

# Occupational asthma induced by the fungicide tetrachloroisophthalonitrile

Izumi Honda, Hirotsugu Kohrogi, Masayuki Ando, Shukuro Araki, Tatsuro Ueno, Makoto Futatsuka, Atsushi Ueda

## Abstract

**A 48 year old male farmer had recurrent episodes of dyspnoea, shortness of breath, and wheezing after being in his plastic greenhouse when the fungicide tetrachloroisophthalonitrile had been sprayed. A bronchial provocation test with a control challenge and a patch skin test confirmed that his asthma was induced by tetrachloroisophthalonitrile.**

(Thorax 1992;47:760-761)

Tetrachloroisophthalonitrile, a fungicide (fig 1),<sup>1</sup> causes contact dermatitis and eczema.<sup>2</sup> In this paper we report the case of a farmer who developed asthma after exposure to tetrachloroisophthalonitrile.

## Case report

In May 1986 a 48 year old male farmer attended Kumamoto University Hospital, with dyspnoea, shortness of breath, and wheezing. He had had his first attack of asthma, lasting five days, 10 years before. Two years previously (1984) he had had five episodes of asthma from March to June, followed by further episodes in 1985 at the same time of year and again in December. He noticed that his symptoms always occurred when he was using tetrachloroisophthalonitrile in his plastic greenhouse or in the evening after working there. He had been using tetrachloroisophthalonitrile for 10 years.

On admission physical examination showed nothing abnormal. His chest radiograph showed slightly overinflated lungs. Total lung capacity, vital capacity, forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC, and residual volume were normal. A methacholine inhalation test<sup>3</sup> showed hyperresponsiveness: the threshold concentration of methacholine required for increasing respiratory resistance was 0.98 mg/ml (normal subjects usually fail to respond to the highest concentration of 25 mg/ml) and reactivity was 7.13 cm H<sub>2</sub>O/l/s/unit. Arterial blood gas tensions were normal. The blood eosinophil count and serum total IgE concentration (radioimmunosorbent test) were normal. The intradermal response to various allergens (house dust, *Alternaria*, *Aspergillus*,

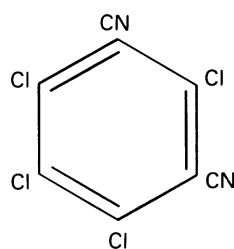


Figure 1 Structure of tetrachloroisophthalonitrile (molecular weight 265.9).

**First Department of Internal Medicine**  
I Honda  
H Kohrogi  
M Ando  
S Araki

**Department of Public Health**  
T Ueno  
M Futatsuka

**Kumamoto University Medical School, 1-1-1 Honjo, Kumamoto 860**

**Department of Hygiene**  
A Ueda

**Faculty of Medicine, Kagoshima University, 35-1 Sakuragaoka, Kagoshima 890, Japan**

Reprint requests to:  
Dr M Ando

Accepted 19 December 1991

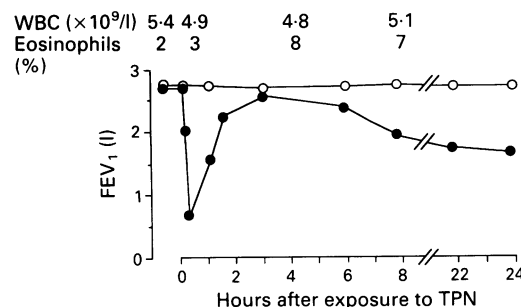


Figure 2 Time course of FEV<sub>1</sub> after exposure to tetrachloroisophthalonitrile and dichlorvos. Tetrachloroisophthalonitrile (closed circle) caused an early and late asthmatic response and it increased the eosinophil count in peripheral blood. Neither dichlorvos (open circle) nor water (not shown) caused any change in FEV<sub>1</sub>.

*Penicillium*, *Cladosporium*, lesser reed mace, ragweed, egg plant, buckwheat) was negative; a positive response to *Candida* was seen after 30 minutes and lasted for more than 24 hours. A patch test with eight pesticides (diluted 200–5000 fold) used in his district (tetrachloroisophthalonitrile, chinomethionate, iprodione, thiophanate methyl, benomyl, captan, methidathion, and dichlorvos) showed a positive reaction to tetrachloroisophthalonitrile only. Specific IgE antibody to tetrachloroisophthalonitrile was not detected by the enzyme linked immunosorbent assay (ELISA).

