Eur Respir J, 1994, 7, 415–417
Printed in UK - all rights reserved

European Respiratory Journal
ISSN 0903 - 1936

CASE REPORT

Occupational asthma due to heated polypropylene

J-L. Malo*, A. Cartier*, L. Pineault, M. Dugas*, A. Desjardins*

Occupational asthma due to heated polypropylene. J-L. Malo, A. Cartier, L. Pineault, M. Dugas, A. Desjardins. ©ERS Journals Ltd 1994.

ABSTRACT: A 35 year-old nonatopic woman was referred to the hospital for possible work-related asthma. She had worked as an operator, at a plant producing polypropylene bags, for the previous four yrs. Her main complaint was a productive cough with dyspnoea and wheezing, as well as rhinitis over the past 3 yrs. She had been absent from work for 6 months on maternity leave, and had improved greatly. She was on a $beta_2$-adrenergic agent and had to take it at least four times daily.

Baseline spirometry whilst at work showed marked airflow obstruction (forced expiratory volume in one second (FEV_1) of 43% predicted (pred). After two months away from work FEV_1 improved to 89% pred; provocative concentration of histamine causing a 25% fall in FEV_1 (PC_{20}) was 3.6 mg·ml^{-1} (mild airway hyperresponsiveness). Return to work resulted in a marked deterioration in FEV_1, and serial peak expiratory flow (PEFR) values. PC_{20} was 0.11 mg·ml^{-1} (severe airway hyperresponsiveness) one week after she had returned to work. Specific inhalation challenges with polypropylene heated to 250°C resulted in a late asthmatic reaction. As formaldehyde is one of the degradation products of heating polypropylene, we exposed her to it for up to 2 h, but we elicited no bronchospastic reaction.

We conclude that heated polypropylene should be listed as one of the agents that causes occupational asthma.

Eur Respir J., 1994, 7, 415–417.

*Dept of Chest Medicine, Höpital du Sacré-Coeur, Montreal, Canada.

Correspondence: J-L. Malo
Dept of Chest Medicine
Sacré-Coeur Hospital
5400 West Gouin
Montreal
Canada

Keywords: Bronchial hyperactivity
bronchial provocation tests
methacholine
peak expiratory flow rate

Received: April 2 1993
Accepted after revision August 8 1993

JLM is a research fellow with the Fonds de la Recherche en Santé du Québec and the Université de Montréal School of Medicine.

Occupational history

A 35 year old woman had been employed at a company that manufactures bags, since the age of 15 yrs. She was exposed primarily to cotton and flax. Over the last 4 yrs, she had been an operator in a different department, working on a machine that transforms polypropylene into threads used in the production of bags, through an extrusion process following melting of pellets. Polypropylene, the chemical formula of which is $(CH_3)_2$-CH-$[CH_2$-CH $(CH_3)]_n$-CH=CH-CH_3 is heated to 250°C in the process. According to information obtained from a chemist, heating polypropylene to this temperature results in the release of several degradation products including: aliphatic hydrocarbons (ethylene, butene); aldehydes (principally formaldehyde); and ketones.

Medical history

The subject had no previous history of respiratory problems. She had stopped smoking 10 yrs ago. One year after being transferred to the department in which polypropylene was heated, she started experiencing progressive symptoms of productive cough, dyspnoea and wheezing, which were worse at work and improved when she was away from work. These symptoms deteriorated to such an extent that she experienced nocturnal awakenings due to asthma on a regular basis and had to visit emergency rooms on two occasions because of it. A year and a half before being seen, she left work for 6 months on maternity leave, and her asthmatic condition improved greatly, although she still required inhaled $beta_2$-adrenergic agent on a *p.r.n.* basis (not daily). Her return to work caused a worsening in her asthmatic condition. She had no personal or familial atopic history (infantile eczema, urticaria, seasonal or perennial rhinitis, migraine). Skin tests performed with a battery of 15 common inhalants were all negative, with a positive control to histamine phosphate (1 mg·ml^{-1}).

