

Clinical aspects of allergic disease

Occupational asthma in a technologist exposed to glutaraldehyde

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Background: Occupational asthma can be caused by several sterilizing agents, including glutaraldehyde, which has been shown to cause irritation of the eyes and upper respiratory tract and skin rash. We report a case of occupational asthma that was caused by exposure to glutaraldehyde.

Methods: To document the diagnosis of occupational asthma in a respiratory technologist, the following tests were performed: preshift and postshift spirometry, serial measurements of peak expiratory flow rate and nonspecific bronchial hyperresponsiveness, and workplace challenge test.

Results: Monitoring of peak expiratory flow rate showed improvement when the subject was away from the workplace. Improvements in forced expiratory volume in 1 second (FEV_1) and provocative concentration causing a 20% fall in FEV_1 were also observed. A workplace challenge test showed a progressive fall in FEV_1 when the subject was exposed to glutaraldehyde in a sterilizing agent used to clean bronchoscopes at her workplace. After the diagnosis of occupational asthma was confirmed, the subject continued to assist with bronchoscopy but no longer cleaned the bronchoscopes.

Conclusions: This case study illustrates the usefulness of a workplace challenge test in confirming the diagnosis of occupational asthma. It also indicates the importance of preventing or reducing exposure to sterilizing agents such as glutaraldehyde by means of effective ventilation and proper storage and enclosure during use. (*J ALLERGY CLIN IMMUNOL* 1993;91:974-8.)

Key words: Occupational asthma, workplace challenge test, glutaraldehyde

Several sterilizing agents such as formaldehyde,¹ chlorhexidine,² chloramine-T³ and glutaraldehyde⁴⁻⁸ have been shown to give rise to occupational asthma. Glutaraldehyde is an effective antimicrobial agent and is used in most hospitals for cold sterilization of endoscopes. It has been shown to cause symptoms of irritation of the eyes and the upper respiratory tract and skin rash.⁴ Occupational asthma as a result of exposure to glutaraldehyde has been reported previously.⁵⁻⁸ In this case report, we describe a patient in whom occupational asthma developed as a result of glutaraldehyde exposure. This was documented by preshift and postshift spirometry, appropriate changes in peak expiratory flow rate (PEFR) and

Abbreviations used

PEFR: Peak expiratory flow rate

PC₂₀: Provocative concentration causing a 20% fall in FEV_1

FEV_1 : Forced expiratory volume in 1 second

provocative concentration causing a 20% fall in forced expiratory volume in 1 second (PC₂₀) at work and away from work, and workplace challenge test.

CASE REPORT

A 33-year-old respiratory technologist was referred to the University of British Columbia Respiratory Clinic for assessment of asthma. She gave a history of asthma since childhood. The symptoms were mild then, and the attacks were relieved readily by bronchodilators. By the age of 15, her asthma symptoms disappeared completely. At the age of 26, her asthma symptoms returned intermittently only after she had a cold. During these episodes the symptoms were also quite

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TABLE I. Preshift and postshift spirometry

	FEV ₁ (L)	FEV (L)	MMF (L/sec)
Exposed day			
Preshift	2.13 (74%)	3.25 (92%)	1.25 (37%)
Postshift	1.55 (54%)	2.33 (64%)	1.07 (32%)
Control day			
Preshift	2.13 (74%)	3.34 (92%)	1.26 (37%)
Postshift	2.12 (74%)	3.30 (91%)	1.23 (37%)

Numbers in parentheses represent percent predicted value.
MMF, Maximum mid expiratory flow rate.

mild and were relieved readily by inhalation of albuterol.

Four years ago, she started to work in a bronchoscopy unit at a local hospital. Since that time her asthma worsened. She had daily symptoms and had to administer albuterol by inhalation three to four times daily. In addition, she had to be prescribed intermittent courses of prednisone for acute exacerbations. In October 1990, she was receiving high-dose inhaled beclomethasone, 1000 µg/day, but this failed to control her symptoms. She was again prescribed prednisone until she went on vacation. Her asthma improved considerably.

In addition to assisting physicians in fiberoptic bronchoscopy, she had to clean bronchoscopes after use with Sporicidin (Sporicidin International Ltd., Rockville, Md.) which contains 3.6% glutaraldehyde, 7% phenol, and 1.2% sodium phenolate. The cleaning and rinsing of bronchoscopes was done in a small room with no ventilation. Sporicidin was placed in a basin that was not enclosed while the bronchoscope was being cleaned.

