

Meat wrapper's asthma: identification of the causal agent

G. PAULI, J. C. BESSOT, M. C. KOPFERSCHMITT,*
G. LINGOT, R. WENDLING,† P. DUCOS and J. C. LIMASSET‡

**Chest Diseases Institute, Strasbourg, and*

†*Caisse Régionale d'Assurance Maladie de Strasbourg, Service Prévention, and*

‡*Institut National de Recherche et de Sécurité, Service Chimie, Toxicologie, Vandoeuvre-les-Nancy, France*

(Received 9 July 1979; accepted for publication 3 October 1979)

Summary

Meat wrapper's asthma is a typical example of occupational asthma due to emissions from chemical products. The authors report three new cases due to the use of the now classic meat packaging techniques in supermarkets. The chemical agents involved were identified. Inhalation tests have been carried out in one patient with the complete wrappings, i.e. the PVC film and the price labels, and separate tests were performed with eight additives of the PVC film, and with phthalic anhydride and di-cyclohexyl-phthalate emitted from heated price labels. These tests incriminate two products: phthalic anhydride seems to be the principal causal agent and epoxidized soybean oil can be suspected as a secondary agent causing this occupational asthma.

Introduction

There have been numerous reports in the past seven years of persons engaged in wrapping meat having respiratory complaints. Since 1963 polyvinyl chloride films have become the predominant meat wrapping material in use. The PVC film contains a high percentage (up to 30% by weight) of additives such as plasticizers, heat stabilizers, antifog agents and colourants. The cutting and sealing of the film are performed in the meat cutting area of the supermarket by means of a more-or-less automatic machine. A hot wire cuts the plastic film. Its ends are folded under the package and sealed by touching the package to the heated sealing pad. The adhesive price labels are usually fixed on the package in the same working area. These labels are heated in order to activate their adhesive coating. They are applied to the package which is then quickly passed over an inclined heating pad forming thus a strong film-label bond. These paper labels are coated with a thermosetting resin and a solid plasticizer which melts during its activation.

The first respiratory manifestations involving PVC films have been reported by R. Vandervort in 1971 (unpublished report of the National Institute for Occupational Safety and Health). In 1973 Sokol *et al.* described asthmatic reactions in three patients

Correspondence: Dr G. Pauli, Chest Diseases Institute, CHU—67000 Strasbourg, France.

employed as meat wrappers. Other similar cases were reported by Stevens (1974), Polakoff, Lapp & Reger (1975), Boushey, Empey & Laitinen (1975), Johnson & Anderson (1976) and Falk & Portnoy (1976).

Jaeger and Hites (1974) showed that a plasticizer, the di(2-ethylhexyl) adipate, was emitted from PVC films. Van Houten, Cudworth & Irvine (1974) confirmed the presence of this plasticizer in the work environment and indicated that the HCl emissions did not reach the threshold for occupational exposure.

Andrasch *et al.* (1975, 1976) using inhalation provocation tests attributed the respiratory symptoms to the fumes emitted from the heat adhesive labels.

Recently Vandervort & Brooks (1977) have described the thermal decomposition product of PVC film and thermal activated price labels; they pointed out that dicyclohexyl-phthalate was the major ingredient of label adhesives. However they concluded that a causal relationship between the emissions from labels and respiratory disorders was not demonstrated.

Levy, Storey & Phashko (1978) also blamed the labels and noted the presence of phthalic anhydride in fumes emitted from the adhesive during heat activation.

This study reports clinical histories of three cases of meat-wrapper's asthma and a chemical study of the material involved. Although inhalation provocation tests have been reported by several authors, these tests were usually performed with complete material, i.e. the PVC films and the price labels, but no separate tests with each chemical agent were made. The knowledge of the compositions of the PVC film and the thermally activated adhesive labels gave us information on the chemical agents to be used for inhalation challenge tests in one volunteer in order to determine the precise agent responsible for this occupational asthma.

