Occupational asthma due to sodium iso-nonanoyl oxybenzene sulphonate, a newly developed detergent ingredient

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ABSTRACT Research with sodium iso-nonanoyl oxybenzene sulphonate (SINOS) for use in a detergent product was complicated by the development of asthma in an atopic 38 year old laboratory technician. Inhalation challenge tests with nebulised SINOS solutions over a dose range of 0.01–32 µg gave reproducible late asthmatic reactions after the higher doses and an increase in bronchial responsiveness to methacholine. The magnitude of the late reaction was related to the challenge dose.

Rashes, rhinitis, and conjunctivitis were noted in three of 60 detergent workers engaged for 12–18 months in research with a newly developed ingredient (sodium iso-nonanoyl oxybenzene sulphonate, SINOS) and investigations suggested that delayed contact hypersensitivity to SINOS was probably responsible for some at least of the rashes. A fourth worker then developed asthma. This paper describes investigations suggesting that this was causally related to SINOS.

Case report

A 38 year old laboratory technician, who had worked in the research and development plant of a detergent manufacturer since the age of 19 years, had had moderately severe asthma as a child from the age of 2 to 14 years but recalled neither rhinitis nor eczema. He had been well until January 1985, when, 18 months after starting work with SINOS, he began to have rhinitis, a rash, a dry cough, and undue breathlessness on exertion. Four weeks later he woke on two successive nights during the working week with wheezing, chest tightness, and breathlessness, the last being severe on the second occasion. He stayed away from work and his symptoms resolved completely within two weeks.

He had never smoked, he had no pets or other relevant domestic exposures, and he took no regular medications. While he was symptom free away from work he had no abnormal physical signs and ventilatory indices were within normal limits, but a chest radiograph showed some evidence of overinflation. Skinprick tests gave positive immediate reactions to various common allergens, and total serum IgE was substantially raised at 1000 (normal range 10–150) IU.

There was no excess binding in antigen specific IgE assays with SINOS directly attached to ELISA plastic plates (Dynatech, Billingshurst) but, in the absence of a positive control serum, the ability of the test to exclude a specific IgE response was not validated. Tests to detect anti-SINOS precipitating IgG antibodies also gave negative results.

Results of a routine biochemical screen and a full blood count were normal apart from an eosinophil count of \(1.18 \times 10^{9}/\text{l}\).

The patient returned to work after three weeks. There was a minimal recurrence of his symptoms, and a mild increase in circadian change in peak expiratory flow (PEF), the mean daily difference between maximum and minimum daily PEF readings increasing from 54 to 97 l/min. The cumulative dose of methacholine required to provoke a 20% decrement in FEV\(_1\) (PD\(_{20}\)) measured by a dosimeter method, fell from 400 and 500 µg when he was absent from work to 280, 240, and 200 µg after his return to work. He ceased work once more after two weeks and SINOS inhalation tests were carried out within a few days, when his symptoms had resolved.

SINOS INHALATION TESTS

It was estimated from workplace exposure measurements that he had tolerated hourly inhalations of 0.02–100 µg SINOS without undue discomfort, so an initial challenge dose of 0.01 µg was chosen. For the maximum dose 100 µg was chosen (equivalent to a full working day's dose at

![Fig 1](http://thorax.bmj.com/).
Fig 2. Dose-response relationship between SINOS and FEV₁ area decrement (numbers indicate the chronological order of the control tests and 32 μg tests).

exposure levels close to the hourly maximum over the preceding six months.

A locally designed dosimeter was used to deliver both methacholine and SINOS. The onset of inspiration from functional residual capacity triggered the nebulisation of 10 μl (±5%) of test solution during the initial 2 seconds of a 5 second inspiration. There was no subsequent breath holding. SINOS was administered in 50 μl doses (five inhalations) from solutions of increasing concentration (0-2-640 μg/ml in phenol saline). Daily increments of about 3.2 fold (√10) were given to provide a dose range of 0.01-32 μg over the course of two weeks, during which three blinded control tests with phenol saline alone were interspersed at random.

Late asthmatic reactions of increasing severity were observed with the higher doses of SINOS, and these were accompanied by a further decrease in PD₉₀ which was 110 μg on the day after the last SINOS challenge despite full recovery of baseline FEV₁. The reaction to the 32 μg dose was considered unequivocal by both patient and physician (fig 1), and no further dose increments were administered. It proved to be reproducible (fig 2). No asthmatic symptoms were noted after the control tests but circadian changes in FEV₁ increased slightly as the level of bronchial responsiveness increased.

The FEV₁ response 2-12 hours after control and SINOS challenge was expressed as the area above the FEV₁-time plot. baseline FEV₁ (mean of five sets of three technically satisfactory measurements at 10 minute intervals before challenge) being used to define the upper boundary of the area measured. Regression analysis, which excluded the results from the control challenges, showed a significant linear relationship (fig 2) between this area decrement (A) and the log challenge dose:

\[ A = 4.53 + 2.74 \times \text{log}_{10} \text{dose} \]

(slope significantly different from 0 (p < 0.001, F₁,₂ = 79).

The patient was transferred to another of the company’s plants and had no further exposure to SINOS. He had no more symptoms and PD₂₀ methacholine increased steadily over three months to 800 μg.

**Discussion**

SINOS appears to be a further example among the wide variety of industrial chemicals capable of inducing occupational asthma. The pathogenic mechanisms remain unclear. In most instances induction of an antibody response has not been demonstrated, possibly because a suitable carrier-hapten complex could not be produced for immunological studies; but the clinical effects have generally been very similar to those induced by conventional common allergens. Thus chemically induced asthma has often been associated with rhinitis, conjunctivitis, and rashes—either in the asthmatic worker himself or in other members of the exposed workforce. Furthermore, when used in inhalation tests in affected workers these chemicals usually provoke a late (or dual—that is, immediate plus late) type of asthmatic reaction and an increase in non-specific bronchial responsiveness. In this they again resemble common allergens, although irritants such as the oxidant gases nitrogen dioxide and ozone may provoke similar reactions and increase non-specific bronchial responsiveness. In all these respects SINOS appears to be typical of occupational inducers of asthma.

The regression analysis of dose against response showed a linear relationship between a cumulative measure of decline in FEV₁ (area decrement) and log dose of SINOS. This linearity and the lack of any obvious threshold dose might suggest an irritant or possibly a pharmacological effect—which is, of some interest in view of the uncertainty surrounding immunological mechanisms in the pathogenesis of occupational asthma in general and the absence of a detectable antibody response in this worker in particular. A similar dose-response relationship, however, might conceivably be observed if hypersensitivity to common allergens were investigated in this way.

A dose-response analysis has not previously been used to investigate occupational asthma. It was useful in allowing us to evaluate the statistical significance of the reactions we had observed, though we recognise that this approach will be suitable only when airway reactivity is low and multiple challenge increments can be administered.

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**References**


