
Occupational asthma due to freeze-dried raspberry

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Objective: To investigate the possibility that inhalation of raspberry powder at work can cause occupational asthma.

Methods: We report the case of a 35-year-old, nonsmoking woman who complained of hay fever symptoms, wheezing, and shortness of breath two or three times a month exclusively in association with coating chewing gum with raspberry powder. Prick test extracts with the five types of fruit powder were produced. Peak expiratory flow rate monitoring five times daily was performed for an 8-week period while the patient was at work. Specific IgE and histamine release tests for raspberry powder were performed. Breathing zone dust measurements were taken.

Results: Baseline lung function and histamine provocation test results were normal. During the 8-week monitoring period, 5 episodes of reduced peak expiratory flow rate were demonstrated. Each period was directly related to working with raspberry powder. A 9-mm prick test result positive for raspberry powder was seen (histamine control, 9 mm). In addition, the result of a radioallergosorbent test for raspberry was positive (0.84 kUA/L). The result of a histamine release test with raspberry powder from work was negative. Breathing zone total dust measurement was 5.9 mg/m³.

Conclusions: To our knowledge, this is the first description of occupational asthma due to the inhalation of raspberry powder. The symptoms of the patient described herein disappeared after she was moved to another part of the factory. Hygienic improvements were performed at the workplace to reduce the sensitization risk of other workers.

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INTRODUCTION

Occupational asthma is defined as asthma both causally and specifically related to airborne exposures at the workplace. It has been estimated that between 4 and 10% of asthma may be occupationally related.¹ Bronchial hyper-reactivity is closely related to the presence of asthma. Only a few cases of asthma without bronchial hyperreactivity have been previously described.^{2,3} Three years ago a chewing gum factory started producing chewing gum with natural fruit flavors, including raspberry (*Rubus ideaus*). This report describes a case of histamine challenge-negative occupational asthma due to the inhalation of freeze-dried raspberry powder. This association has not been previously reported. The objective of our report is to investigate the possibility that inhalation of raspberry powder at work can cause occupational asthma.

CASE REPORT

A 35-year-old, nonsmoking woman was referred by the local occupational health service center. She complained of typical hay fever symptoms in the spring and itching of the palate after eating apples and nuts for the past 10 years. On August 1, 2000, she started working with mixing machines that coated chewing gum. A few weeks later, she began complaining of severe hay fever symptoms, dry cough, and shortness

of breath with wheezing. This was the first time she experienced shortness of breath with wheezing and had not had an upper or lower respiratory tract infection within the previous 6 months. She only had shortness of breath on the days that she coated chewing gum with raspberry powder, which occurred two or three times a month. Her symptoms started within the first couple of hours of the working day and disappeared in the evening. She had no symptoms when she coated chewing gum with the other materials (strawberry, orange, black currant, or menthol powders). The only medication she was taking was terfenadine, which she started taking in the spring. The results of physical examination were normal without sibilant rales.

WORK PROCESS

Material safety data sheets and information from the producer indicated that all five fruit powders were produced by freeze-drying without any additives (Molda AG, Dahlenburg, Germany). Experimentally, 3% silicium was added to raspberry powder in an effort to improve coating. Thus, two forms of raspberry powder were used: with and without silicium.

During her workday from 6:00 AM to 2:15 PM, the patient operated six to eight coating machines. Sugar and flavored powder were automatically added to closed mixing machines with an internal rotating drum. Twenty kilograms of fruit powder from paper sacks was poured into a funnel above the coating machines. During production, the machine lid was periodically opened to either add talcum powder (to prevent sticking) or to scrap and loosen chewing gum, which was stuck to the walls of the drum.

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METHODS

Clinical evaluation included blood testing, spirometry (S-model No. 20.600; Vitalograph Ltd, Buckingham, England), histamine provocation testing as described by Cockcroft et al,⁴ and peak expiratory flow rate monitoring 5 times daily for 8 weeks at work (Mini-Wright Peakflow Meter; Clement Clarke International Ltd, Essex, England). A minimum of three peak expiratory flow rate measurements were obtained with at least two measurements within 20 L/min of each other. The best peak expiratory flow rate measurement was selected. Peak expiratory flow rate values were corrected according to temperature, humidity, and altitude.⁵

After obtaining informed consent from the patient, we performed standard prick tests and prick tests with freeze-dried fruit powder diluted with sterile saline to an appropriate consistency: pure raspberry powder, 0.14 g/mL; raspberry powder with 3% silicium, 0.14 g/mL; pure strawberry powder, 0.13 g/mL; orange powder with 3% silicium, 0.17 g/mL; and pure black currant powder, 0.17 g/mL. Nine control individuals were also prick tested with all fruit powder extracts, with no positive reactions.