Materials and methods

Report of cases

Case 1. N.L., a 49-year-old man, had no previous history of respiratory disorders or allergy. The patient had worked for several weeks in the butcher's shop of a food-store when the first symptoms, wheezing and coughing, appeared at the end of the day's work. Four weeks later the patient had a severe attack of asthma and a corticosteroid treatment was required. When he left his job, the symptoms disappeared. He tried to return to work, but shortly after entering the butcher's shop he developed severe symptoms and was hospitalized.

There was no asthma or allergy in the family history, and the patient was a heavy smoker (one pack of cigarettes a day). The skin tests to common-allergens were all negative and the total serum IgE level was low: 66.5 u/ml. There was no blood eosinophilia. An acetylcholine challenge test showed abnormal bronchial reactivity with decrease in FEV₁ of 31% after inhalation of 1000 µg of acetylcholine. Spirometry revealed completely reversible airways obstruction.

The patient changed to another job and has had no further asthma crises.

Case 2. B.J., a 32-year-old man, non-smoker, with no personal or family history of respiratory disorders or allergy, had worked for 5 months in the same butcher's shop when he first developed symptoms. He complained of cough, wheezing and typical nocturnal asthma attacks. Skin tests for common-allergens were all negative. The total serum IgE was 72 u/ml. There was no blood eosinophilia. The patient left the meat wrapping area but he continued to work as a butcher without respiratory symptoms.

Case 3. O.J., a 26-year-old man, non-smoker, was cutting meat in a butcher's shop of a food-store and occasionally he was also packaging meat. He complained of nocturnal asthma attacks only when he was employed in meat-wrapping.

Clinical investigations showed negative skin tests to common allergens. Oral bronchodilators were administered and the patient returned to work. Asthmatic symptoms recurred and an occupational factor was suspected.

The quantitative acetylcholine challenge test revealed abnormal bronchial reactivity with a decrease in FEV₁ of 25% after inhalation of 1000 µg of acetylcholine.

An 11% eosinophilia was found and the total serum IgE was 566 u/ml. Spirometry revealed completely reversible airways obstruction. More precise investigations were carried out by challenge tests with complete material i.e. the PVC films and the price labels, and with separate chemical agents (Fig. 1).

Determination of chemical agents involved

PVC film and additives for the plastic film. The following ingredients made up PVC powder, di(2-ethylhexyl)adipate, di(2-ethylhexyl)phthalate, glycerol monooleate, ethylglycol laurate, epoxidized soybean oil, zinc stearate, calcium stearate, thiocarbonyl.

Labels. An analysis of the paper labels was performed as follows: rapid extraction of the labels in acetone, filtration, concentration, and immediate determination by gas chromatography on an APIEZON column at 180°C. Laboratory tests reproducing working conditions were used to verify if the quantity of product collected on a Whatman GF/C glass filter and placed at the distance of 10 cm from the hot-plate was consistent with the initial label amount.

Other series of labels (used in supermarkets in Nancy and Rennes) which had provoked asthma in meat wrappers were examined.

Challenge tests

The tests were performed in a closed chamber (3.5 m³). A known quantity of the above mentioned products was heated by means of a Kofler Hot Bench to temperatures generating emissions (visible evaporation or decomposition) i.e. between 150 and 240°C depending upon the compounds tested.

The film, the samples of the pure PVC, and the labels were heated to temperatures used for their thermoprocessing (180 and 250°C).

Inhalation exposures were given for 20 min except when there was an immediate reaction. Continuous clinical examination of both the patient and a volunteer control subject, took place during the test. Respiratory function measurements (FEV₁, PEFR or Raw) were performed 20 min after exposure and then 6 hours after the end of the test period.

Thirteen substances have been tested, however some of them were grouped in order to shorten the test period. A two day interval was required between each challenge test. The return to base line value was verified by spirographic control before the inhalation tests.

