

Occupational asthma due to inhaled carmine

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Summary

Two patients are described with occupational asthma due to carmine, a natural dye extracted from the insect *Coccus cactus*. Both had dual asthmatic reactions after carmine inhalation. Oral challenge provoked gastrointestinal symptoms in one patient, and asthma in them both, perhaps accounting for their continuing symptoms. One patient worked extracting carmine from the insects and the other used carmine as a cosmetic colouring agent.

Introduction

Carmine is a natural dye, extracted from the dried females of the insect *Coccus cactus*, which principally feeds on the prickly pear.

The extraction process starts by mixing the dried insects with sodium carbonate, citric acid and water. After filtration the filtrate is treated with sodium sulphate and calcium carbonate to precipitate the carmine, which is recovered from filter presses by hand. After sterilization with hot steam the extract is dried in ovens. The resulting powder is stored before different batches are mixed in a blender, when sucrose may be added to standardize the colour. The carmine is then bagged. There is an exposure to carmine dust at the drying, mixing and bagging stages.

The extracted carmine is used for cosmetic manufacture and biological dyes. It is also the basis of cochineal, which is widely used as a food colouring, and is added in the manufacture of Campari.

There are no previous reports of respiratory disease due to carmine, but it has caused allergic cheilitis when used as a lip salve (Sarkany, Meara & Everall, 1961), with positive patch tests in three affected patients.

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Case reports

Case 1

A 36 year old process worker in a factory making natural and synthetic dyes. He was said to be the only affected worker out of a work force of fifty-two. 4 months after starting work extracting carmine, by the process previously described, he had his first attack of asthma which woke him from sleep. He had been mixing carmine powder and blending it on the previous day. Later wheezing and sneezing started while at work, and would persist in the evening at home. He was moved to tartrazine manufacture in the same factory where he was much improved. He had one subsequent attack of asthma after taking an ampicillin capsule. During his illness he lost 6.0 kg in weight. He was a non-smoker with no allergic disease in his parents or siblings. Examination while away from work was normal.

Investigations

His eosinophil count was $320/\text{mm}^3$ and skin prick testing with twenty-three common allergens was negative. Prick testing with carmine extract at 10 mg/ml was also negative. The IgG level was 230 iu/ml (57–172), IgA 172 iu/ml (75–268), IgM 163 iu/ml (58–196) and IgE 230 iu/ml (<150). No precipitins were found to carmine extract at 10 and 30 mg/ml. Chest X-ray was unremarkable. When away from work, lung function gave FEV_1 as 3.63 (3.68 expected), FVC as 4.45 (4.62 expected).

Bronchial provocation tests. Day 1: Bronchial reactivity to histamine was negative at 32 mg/ml for 30 sec. Day 2: 30 g dried *Coccus cacti* ground in mortar and pestle for 30 min gave no reaction. Day 3: 30 g dried *Coccus cacti* ground in mortar and pestle for 60 min gave rhinitis and eye irritation, but no wheezing. Day 4: carmine extract in Coca's solution at 10 mg/ml inhaled via a rebreathing bag for 5 min. There was a dual asthmatic reaction with a 31% fall in FEV_1 at 5 hr. Day 5: exercise test of 6 min free running gave an immediate asthmatic reaction with a 26% fall in FEV_1 after 5 min. Day 8: 1.0 ml cochineal diluted in 100 ml of water and drunk.