There was no history of eczema or allergic rhinitis and no history of atopic disease in the patient's immediate family. She did not smoke.

Physical examination revealed no nasal polyps. Her lungs were clear with no crackles or rhonchi. The patient's hemoglobin, white blood cell count, and differential count were normal. Her absolute eosinophil count was 70/mm³. Her chest radiograph was normal. Allergy skin tests were done with the prick method with 25 common allergens. She showed positive immediate skin reaction to extracts of feathers and cat fur. When she was first seen in the clinic in March 1991, she was still working in the bronchoscopy unit. Her lung function test results were as follows: forced expiratory volume in one second (FEV₁) 65% of predicted value, forced vital capacity, 80% of predicted value; and maximum mid expiratory flow rate, 34% of predicted value. Her FEV₁ improved by 25% after inhalation of albuterol.

METHODS

Preshift and postshift spirometry

At the time of her first visit, she was receiving beclomethasone 2000 µg/day and albuterol by inhala-

tion. She was asked to come to the laboratory before starting work and at the end of her work shift for spirometric measurements on 2 separate days: one day when she performed her duties in the bronchoscopy unit including cleaning and rinsing of bronchoscopes and another day when she performed only administrative duties without assisting at bronchoscopies. She was told to take beclomethasone by inhalation four times daily at the same times on both days. Table I shows that on the day that she cleaned and rinsed the bronchoscopes, there was a postshift drop of 23% in FEV₁ from the baseline level, which was associated with cough and difficulties in breathing even though she took beclomethasone regularly. There was no postshift fall in spirometry on the day that she performed only administrative duties.

Serial measurements of PEFR and nonspecific bronchial hyperresponsiveness

The patient was also asked to monitor her own PEFR every 2 hours during waking hours for 1 week while she was working and for 2 weeks while she was on vacation. On each occasion she was told to perform maximally at least three times. The readings should be within at least 5% of each other. She was also asked to record her symptoms and medication requirement during the entire period.

A methacholine challenge test was also carried out before the patient went on her vacation. It was repeated on the first day that she returned to work after her vacation. Methacholine challenge test was done according to our standardized protocol⁹ with a Bennett twin nebulizer (Puritan Bennett Corp., Kirkland, Quebec, Canada). The PC₂₀ was obtained by interpolation from the dose-response curve drawn on a semilogarithmic noncumulative scale.

RESULTS

Fig. 1 shows serial measurements of peak expiratory flow rates for 1 week at work and 2 weeks on vacation together with spirometric measurements and measurements of nonspecific bronchial hyperresponsiveness before and after 2 weeks of vacation. There was a progressive improvement in

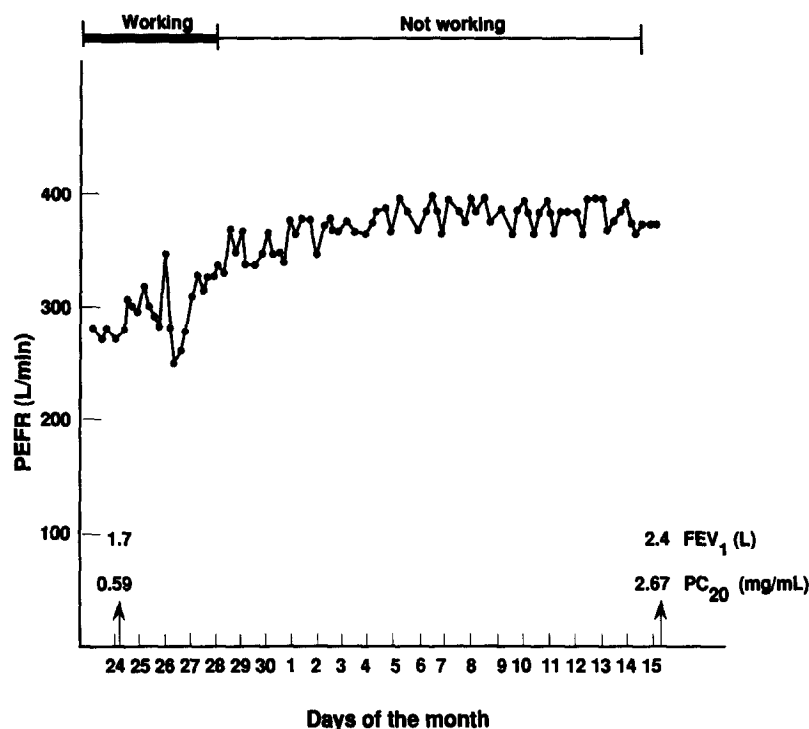


FIG. 1. PEFR monitoring of the patient for 1 week at work and 17 days away from work showing the improvement of her PEFR when she was away from work. Her FEV₁ and PC₂₀ were also improved after she returned from her vacation.