Results

Emissions from thermal activation of packaging films and price labels in the working environment

One of the major products emitted from the labels during thermal activation was

Table 1. Emissions from thermal activation of packaging films and price labels in working environment

Fields of determination	Products		
	Di (2 ethylhexyl) adipate (mg/m ³)	Di (2 ethylhexyl) phthalate (mg/m ³)	Dicyclohexyl phthalate (mg/m ³)
At 30 cm from the cutting wire	0.54	0.25	0.37
In breathing zones	0.33	0.22	0.28
At 30 cm from the hot plate	1 0.43	—	0.77
	2 0.47	0.24	0.80

Analyses (1) and (2) were repeated at 3 months' interval.

dicyclohexyl phthalate (Table 1), about 0.80 mg/m³ at a distance of 30 cm from the hot plate.

Under the operating conditions small concentrations of phthalic anhydride could not be detected due to the limits of the analysis technique.

Paper label analysis

The paper labels coated with a thermosetting resin (styrenated alkyd resin) and containing a substantial amount of dicyclohexyl phthalate (about 30 mg per label) showed an abnormally high proportion of phthalic anhydride (120 µg per label). The origin of the latter could not be specified: probably the dicyclohexyl phthalate or the alkyd resin. In a label containing about 120 µg phthalic anhydride, 60 µg were found at 200°C and 60 to 90 µg were found at 250°C. In other series of labels used in different supermarkets, we have found 300 µg of phthalic anhydride from a 17% smaller paper surface.

Challenge tests

Results of inhalation tests are shown in Fig. 1.

PVC films. Inhalation tests performed with the complete PVC film (PVC + additives) elicited a decrease in FEV₁ of 1500 ml after 20 min exposure accompanied by audible wheezing. Six hours after exposure airway obstruction still remained and a decrease in FEV₁ of 900 ml was noted.

Inhalation tests performed with samples of pure PVC gave a transient reaction after 20 min exposure, with a decrease in FEV₁ of 900 ml. The patient recovered rapidly and the normal base line value was reached 10 min after the end of the exposure. Late reactions were not noted during the 6 subsequent hours.

Eight additives have been tested. One of them, epoxidized soybean oil, produced 5 minutes after exposure a FEV₁ decrease of 1100 ml. The asthmatic symptoms persisted for 12 hours. There was no reaction in the patient with the seven other additives.

Labels. After a short exposure (3 min) to emissions from a label heated to 250°C, the patient developed an acute attack of asthma. The intensity of the bronchospasm was shown by an immediate increase in airway resistances (from 1.19 cm H₂O/l/sec to 14.84 cm H₂O/l/sec); simultaneously we observed a fall in FEV₁ from 4.700 ml to 2.100

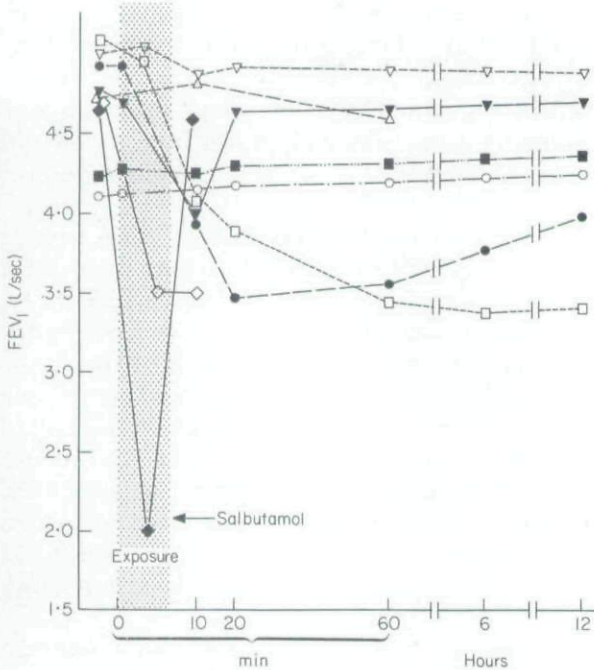


Fig. 1. Changes in FEV₁ following inhalation of PVC film and/or additives and chemicals from labels in Patient 3. □, Additive 1; ▽, additive 2; ●, PVC film + additives; ▼, pure PVC; ■, additive 3; ○, additive 4; ◆, labels; △, dicyclohexyl phthalate; ◇, phthalic anhydride.

ml. A B2 bronchodilator aerosol was administered and complete reversibility of the bronchospasm was observed. No late reactions were noted.

