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ENVIRONMENTAL CHEMICALS AND EXPERIMENTAL ALLERGIC CONJUNCTIVITIS

Mikio MIYATA, Tatuto NAMBA, Gin LI,
Shigeru AOKI, Mitsushi ABE and Satoshi ISHIKAWA

*Department of Ophthalmology, School of Medicine, Kitasato University,
1-15-1 Kitasato, Sagami-hara, Kanagawa 228, Japan*

Introduction

About 30 years ago, hay fever-like disease was unheard of in Japan. However, within the past 20 years, severe allergic conjunctivitis of the eyes and nose in early spring has become a major diseases among the Japanese people. Chemical substances in the environment may be contributing to this situation. The present study was conducted to confirm this point.

1. Material and Method

Experimental allergic conjunctivitis was induced by passive immunization followed by challenge with Japanese cedar pollen in the conjunctival sac (Ovary *et al.*, 1976; Iso *et al.*, 1980). Seven-week-old Hartley strain male guinea pigs were immunized intraperitoneally with a solution of Japanese cedar pollen. Antiserum with titer exceeding 1 : 160 as measured by passive cutaneous anaphylaxis was pooled for the present experiment. The guinea pigs were passively immunized with intravenous injection of 1 ml antiserum. Ten days later, the animals were topically challenged with homogenates of cedar pollen immediately following intravenous injection of 10 mg Evans blue in 1 ml physiological saline.

A single subcutaneous administration of trichlorfon, fenitrothion, or paraquat dichloride

was given 2 days before the challenge, with various concentrations being tested. Chloroform as trihalomethane in drinking water was administered for 2 days before the challenge. p-Dichlorobenzene was inhaled at one of several concentrations for 2 days before the challenge.

The animals were sacrificed 30 min after the challenge by exsanguination under deep anesthesia. The conjunctivae were excised and any extravasated Evans blue in the tissue was extracted. The absorbance of Evans blue was spectrophotometrically measured at 620 nm and expressed as relative intensity of allergic conjunctivitis.

2. Results

The results of quantitative dose-response analysis of the allergic reaction of the conjunctiva exposed to trichlorfon are shown in Fig. 1. The open circles represent reactions with the challenge of cedar pollen and the close circles, reactions without the challenge. Each circle stands for the value of an average of 10 eyes. Allergic reaction was aggravated by trichlorfon even at the very low level of 3×10^{-5} mg/kg and was greatest at 3×10^{-3} mg/kg. Aggravation was rather weak at high doses, rising to a bell-shaped curve. Similar curves were obtained in the experiment with fenitrothion.

Exposure to paraquat aggravated the allergic reaction. Aggravation was noted from 10^{-4} mg/kg and reached a maximum at 10^{-2} mg/kg body weight. Aggravation was rather weak at the

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Correspondence : Mikio MIYATA at the above address.

Fig. 1. Allergic intensity plotted against concentration of trichlorfon.

higher doses, and a bell-shaped dose-response curve was obtained.

Allergic conjunctivitis was thus appeared to be aggravated by very low concentrations of chloroform, at 0.1 ppm in drinking water, and of p-dichlorobenzene, at 3.2 ppb in air. Aggravation was found to be greatest at 1 ppm chloroform and 32 ppb p-dichlorobenzene, again diminishing at higher doses, so that the dose response curve was consequently bell-shaped.

3. Discussion and summary

Residues of chemicals in the body and minimum effective doses are important factors of chemical toxicity. It has been shown that effect of organophosphorus pesticides persist for more than 70 days (Homma, 1991) and the minimum effective doses on electroretinogram is 5 $\mu\text{g/kg}$ of body weight (Imai, 1974). The aggravating effects of the organophosphorus pesticides, trichlorfon and fenitrothion, were shown in this study to start at 10^{-4} mg, i.e. 1/100 the minimum effective doses specified in the above re-

port. This parameter for paraquat was also extremely low. The minimum effective dosage of chloroform as trihalomethan in drinking water was 1 ppm, this almost compliance with the regulation. Contamination by p-dichlorobenzene in room air and even in highway air (Hanai *et al.*, 1985) presumably from moth balls and toiletary exceeds the present minimum effective dosage. Another point of interest from the present study is that aggravating effects diminished at higher concentrations. Thus aggravation may possibly occur at relatively safe levels that would not require to treat in standard toxicology treatment.

In summary, chemical substances appear to be major factors for allergy and aggravations may become severe at extremely low doses.

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