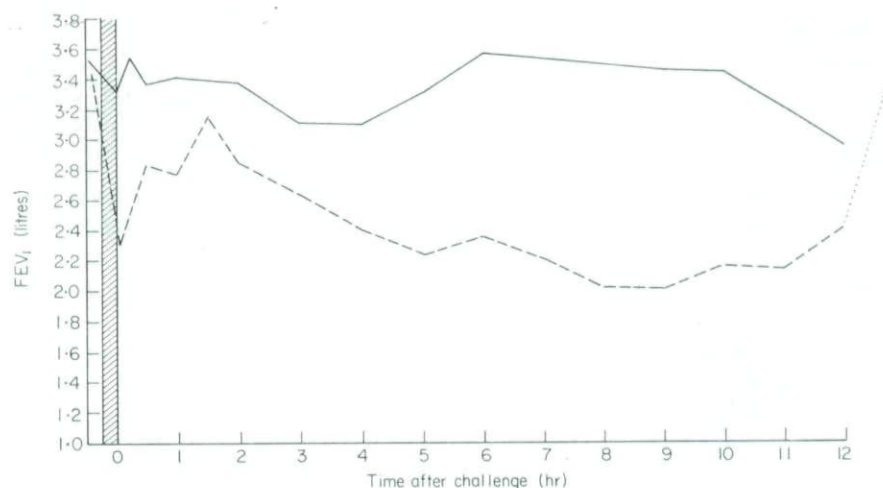


Fig. 1. (—) Citric acid and salts (30 min); (---) carmine extract (5 min); (▨) challenge.

This was followed by severe colicky abdominal pain after 4 hr, lasting 8 hr. The FEV₁ fell by 16% of maximal after 11 hr. Day 9: 500 g mixture of extracting salts tipped between 2 trays for 30 min (sodium carbonate, citric acid, calcium carbonate, sodium sulphate and sucrose) gave no reaction. Day 10: 50 g carmine extract tipped between two trays for 30 min. This was followed by a dual asthmatic reaction, with a 33% immediate fall in FEV₁ followed by a 41% fall after 9 hr. Fig. 1 shows the result of provocation testing on days 4 and 9.

Follow-up

He still works in the same factory, but at night when the carmine process is not used. He has been left with exercise-induced asthma which was not present beforehand and has had occasional attacks of wheeze at work.

Case 2

A 54 year old man who had worked as a blender of cosmetics for 15 years. 5 years after starting work carmine was introduced as a colouring agent. 5 years after starting to use carmine he developed attacks of breathlessness, starting during the day at work. He had to stop several times to rest while cycling home from work in the evening. Jobs requiring carmine were run in batches lasting about 6 weeks, three or four times a year. His breathlessness was much worse during these periods. Eventually, his breathlessness would start within 20 min of exposure and was associated with a running nose. He improved while at home at the weekend and would considerably improve while on holiday.

He smoked 10-30 cigarettes a day, but had had no previous respiratory disease. One brother had asthma.

His job involved blending talcs, zinc stearate, magnesium stearate, kaolin pond, zinc oxide and microcel-C, with various colouring agents including carmine, aluminium dust and blue and brown pigments.

Table 1. Lung function tests in case 2

Parameter	Predicted	1 month after exposure	3 months after exposure	1 year after exposure
FEV ₁ (ml)	2730-3700	950	1550	1150
FVC (ml)	3640-4930	2650	3680	3000
FEV ₁ /FVC	66-77	36	42	38
TLC (ml)	5390-7300	8690	8450	6880
RV (ml)	1870-2540	6290	4700	3980
FRC (ml)		7160	5850	4130
Va (ml)	5020-6790	4420	5500	5210
VC (ml)	3640-4930	2400	3750	2900
Inspiratory AWR (Kpa/l/sec.)	<0.2	0.96	0.3	0.77
S Gaw (sec/KPa)	1.3-3.6	0.15	0.56	0.31
DLCO (m.mol/min/KPa)	8.07-10.92	3.63	5.30	5.47
KCO (m.mol/min/KPa/Litre)	1.26-1.71	0.82	1.0	1.05
After salbutamol (200 mg by inhalation)				
FEV ₁ (ml)		1100	1800	1470
FVC (ml)		3000	4250	3610
FEV ₁ /FVC		37	42	41

Investigations

On examination, he was breathless at rest with an overinflated and wheezy chest. Chest X-ray showed overinflation but no other abnormality. His eosinophil count was $110/\text{mm}^3$, and his IgG level was 108 iu/ml (57–172), IgA 212 iu/ml (74–268), IgM 218 iu/ml (58–197) and IgE 100 iu/ml (<150). Skin prick testing with twenty-three common allergens was negative, as was prick testing with carmine extract at 10 mg/ml. No specific IgE antibodies were found to a *Coccus cactus* extract by RAST, but precipitating antibodies were present to carmine extract at 30 mg/ml.

Lung function tests are shown in Table 1.