Breathing zone dust measurements under normal working conditions were taken for a period of 118 minutes using a constant flow pump (SKC High Flow Sampler HFS 113; SKC Inc, Eighty Four, PA). Dust was collected on a 37-mm membrane filter with air flow of 1.9 L/min, resulting in a suction velocity of 1.25 m/s. Particle size was not determined.

RESULTS

Blood testing demonstrated normal levels of eosinophilocytes ($0.2 \times 10^9/L$), IgE (28 kU/L), and α_1 -antitrypsin (29 $\mu\text{mol/L}$). A radioallergosorbent test (RAST) for grass (*Phleum pratense*, 6.4 kU/L), birch (*Betula verrucosa*, 4.4 kU/L), and hassel (2.1 kU/L) produced elevated results. A RAST for house dust mites produced normal results (<0.4 kU/L). Standard prick test results were positive for birch (5 mm), grass (6 mm), and hassel (4 mm), with histamine control of 9 mm. Prick tests with the fruit powders revealed the following results: orange with 3% silicium, negative; pure black currant, negative; raspberry with 3% silicium, 9 mm with a pseudopod; pure raspberry, 7 mm; and pure strawberry, 6 mm. Results of a RAST for raspberry (Rf343; 0.84 kUA/L) and strawberry (f44; 1.78 kUA/L) were positive (normal, <0.35 kUA/L; Pharmacia AS, Copenhagen, Denmark). Results of a histamine release test with raspberry powder from work were negative (Reference Lab, Copenhagen, Denmark).

Lung function was normal: forced expiratory volume in 1 second (FEV₁), 2.90 L (97% of expected); forced vital capacity (FVC), 3.50 L (97% of expected); and FEV₁/FVC ratio, 83%. The results of a histamine provocation test during an employment period were normal with a provocation concentration that caused a decrease in FEV₁ of 20% of more than 8 mg/mL.

The total respirable dust measurement was 5.9 mg/m³. Peak expiratory flow rate monitoring during 8 weeks of

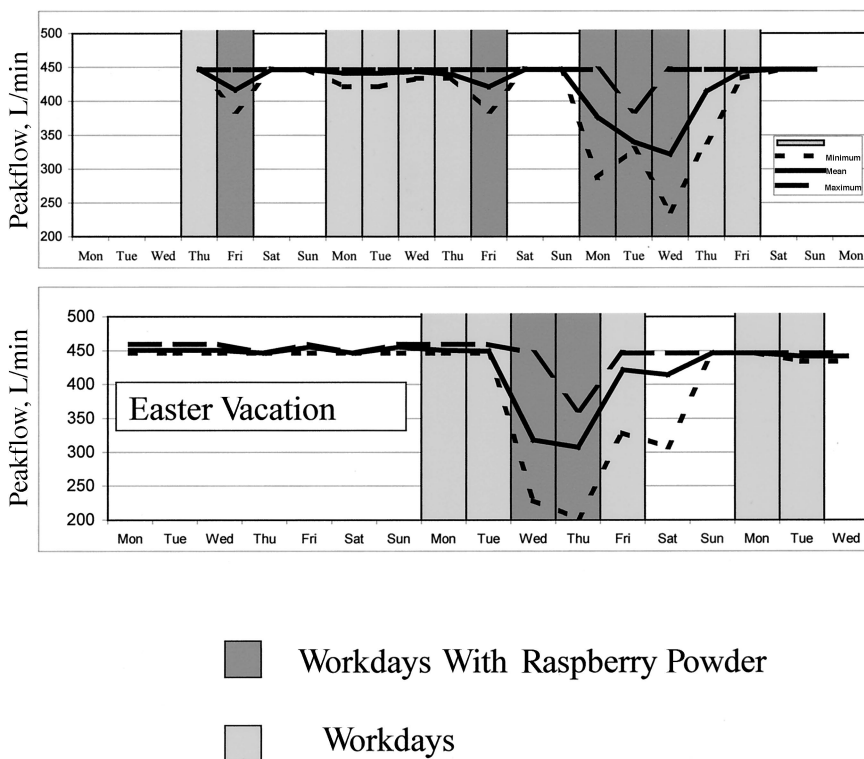


Figure 1. Peak expiratory flow rate monitoring five times daily with corrected minimum, maximum, and mean values.