Assessment of spirometry, bronchial responsiveness and peak expiratory flow rates

When she was first seen, at a time when she was still at work, spirometry carried out according to accepted standards [1], showed marked airflow obstruction, with a forced expiratory volume in one second (FEV_1) value of 1.3 *l*, corresponding to 43% of the predicted value [2]. She was prescribed inhaled steroids (beclomethasone, 2,000 µg daily) and kept away from work. Two weeks later, her FEV_1 had improved to 1.63 *l*, and bronchial responsiveness to methacholine assessed using a standardized method (output of nebulizer=0.14 ml·min^{-1}) [3] showed significant bronchial hyperresponsiveness (provocative concentration causing a 20% fall in FEV_1 (PC_{20}) 0.24 mg·ml^{-1}). She remained away from work. FEV_1 further improved to 2.4, 2.7 and 2.5 *l* and PC_{20} to 0.7, 3.6 and

3.4 mg·ml^{-1} when they were assessed 3, 5 and 7 weeks away from work, respectively, at a time when she was still on beclomethasone, 2,000 µg daily. During this period, she was given a mini-Wright peak flow meter to assess her peak expiratory flow rates (PEFR) every 2 h whilst awake. This showed minimal changes (fig. 1). She was then asked to return to work, her medication being unchanged. This resulted in the reappearance of symptoms on the first day of exposure, with a progressive fall in PEFR, that remained constant during the weekend (fig. 1). Her FEV_1, measured after 5 days at work with a two day break at the weekend, dropped to 2.0 *l*, and PC_{20} to 0.11 mg·ml^{-1}. She was put on sick leave and continued to assess her PEFR. Values improved progressively, and two months later, there were no significant changes in daily PEFR, FEV_1 had increased to 3.2 *l* (normal value), and PC_{20} was 3.1 mg·ml^{-1} (mild airway hyperresponsiveness).

Specific inhalation challenges

The subject underwent specific inhalation challenges in the following way: she had a first series of tests in which no significant (<10%) changes in FEV_1 occurred after a control day of nonexposure and after exposure to a control diluant (polyol), nebulized for 30 min at a distance of 1 m from her mouth in a challenge room [4]. The next day, the subject was exposed to heated polypropylene for 4 min. This was done using the same material as that used at work, which, according to the safety data sheet, contained no other contaminants besides polypropylene. There was a maximum fall in FEV_1 of 16% recorded 20 min after exposure ended, with partial recovery to -11% compared to the pre-exposure value. This was followed by a progressive late reaction (maximum fall in FEV_1 of 34% 6 h after exposure ended). Oral temperature increased to 37.5°C (from a baseline value of 36.3°C), but white blood counts (WBC) were normal (6,600 cells·mm^{-3}). These tests were repeated one month later. This time the subject was exposed to heated polypropylene for progressive periods of 4, 8 and 20 min (fig. 2). There was a significant late reaction after the last exposure, with a maximum fall in FEV_1 of 31% 7 h after exposure ended. Oral temperature increased to 37.5°C from 36.4°C. WBC was 8,100 cells·mm^{-3} at the time of the maximum reaction and 7,000 cells·mm^{-3} the following morning. There were no significant changes in vital capacity. The next morning, the patient underwent a bronchoscopy with bronchoalveolar lavage. The total number of cells was 11.3×10^6 (normal value), but neutrophils (9%) and eosinophils (6%) were increased. Lymphocytes were normal (11%).

Heating polypropylene to 250°C results in the release of various degradation products (aliphatic hydrocarbons, aldehydes (mainly formaldehyde), and ketones) [5]. As formaldehyde is recognized as causing occupational asthma [6, 7], we decided to expose the patient to formaldehyde by nebulizing it at a distance of one metre from her mouth in a challenge room. Exposing the patient to formaldehyde for increasing periods up to a maximum of 2 h elicited no significant change in FEV_1 in the hours that followed.

