

2. Dubourg A, Scamuffa RF. An experimental overview of a new vasoactive drug: buflomedil HCl. *Angiology* 1981;32:663-675.
3. Le Quentrec P, Lefebvre ML. Double-blind placebo-controlled trial of buflomedil in the treatment of Raynaud's phenomenon: six-month follow-up. *Angiology* 1991;42:289-295.
4. Jacobs MJ, Lemmens HA. Microcirculatory changes in patients with primary Raynaud's phenomenon after treatment with buflomedil. *Int J Microcirc Clin Exp* 1985;4:63-68.

Occupational asthma to diacrylate

K. Weytjens, A. Cartier, C. Lemi re, J.-L. Malo*

Key words: acrylates; asthma; cross-reactions; cyanoacrylates; methacrylates; occupational diseases.

● ACRYLIC compounds are used increasingly in various industries (paints and coatings, adhesives, printing inks, plastic glass) and health professions (dental prostheses and fillings, bone cement in orthopedic, histologic preparations, soft contact lenses), as well as in home repairs and hobbies

(instant glues). Skin sensitization and irritation of mucous membranes are well known properties of these compounds. Since 1985, several cases of occupational asthma (OA) to methacrylate (MA) and cyanoacrylate (CA) have been described, as reviewed (1). The mechanism of sensitization is not known.

We report for the first time, to our knowledge, OA to a diacrylate, without evidence of bronchial cross-reactivity with CA and MA.

A 44-year-old man started work in an auto body shop in January 1997. At work, he used a primer containing ethoxylated-(2)-bisphenol-*a*-diacrylate and additives. After 3 months, he progressively developed nasal congestion, sneezing, and rhinorrhea, followed by chest tightness, dyspnea, cough, and wheezing a few weeks later. Symptoms started after 2 h at work and often caused nocturnal awakenings. They improved after he started taking

antihistamines and began to wear a mask at work. When he interrupted his work for 2 months after minor surgery, he became asymptomatic, but his symptoms returned soon after returning to work. The patient stopped working in August 1997 and again became asymptomatic. He had no previous history of rhinitis or asthma but had a smoking history of seven pack-years, having stopped 11 years earlier.

We first examined him in October 1997. Skin prick tests with 22 common inhalants were all negative with a positive histamine control. FEV₁ was 3.28 l (107% predicted) and FVC 4.03 l (107% predicted) (2); methacholine bronchial responsiveness was normal (PC₂₀M=29 mg/ml) (3). In November 1997, specific inhalation challenges (SIC) were carried out according to a standardized procedure (4). On a control day, the patient was exposed to a nebulized diluent (a commercial mixture of polyols) for a total of 30 min. No significant change in FEV₁ occurred in the following 8 h; PC₂₀M at the end of the day was >128 mg/ml. Exposure to diacrylate was done by nebulizing it in a challenge room for progressively increasing periods of time on subsequent days (total of 4,

A nonatopic patient showed positive inhalation challenge to ethoxylated-(2)-bisphenol-*a*-diacrylate but no cross-reactivity with metha- and cyanoacrylate.

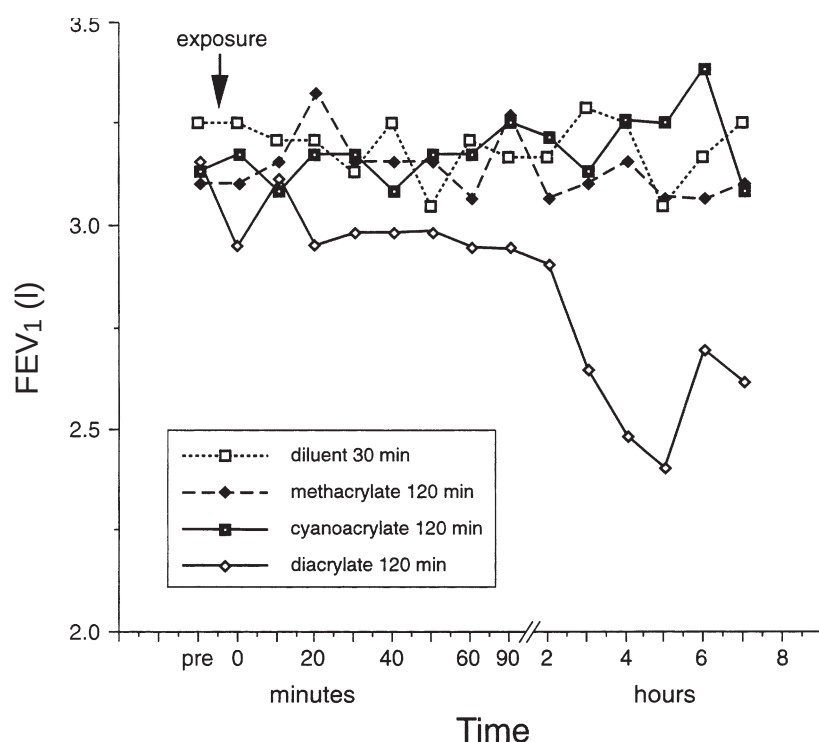


Figure 1. Results of specific inhalation challenge tests.