The inhalation tests performed with dicyclohexyl phthalate (40 mg) did not provoke any bronchospastic reactions.

The inhalation tests performed with phthalic anhydride (thermal decomposition of 30 mg, i.e. less than 2 p.p.m.) produced after 5 min an increase in the airway resistance from 2.51 to 6.54 cm H₂O/l/sec and a fall in FEV₁ from 4.700 ml to 3.500 ml. Simultaneously acute wheezing was noted.

The same pulmonary function studies were performed in a control subject who was exposed at the same time and at the same concentrations of phthalic anhydride: no modifications in the spirographic values were noted.

Discussion

The inhalation tests performed in our third patient, incriminate several possible aetiological agents.

The packaging film heated at about 180°C produced a bronchospastic reaction persisting for 6 h and the inhalation of the vapours emitted from the pure PVC film heated at 180°C produced only a transient bronchospastic reaction. This reaction could be attributed to the decomposition of the PVC, particularly to the irritative action of HCl (Cornish & Abar, 1969). We emphasize, however, that the decomposition of such a PVC sample without additives is faster and more important than the decomposition of a stabilized sample.

The inhalation tests performed with seven of the eight additives to the PVC film were negative. Epoxidized soybean oil provoked a persistent bronchospastic reaction. This additive acts as a plasticizer and a stabilizer. It is a complex compound produced by hydrogen peroxide epoxidation of soybean oil and a thermal degradation is possible. It is noted that inhalation tests with another plasticizer di (2 ethylhexyl) adipate which has been detected in the working environment by several authors remained negative.

The most severe bronchospasm was observed after inhalation of fumes emitted from the labels. These results are in accordance with the findings of Andrasch *et al.* (1976) who first demonstrated the importance of emissions from heated labels. However, they could not determine the causal chemical agent. The negative dicyclohexyl-phthalate inhalation test excludes a possible bronchospastic action of this major ingredient. In contrast, exposure to phthalic anhydride led to an immediate and severe bronchospasm. Levy *et al.* (1978) reported bronchospasm from the fumes of labels and the presence of phthalic anhydride in the fumes emitted but could not provoke bronchospasm by means of inhalation tests with a solution of phthalic anhydride. They suggested that it would be necessary to perform tests with phthalic anhydride vapours. Our method of administration may explain our positive results, which should be confirmed by similar tests in other meat wrappers presenting the same respiratory disorder.

The importance of phthalic anhydride as an agent of occupational asthma has been reported in several studies (Chester *et al.*, 1977; Fawcett *et al.*, 1977; Ghezzi & Scotti, 1965; Kern, 1957; Maccia *et al.*, 1976).

In meat wrapper's asthma phthalic anhydride is produced by thermal decomposition of di-cyclohexyl-phthalate and can also be present as an impurity in alkyd resins. However, we were unable to demonstrate that this asthma is a result of hypersensitivity to phthalic anhydride. We have no direct proof that these reactions are due to an immunological mechanism. The existence of a latent period preceeding the first respiratory complaint in butchers, the reaction to the presence of very small concentrations well tolerated by other subjects and previously by themselves, are in agreement with the traditional criteria for hypersensitivity.

Meat wrapper's asthma is a typical example of occupational asthma due to emissions from chemical products. The three cases described in this study must be added to the observations published since 1973. The tests performed in one patient permit us to incriminate two products: phthalic anhydride contained in the adhesive coating of the thermosetting labels which seems to be the principal causal agent and epoxidized soybean oil should be suspected as a secondary agent.

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