employment demonstrated five periods with reduced peak expiratory flow rate measurements with wheezing, shortness of breath, sneezing, and rhinorrhea that required treatment with terbutaline inhalation. Between these episodes, peak expiratory flow rate was consistently around 500 L/min (450 L/min corrected). Peak expiratory flow rate reduction was only seen during the five periods during which raspberry fruit powder was used. There were two minor episodes with peak expiratory flow rate reduction to 450 L/min (386 L/min corrected) and three more serious episodes with maximum peak expiratory flow rate reduction to 310 and 300 L/min (238 and 229 L/min corrected; Fig 1).

DISCUSSION

Type 1 allergic responses have been described in association with a large number of fruits: apple,⁶ peach (*Prunus persica*),⁷ banana,⁸ pomegranate,⁹ mango,¹⁰ melon (*Cucumis melo*),¹¹ papaya,¹² and fig.¹³ Pectin has been described as a cause of allergy.^{14,15} Fruits may be treated with sulfur dioxide gas to extend the length of healthy appearance. Sulfur dioxide in the fruit can degrade to bisulfite or sulfite with allergenic potential.¹⁶ The red citrus mite has been described as a cause of asthma in children.¹⁷ No reports concerning raspberry exposure and allergic responses could be found in the literature.

Birch (*Betula verrucosa*) pollinosis, a PR10-homologous allergen, is a main cause of allergic rhinitis and asthma in Western Europe. Bet v 1 appears to be the major allergen in birch pollen.¹⁸ Birch pollen–hypersensitive patients often have oral allergy syndrome after ingestion of apples, pears, cherries, apricots, hazelnuts, celery tubers, carrots, or other vegetables.¹⁹ Many of these fruits and vegetables have PR10 allergens with sequence homology to Bet v 1.¹⁸ There may be similar phosphate-loop region structural elements in the domain common to these allergens.²⁰ This information suggests that there also may be cross-reactivity between raspberry and birch pollen, although this possibility has not yet been investigated.

Inhalation of pure freeze-dried raspberry powder is the apparent cause of asthma in the patient described herein. No additives were added during the production of fruit powders according to the manufacturer. It is unlikely that the powder could have been contaminated during transportation or storage, because it was packed in closed, thick paper sacks. This patient only had asthmatic attacks on the days that she worked with raspberry powder. Hygienic measurements demonstrated significant dust exposure during the coating process. Peak expiratory flow rate monitoring showed a conclusive connection between asthma attacks and exposure to raspberry powder. In addition, positive results on prick tests and RASTs for raspberry were demonstrated. The patient's work-related exposure was thought to constitute an excellent and specific provocation. Therefore, a specific bronchial provocation test in a controlled laboratory setting was not performed. Thus, it was not possible to evaluate the presence or absence of a late-phase response.

A type 1 allergic response was demonstrated by a positive result on prick test for raspberry powder extracts. Prick testing with varying dilutions was not performed. It is unlikely that the positive prick test result was caused by an irritative response, because it was large with a pseudopod. None of the control subjects had a positive prick test result to the fruit powder extracts. In addition, the RAST result was weakly positive. It is interesting that the histamine release test result using raspberry pulver from the workplace was negative. Thus, RAST was more reliable in this case.

There was no evidence of bronchial hyperresponsiveness to histamine in this case of occupational asthma. Bronchial hyperresponsiveness is variable and relates to the severity of disease. Although the results of bronchial hyperresponsiveness tests are usually positive, they may be negative even in the presence of disease.^{2,3,21,22} This patient had variable and mild bronchial hyperresponsiveness, which may explain why her histamine challenge result was negative. She was not taking any asthma medication at the time of the challenge test.

The patient could eat whole fresh raspberries without any adverse reaction. Thus, her allergic responsiveness only occurred in association with the inhalation of powder. This pattern of response can be explained by extensive contact with respiratory mucosal surface and immunocompetent cells. Bronchial hyperresponsiveness due to an infection was not likely, since the patient had no reported illness in the preceding 6 months. All symptoms disappeared after the patient was moved to another part of the factory.

Because of this case, the hygienic conditions at the workplace were improved. On-line respirators were provided to all workers. Disposable coats were also issued. The company is investigating possibilities of replacing powder with solutions of fruit to reduce or eliminate dust exposure.

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