30, and 120 min). After the 120-min exposure, the subject developed an atypical reaction of the progressive type (maximum fall in FEV₁ of 22% at 390 min after exposure); 8 h after exposure, FEV₁ was still 19.6% lower than baseline and returned to baseline after salbutamol. The next morning, PC₂₀M was assessed at 24 mg/ml. Three weeks later, we re-exposed him with simultaneous measure of lung volumes: an early-late reaction (24% fall in FEV₁ at 210 min after exposure) occurred (Fig. 1) with a rise in residual volume of 32%, in functional residual capacity of 23%, and in total lung capacity of 8% of baseline. PC₂₀M at the end of the day was 128 mg/ml. Handling methacrylate- and cyanoacrylate-based adhesives in a challenge room for 120 min each did not provoke any significant change in FEV₁ or in PC₂₀ (Fig. 1). Such an exposure had induced asthmatic reactions in sensitized subjects in our laboratory.

The possibility of bronchial cross-reactivity between acrylates was examined in two other subjects. A 57-year-old male, nonatopic ex-smoker developed rhinitis and asthma 1 year after starting exposure to CA- and MA-based adhesives. Exposure to CA for 30 min in the laboratory was followed by an early-late fall in FEV₁ (maximum fall of 25% at 300 min after exposure) and a simultaneous rise in lung volumes (FRC +36% of baseline); there was a change in PC₂₀M from 18 mg/ml to 3.6 mg/ml. Exposure to MA in the same way for 120 min did not cause any change in FEV₁ or in PC₂₀M in the following 8 h. The second subject was a 23-year-old dental technician, a nonatopic smoker, who developed OA 3 years after starting work. Exposure to MA for 120 min in the laboratory did not provoke a significant change in FEV₁ or PC₂₀M. However, SIC with CA caused an early-late reaction with a maximum fall in FEV₁ of 47.8% at 180 min after a progressive exposure of 30 min; hydrocortisone was administered intravenously, leading to functional recovery.

We report a case of work-related rhinitis and asthma due to diacrylate, confirmed by SIC, without bronchial cross-reactivity to other

acrylates (CA, MA). To our knowledge, diacrylates do not cause OA. Estlander et al. described a patient with allergic conjunctivitis, but no chest or nasal symptoms, who was sensitized to several methacrylates as well as to diacrylates, as confirmed by patch testing (5). We knew that unknown additives were in the product to which our patient was exposed, but pure diacrylate was not available for testing. As forced expiratory maneuvers are effort-dependent, we confirmed that the fall in FEV₁ was associated with airway obstruction by measuring lung volumes; this showed air trapping and hyperinflation. Acrylates are known irritants; however, the latency period before development of symptoms and the nonimmediate response after SIC in our subject are more suggestive of a specific and sensitizing mechanism, despite the absence of nonspecific bronchial hyperresponsiveness. However, as for most low-molecular-weight agents, the immunologic mechanism cannot be elicited. Changes in bronchial responsiveness were not observed after the late asthmatic reaction, but such changes are not constant in these circumstances (6). OA without evidence of bronchial hyperresponsiveness has been described by others (7, 8).

We found no clinical cross-reactivity between CA and MA in two other subjects with OA to CA, nor between diacrylate and monoacrylates in our subject. As is the case for formaldehyde, the physical state of the agent (vapor for monoacrylates, aerosol for diacrylate) may explain this finding (9).

In conclusion, we report two new interesting findings:

- 1) a new occupational sensitizing agent, diacrylate, causing rhinitis and asthma
- 2) the absence of clinical bronchial cross-reactivity between different acrylates.

However, further studies on this last finding are warranted.

Acknowledgment We thank Lori Schubert for reviewing this paper.

*Department of Chest Medicine, Hôpital du Sacré-Coeur, 5400 W. Gouin Blvd, Montréal HA1 1C5, Canada, Tel. 514-338-2796, Fax: 514-338-3123, E-mail: malojl@alizer.ere.umontreal.ca

Accepted for publication 3 November 1998
Copyright © Munksgaard 1999
ISSN 0105-4538

References

1. Savonius B, Keskinen H, Tuppurainen M, et al. Occupational respiratory disease caused by acrylates. *Clin Exp Allergy* 1993;23:416-424.
2. Knudson RJ, Lebowitz MD, Holberg CJ, et al. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 1983;127:725-734.
3. Cockcroft DW, Killian DN, Mellon JJA, et al. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977;7:235-243.
4. Cartier A, Malo JL. Occupational challenge tests. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI. *Asthma in the workplace*. New York: Marcel Dekker, 1993:215-247.
5. Estlander T, Kanerva L, Kari O, et al. Occupational conjunctivitis associated with type IV allergy to methacrylates. *Allergy* 1996;51:56-59.
6. Malo JL, Ghezzi H, L'archevêque J, Cartier A. Late asthmatic reactions to occupational sensitizing agents: frequency of changes in nonspecific bronchial responsiveness and of response to inhaled beta-2 adrenergic agent. *J Allergy Clin Immunol* 1990;85:834-842.
7. Smith AB, Brooks SM, Blanchard J, et al. Absence of airway hyperreactivity to methacholine in a worker sensitized to toluene diisocyanate. *J Occup Med* 1980;22:327-331.
8. Banks DE, Barkman HW Jr, Butcher BT, et al. Absence of hyperresponsiveness to methacholine in a worker with methylene diphenyl diisocyanate (MDI)-induced asthma. *Chest* 1986;89:389-393.
9. Lemièrre C, Desjardins A, Cloutier Y, et al. Occupational asthma due to formaldehyde resin dust with and without reaction to formaldehyde gas. *Eur Respir J* 1995;8:861-865.

Asthma to latex in a seamstress

K. Weytjens, M. Labrecque, J.-L. Malo, A. Cartier*

Key words: asthma; occupational diseases; latex; textile industry.