Bronchial provocation testing. Day 1: 20 g carmine powder tipped between two trays for 15 min. There was a dual asthmatic reaction with a 23% immediate fall in FEV_1 and a 47% fall at 3 hr. Day 2: a mixture of talcs, magnesium and zinc stearates, blue, brown, yellow and black pigments, zinc oxide and kaolin pond were mixed and tipped between two trays for 15 mins, and gave no significant reaction. Day 3: *Coccus cactus* extract, 10 mg/ml, inhaled via a rebreathing bag for 5 min. There was a dual asthmatic reaction with a 27% immediate fall in FEV_1 followed by a 29% fall after 3.75 hr. This reaction lasted for 3 days. Day 6: 100 ml Campari drunk. There was a dual asthmatic reaction with a 15% fall in FEV_1 after 45 min followed by an 18% fall at 4.5 hr. Fig. 2 shows the results of provocation testing on days 1 and 2.

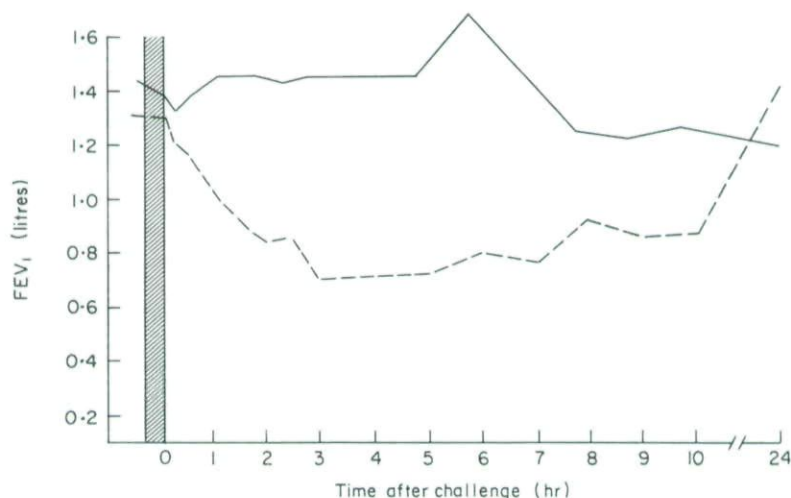


Fig. 2. (—) Other powder constituents (15 min); (---) carmine dust (15 min); (▨) challenge.

Follow-up

Carmine has now been replaced by other synthetic red dyes in this man's factory. He is now considerably improved but still has severe exercise-induced asthma. He also wheezes on most days.

Discussion

Bronchial provocation testing in these two men has established that carmine is responsible for their wheezing attacks. In the first case an attempt was made to induce asthma by grinding the actual insects. This probably failed as very little dust was produced, because of the fat content of the insects.

Both patients were tested with an extract of *Coccus cactus* insects prepared in Coca's solution. Inhalation of this provoked their asthma. Both patients wheezed after inhalation of carmine in powder form. This is likely to be a specific reaction as inhalation of powders of the other constituents used by these two men did not provoke asthma. The red colour of carmine is due to carminic acid secreted into intracellular vesicles of the *Coccus cacti* insects. It is not clear whether this, or other insect-derived materials, is responsible for these patients' asthma. Related insects have been used to produce kermesic acid, used for the red dye on Fezs, and lac used for paints.

Both these patients have been much improved by avoiding exposure to carmine at work, but both still have symptoms. Lung function studies in the second patient suggest associated emphysema, but he also still has attacks of asthma. Both patients still have exercise-induced asthma. It is possible that ingested carmine is responsible for their continuing symptoms as cochineal (derived from carmine) is widely used as a food dye. Both patients reacted, with wheezing, and one with severe abdominal pain, after ingesting dilute cochineal or Campari (containing carmine). Davies, Hendrick & Pepys (1974) described similar gastrointestinal and respiratory symptoms in workers manufacturing penicillin, after oral challenge with the penicillins. In another case, a maintenance engineer, sensitized to Spiramycin, manufactured in his factory, had persisting symptoms after leaving. This eventually stopped after avoiding hens' eggs, which contain trace amounts of spiramycin (Davies & Pepys, 1975).

Alanko *et al.* (1978) described four patients sensitized to reactive dyes. Three of these had elevated total IgE levels and a positive IgE RAST to the specific dyes. Our patients had low IgE levels and negative prick tests with carmine extract, making an IgE-mediated reaction less likely. The underlying immunological mechanisms in these two patients has yet to be elucidated, although precipitating antibody to carmine was found in one patient.

Acknowledgments

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