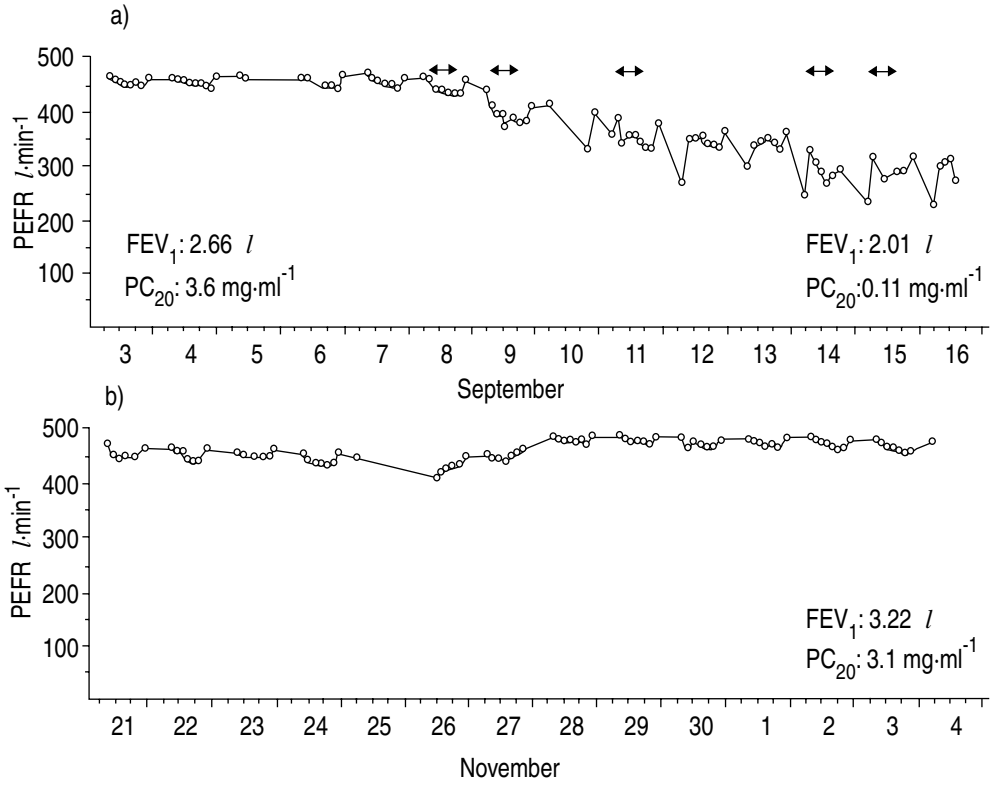

Fig. 1. – a) Significant fall and increase in daily fluctuations in PEFR after return to work, with fall in FEV_1 and increase in responsiveness to methacholine (fall in PC_{20}). The horizontal lines on the upper panel represent periods spent at work. b) No significant changes in PEFR and improvement in FEV_1 and PC_{20} after a period away from work. PEFR: peak expiratory flow rate; FEV_1: forced expiratory volume in one second; PC_{20}: provocative concentration producing a 20% fall in FEV_1.

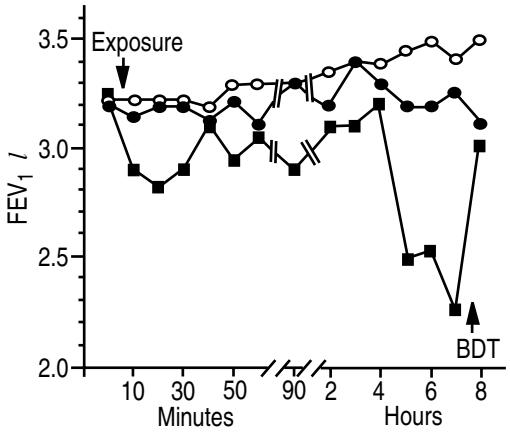

Fig. 2. – Specific inhalation challenges by exposing the subject to polypropylene (arrow) for the indicated intervals. A late reaction is shown after exposure for 20 min with recovery after administering an inhaled $beta_2$-adrenergic agent (BDT). Abscissa cut off from zero. —○— : control no exposure day; —●— : exposure for 8 min to heated polypropylene; —■— : exposure for 20 min to heated polypropylene. FEV_1: forced expiratory volume in one second.

Discussion

Occupational asthma can be caused by high and low molecular weight agents. Interesting differences, summarized elsewhere, exist between the two types of occupational asthma that have a latency period [8]. From a clinical point of view, the latency period before the onset of symptoms is longer in the case of high molecular weight agents [9]. The type of asthmatic reaction after specific inhalation challenges is different, with isolated late or atypical reactions being more common after exposure to low molecular weight agents [10]. The mechanism of reaction is often immunoglobulin E (IgE)-dependent for high molecular weight agents, whereas it remains unknown for most low molecular weight agents.