her PEFR during the first 3 to 4 days of her vacation. Her PEFR remained at a steady level between 370 to 400 L/min for the rest of her vacation. Her FEV₁ improved from 1.8 L before her vacation to 2.4 L on the morning of the first day she returned from vacation. In addition, her PC₂₀ increased from 0.59 mg/L to 2.67 mg/ml methacholine.

Workplace challenge test

The patient was asked to perform her usual duties on 2 separate days, and spirometric measurements were made before and every half hour thereafter from 8:00 AM to 4:00 PM. She was also asked to monitor her PEFR every hour during the day and in the evening. On one day she assisted in three bronchoscopic examinations and washed and rinsed bronchoscopes after each examination from 8:00 AM to 4:00 PM. On another day she also assisted in three bronchoscopic examinations, but another technologist cleaned and rinsed the bronchoscopes on her behalf. There was no exposure to Sporicidin. On both days she was told to use the same dose of beclomethasone (2000 µg/day) by inhalation regularly.

Fig. 2 shows the results of the workplace challenge test. On the day that she was exposed to Sporicidin, her FEV₁ fell progressively during the

day and was associated with shortness of breath and wheeze. The FEV₁ was lowest at the end of the rinsing of the third bronchoscope. The changes in PEFR were similar to those in FEV₁. Her lung function tests (both FEV₁ and PEFR) did not return to normal at 24 hours after challenge, which indicates that she had a late asthmatic reaction as well, despite the use of beclomethasone by inhalation. On the day that she was not exposed to Sporicidin, she was free of symptoms, and her FEV₁ and PEFR showed no significant change.

Follow-up

After the diagnosis of occupational asthma caused by glutaraldehyde exposure was made, the patient continued to assist with bronchoscopy, but her duties no longer included cleaning and rinsing bronchoscopes with Sporicidin. Her symptoms decreased, she gradually reduced the dose of inhaled beclomethasone to 500 µg/day without recurrence of symptoms, and her lung function tests were within normal limits.

DISCUSSION

This report describes an atopic subject with a history of childhood asthma who experienced severe acute exacerbations of asthma since she

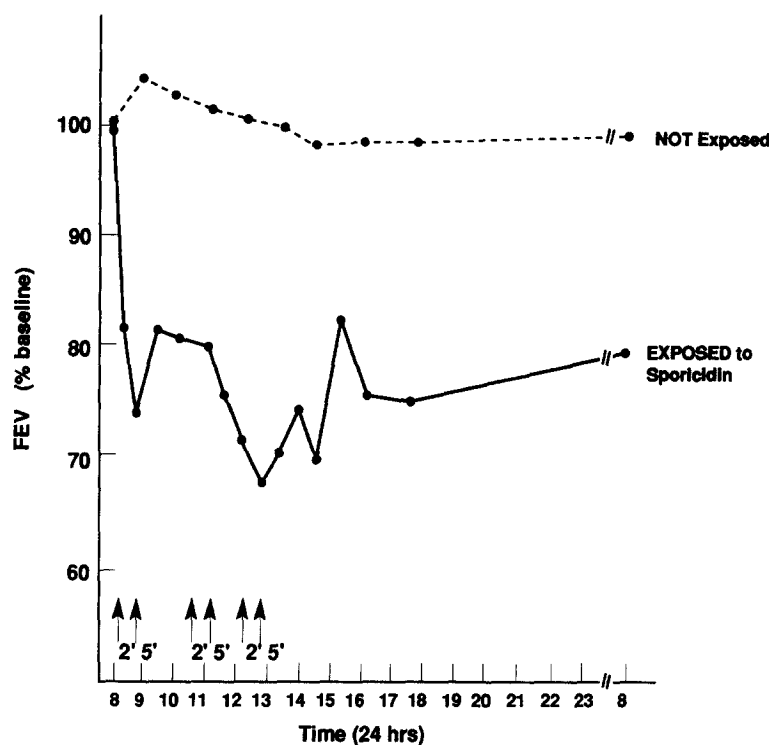


FIG. 2. Workplace challenge test showing the lack of changes in FEV₁ on the day that she was not exposed to Sporidicin and the progressive fall in FEV₁ on the day that she had to wash and rinse the bronchoscope three times. Arrows indicate the time of washing (2 minutes) and rinsing (5 minutes).