We measured FEV<sub>1</sub> before and after the patient entered his plastic greenhouse, in which both tetrachloroisophthalonitrile and dichlorvos (both at concentrations of 3.0–10.0 ppb) had been sprayed by another farmer two hours previously. Before the test his FEV<sub>1</sub> was 2.87 l. Two minutes after entering the greenhouse he complained of dyspnoea, shortness of breath, and wheezing and his FEV<sub>1</sub> had fallen to 1.40 l.

With the informed consent of the patient we performed tests to find out which chemical had induced asthma in the plastic greenhouse. In a double blind fashion we sprayed 0.1% tetrachloroisophthalonitrile, 0.1% dichlorvos, or water (control) in three different rooms in the hospital on different days. We measured FEV<sub>1</sub> before and after the exposure. Neither tetrachloroisophthalonitrile nor dichlorvos had a detectable odour at the concentrations used. Two minutes after entering the room where tetrachloroisophthalonitrile had been sprayed he complained of dyspnoea and came out of the room. Tetrachloroisophthalonitrile induced an early and late asthmatic response lasting for 48 hours (fig 2). He had no symptoms in the room where dichlorvos or water had been sprayed. A normal man (aged 25 years) did not respond to tetrachloroisophthalonitrile, dichlorvos, or water. The concentrations of tetrachloroisophthalonitrile and dichlorvos in the rooms were 1.3–9.8 ppb.

## Discussion

This is the first report of tetrachloroisophthalonitrile induced asthma. The diagnosis of occupational asthma is best confirmed by showing a fall in lung function in relation to

exposure in the working environment to airborne dusts, gases, vapours, or fumes.<sup>4</sup> In this case a provocation test showed that the asthmatic response occurred in the plastic greenhouse where tetrachloroisophthalonitrile and dichlorvos had been sprayed. The double blind provocation test showed that tetrachloroisophthalonitrile caused an early and late asthmatic response whereas dichlorvos and water (control) produced no response. The patient showed a positive reaction to tetrachloroisophthalonitrile in a patch test with eight pesticides used in his district. These results strongly suggest that tetrachloroisophthalonitrile caused asthma in this patient. We could not find any specific IgE antibody to tetrachloroisophthalonitrile using an enzyme linked immuno-

sorbent assay, but specific IgE antibody is not always found in asthma induced by chemicals.<sup>5</sup>

We are grateful to Dr K Fukuda for the measurement of methacholine reactivity and to Dr K Nishigami for his valuable help in the provocation test.

- 1 Turner NJ, Limpel LE, Battershell RD, Bluestone H, Lamont D. A new foliage protectant fungicide, tetrachloroisophthalonitrile. *Contributions from the Boyce Thompson Institute* 1964;22:303-10.
- 2 Bach B, Pedersen NB. Contact dermatitis from a wood preservative containing tetrachloroisophthalonitrile. *Contact Dermatitis* 1980;6:142.
- 3 Takishima T, Hida W, Sasaki H, Suzuki S, Sasaki T. Direct-writing recorder of the dose-response curves of the airway to methacholine. *Chest* 1981;80:600-6.
- 4 Newman Taylor AJ. Occupational asthma. *Thorax* 1980;35:241-5.
- 5 Pezzini A, Riviera A, Paggiaro P, Spiazzi A, Gerosa F, Filieri M, et al. Specific IgE antibodies in twenty-eight workers with diisocyanate-induced bronchial asthma. *Clin Allergy* 1984;14:453-61.

---

## NOTICES

---

### Pharmacology of asthma course

A course on the pharmacology of asthma will be held from 30 November to 3 December 1992 at the Royal Brompton National Heart and Lung Institute. The course is organised in two modules, on basic mechanisms (30 November, 1 December) and on therapy (2 and 3 December). It is suitable for physicians or scientists with an interest in the pharmacology and therapeutics of asthma. The link between basic mechanisms and clinical application will be emphasised. The course organiser is Professor Peter Barnes. Enquiries should be made to the Postgraduate Education Centre, National Heart and Lung Institute, London SW3 6LY (tel 071 352 8121, fax 071 376 3442).

### Teaching clinical communication skills

The Cancer Research Campaign's Communication and Counselling Research Centre is running courses for senior oncologists and clinicians caring for patients with cancer. These are three day residential workshops in luxury accommodation designed to help senior clinical staff enhance their communication skills and develop expertise in teaching these to junior staff. Participants will work in small groups (four per tutor) run by experienced facilitators. The cost of the course is £250 and includes a teaching package of five purpose made videos with accompanying notes for participants' own use. These videos all relate to communication difficulties that may arise in communicating with patients with cancer. For further details please apply to: Dr Lesley Fallowfield, CRC Communication and Counselling Research Centre, London Hospital Medical College, London E1 2AD (tel/fax 071-247 7503).