Polypropylene is a product that, when heated, releases several low molecular weight agents. Polypropylene has not been described as causing occupational asthma. It is likely that propylene itself is not the causal agent, as asthma was generated when the product was heated as for other "plastic-related" products, such as polyethylene [11]. Degradation products include several low molecular weight chemicals (aliphatic hydrocarbons, aldehydes, crotonaldehyde, ketones), which may have been responsible for the reaction. We excluded the possibility that the reaction was specifically induced by formaldehyde, because exposing our subject for 2 h caused no significant bronchoconstriction. As our subject had already undergone PEFR monitoring for quite a long interval, specific inhalation challenges with polypropylene and formaldehyde as well as bronchoscopy, she was reluctant to accept specific inhalation challenges with several agents. No attempt was made to examine the possibility of specific antibody production, as the nature of the degradation product responsible for the reaction could not be determined. This would indeed have been tedious, as several by-products should have been tested both *in vitro* (specific IgE and immunoglobulin G (IgG) antibodies) and with specific inhalation challenges.

Our subject had an increase in oral temperature at the time of the late reaction. However, this was not accompanied by significant increase in white blood count or by a reduction in vital capacity, which makes the possibility of alveolitis less likely. Bronchoalveolar lavage revealed the presence of increased percentages of eosinophils and neutrophils. Although the increase in eosinophils is typical of late reactions, the increase in neutrophils is not, except, according to some researchers, in the case of toluene diisocyanate, which is a low molecular weight agent [12].

We conclude that one or other of the degradation products of heated polypropylene is a cause of occupational asthma. The prevalence of this new type of occupational asthma remains to be explored.

Acknowledgements: The authors would like to thank K. Tallman for reviewing the manuscript.

References

1. American Thoracic Society. Standardization of spirometry, 1987 Update. *Am Rev Respir Dis* 1987; 136: 1285–1307.
2. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. 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, Hargreave FE. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977; 7: 235–243.
4. Pepys J, Hutchcroft BJ. Bronchial provocation tests in etiologic diagnosis and analysis of asthma. *Am Rev Respir Dis* 1975; 112: 829–859.
5. Jarvisalo J, Pfaffli P, Vainio H. Industrial hazards of plastics and synthetic elastomers. Proceedings of the international symposium on occupational hazards related to plastics and synthetic elastomers. New York, Alan R. Liss, Inc., 1984.
6. Nordman H, Keskinen H, Tuppurainen M. Formaldehyde asthma. Rare or overlooked? *J Allergy Clin Immunol* 1985; 75: 91–99.
7. Grammer LC, Harris KE, Shaughnessy MA, *et al.* Clinical and immunologic evaluation of 37 workers exposed to gaseous formaldehyde. *J Allergy Clin Immunol* 1990; 86: 177–181.
8. Malo JL. Occupational asthma: a model for environmental asthma. *In*: Godard P, Bousquet J, Michel FB, eds. Advances in Allergology and Clinical Immunology. Carnforth, UK, Parthenon Publishing Group, pp. 391–400.
9. Malo JL, Ghezzo H, D'Aquino C, L'Archevêque J, Cartier A, Chan-Yeung M. Natural history of occupational asthma: relevance of type of agent and other factors in the rate of development of symptoms in affected subjects. *J Allergy Clin Immunol* 1992; 90: 937–944.
10. Perrin B, Cartier A, Ghezzo H, *et al.* Reassessment of the temporal patterns of bronchial obstruction after exposure to occupational sensitizing agents. *J Allergy Clin Immunol* 1991; 87: 630–639.
11. Gannon PFG, Burge PS, Benfield GFA. Occupational asthma due to polyethylene shrink-wrapping (paper wrapper's asthma). *Thorax* 1992; 47: 759.
12. Fabbri LM, Boschetto P, Zocca E, *et al.* Bronchoalveolar neutrophilia during late asthmatic reactions induced by toluene diisocyanate. *Am Rev Respir Dis* 1987; 136: 36–42.