started to work in a bronchoscopy unit. The features that supported the diagnosis of occupational asthma were the decrease in symptoms and improvement in PEFR and FEV₁ after 2 weeks away from work. Although her PC₂₀ also increased after she was away from work, it is difficult to attach too much significance to the finding because of improvement in the baseline FEV₁ as well. The fact that her FEV₁ fell by 23% after her shift on the day that she was working in the bronchoscopy unit with exposure to Sporidicin suggested that her symptoms were related to the exposure. Workplace challenge test showed that exposure to Sporidicin led to a progressive fall in FEV₁, which was associated with symptoms of asthma, whereas absence of exposure was not associated with a fall in FEV₁ during the control day. Despite administration of high-dose inhaled beclomethasone (2000 µg) by inhalation on the day of workplace challenge test, a late asthmatic reaction was induced. A more severe late asthmatic reaction would have been induced if she had not been receiving beclomethasone. Finally, avoidance of Sporidicin led to a progressive decrease in her symptoms, reduction in medications for the control of symptoms, and improvement in lung function. These findings confirmed that her

asthma during the recent 4 years was work-related and that Sporidicin was the offending agent.

Sporidicin contains 3.6% glutaraldehyde. Glutaraldehyde is not only an irritant but a sensitizer as well. In some workers occupational asthma was demonstrated by prolonged monitoring of PEFR.⁵ Late asthmatic reaction had been induced in a patient after bronchoprovocation test with 2% alkaline glutaraldehyde, suggesting an allergic rather than irritant reaction.⁶ Glutaraldehyde is the likely cause of this patient's asthma even though specific challenge test with glutaraldehyde was not carried out. Because measurement of glutaraldehyde level was not done during workplace challenge test, it is not possible to know whether the patient was exposed to an irritant dose rather than a subirritant level of glutaraldehyde. Irritant bronchial reactions usually occur immediately on exposure and are transient. The occurrence of a late asthmatic reaction is more in line with an allergic reaction than an irritant reaction. The type of allergic mechanism responsible for glutaraldehyde-induced asthma is not known because specific IgE antibodies have not been demonstrated in affected subjects.

It is uncommon for occupational asthma caused by low molecular weight compounds to develop in

subjects with a preexisting asthma. However, a history of asthma should not exclude the diagnosis of occupational asthma caused by a workplace agent. Measurement of cross-shift change in spirometry has not been shown to be a good confirmatory test for diagnosis of occupational asthma.¹⁰ However, if there is a cross-shift change in FEV₁ of more than 10%, it is an indication that further tests should be done to confirm the work-relatedness of asthma. This case also illustrates the usefulness of a workplace challenge test in the diagnosis of occupational asthma. Although specific challenge testing in the laboratory has been considered the "gold standard" in the diagnosis of occupational asthma, there are very few centers with facilities to perform these tests. When multiple agents in the workplace are capable of causing occupational asthma, specific challenge tests become very time-consuming. Moreover, specific challenge testing in the laboratory cannot reproduce the work situation completely. The use of a workplace challenge test can be very helpful in establishing a relationship between work and asthma. However, workplace challenge tests can also be problematic. It is not always possible to obtain permission from employers to conduct environmental and physiologic measurements at the work site. When there are multiple agents that are capable of causing asthma in the workplace, a positive workplace challenge test can only indicate that there is a relationship between work exposure and asthma and will not identify which agent is responsible.

Glutaraldehyde is being used more frequently in hospitals. It is important to prevent or reduce exposure to glutaraldehyde by providing effective ventilation, an enclosed washing machine for bronchoscopes, and the use of a ventilated cabinet for the storage of glutaraldehyde solution and for carrying out cold-sterilizing procedures until an effective and less toxic chemical disinfectant is found.

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