February 1999</td>
</tr>
<tr>
<td>Maximum cumulative dose of methacholine</td>
<td>640 μg</td>
<td>1280 μg</td>
<td>640 μg</td>
<td>640 μg</td>
</tr>
<tr>
<td>Percentage of fall in FEV1</td>
<td>–24%</td>
<td>–23%</td>
<td>–28%</td>
<td>–22%</td>
</tr>
<tr>
<td>Presence of other pulmonary disease at the time of incident</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Diagnosis of RADS</td>
<td>Definite</td>
<td>Definite</td>
<td>Definite</td>
<td>?</td>
</tr>
</tbody>
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*The spirometric relative values were calculated using the reference values established by Quanjer et al.**

†The methacholine challenge was performed with an aerosol nebuliser (FDC88, Mediprom) which delivered successively increasing doses of methacholine (80 μg, 160 μg, 320 μg, 640 μg, 1280 μg, 2560 μg & 5120 μg). Delivered doses were calculated from the flow rate of the aerosol and duration of delivery. At each methacholine dose, the FEV1 measurement was done, starting 90 seconds after the inhalation. The test was stopped when a fall of at least 20% of FEV1 was observed. Total duration of the methacholine challenge and FEV1 measurements generally lasted about 20 minutes.

‡RADS, reactive airways dysfunction syndrome.
and dizziness, which lasted six hours after the incident. She only received salbutamol (self prescribed). The respiratory symptoms improved within 24 hours, but she experienced dyspnoea in a smoky environment at night two or three times a week. When she consulted the department of occupational medicine on April 1999, she reported dyspnoea on exertion. Chest auscultation and chest x ray examination were normal. Baseline lung function parameters were: FEV1, 95% predicted; FEV1/FVC ratio, 87%; and FEF25–75, 77% predicted. The methacholine challenge test was positive at the dose of 640 µg with a 38% decrease in FEV1 from the baseline value. Inhaled steroid (beclomethasone) and bronchodilator (salbutamol) were prescribed. In September 1999, she no longer experienced any respiratory symptoms on effort. Baseline spirometric parameters were normal.

**DISCUSSION**

The four subjects were exposed under similar conditions to inhalation of bromochlorodifluoromethane. All subjects developed symptoms of respiratory irritation with dizziness, and the steward, who probably experienced the highest level of exposure, also presented neurological symptoms.

In our study, the symptoms presented by patients A1, A2, and A3 correspond to the criteria of RADS7 (table 1). All subjects presented symptoms of upper airway irritation and bronchial hyperreactivity immediately after a single exposure to a high concentration of bromochlorodifluoromethane. Halon 1211 was the only Halon in the fire extinguisher. For our subjects were exposed to Halon 1211 itself and not the fluorocarbon. It should be emphasised that symptoms were persistent (lasting more than two years) in at least two subjects.

Previous publications on the effects of Freons on human health have mainly concerned the neurological and cardiovascular effects; the respiratory effects of Freons have been less extensively studied. Brooks and colleagues8 reported that inhalation of bronchodilator containing dichlorodifluoroethane as propellant induced an increase in airway resistance and hypoxaemia in several of a group of 13 subjects with mild to severe asthma.

Recently, de la Hoz et al reported a case of RADS after a 10–15 minute exposure to bromotrifluoromethane, a fluorocarbon widely used in automatic fire extinguishing systems. Prolonged respiratory symptoms were recently reported following exposure to thermal degradation products of Freons. According to the authors, these subjects could have been exposed to hydrogen fluoride, hydrogen chloride, carbonyl fluoride, or chlorine. It should be emphasised that our subjects were exposed to Halon 1211 itself and not the products of thermal degradation, as exposure resulted from accidental release at room temperature.

To our knowledge, the cases presented here are the first reported cases of RADS following exposure to bromochlorodifluoromethane, mainly used in portable fire extinguishers, which probably explains why no occupational exposure limit has been defined for this agent in France. It is difficult to establish occupational exposure limits because the concentration of the compound must be sufficiently high to extinguish fire without causing any toxic effects on human health. This emphasises the need for preventive actions such as information for employees about the possible toxic effects of bromochlorodifluoromethane in the case of accidental inhalation of high levels of this agent.

Our study also indicates that bromochlorodifluoromethane must be added to the list of substances likely to cause RADS.

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Accepted 28 November 2003

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*Occup Environ Med* 2004 61: 712-714
doi: 10.1136/oem.2003.009837