Short Report

Bronchial Responses to Inhaled Histamine and Methacholine after Influenza Virus Vaccination in Monkeys

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ISHIHARA, T., MUE, S., OHMI, T., TAMURA, G., YAMAUCHI, K., IDA, S., FUYUKI, T., CHONAN, T., SHINDOH, C., SATO, K., OTSU, H., TANIGUCHI, Y. and TAKISHIMA, T. Bronchial Responses to Inhaled Histamine and Methacholine after Influenza Virus Vaccination in Monkeys. Tohoku J. exp. Med., 1983, 140 (3), 335-336 — Bronchial responses to inhaled histamine significantly increased on the 2nd day and the 7th day after influenza virus vaccination in monkeys. Bronchial responses to inhaled methacholine also significantly increased on the 14th day and the 21st day after the vaccination.

Asthmatic patients are known to develop easily an attack after a respiratory infection. There are many studies suggesting that viral infection and vaccination of microorganisms increased the bronchial response to histamine and methacholine, especially in asthmatic patients. However, the mechanism of bronchial hypersensitivity has not been clarified, especially in relation to the infection. In order to investigate if viral infection could change the bronchial hypersensitivity in monkeys, bronchial responses to inhaled histamine and methacholine after the vaccination were studied. The influenza virus HA vaccine 0.5 ml (A. Kumamoto, A. Bangkok, B. Kanagawa, total 700 ccA/ml) was injected subcutaneously to 6 Japanese monkeys (Macaca fuscata). Under anesthesia with ketamine hydrochloride 10 mg/kg, a tracheal tube was inserted into the monkeys and the total respiratory resistance (Rrs) was estimated by the oscillation method (Grimby et al. 1968). Histamine and methacholine were dissolved to a serial solution from 0.015% to 2%.

Monkeys inhaled the aerosol in an incremental fashion for 1 min with tidal breathing. In a dose-related fashion, an increase of the total respiratory resistance was observed (Mue et al. 1980), which is instantaneously calculated from the respiratory impedance according to Hyatt's formula (Hyatt et al. 1970). The threshold concentration of these bronchoconstrictors that produced Rrs twice the control value (during inhalation of physiological saline) was examined.

Each experiment was carried out at intervals of at least one week. Fig. 1 shows the change of threshold concentration of histamine for bronchoconstriction in the 6 monkeys after the vaccination. The upper figure shows the monkeys with the increased titer of neutralizing antibody and the lower figure shows those with the unchanged titer of the antibody. In all monkeys with increased antibody titer, an increased bronchial response to histamine was observed on the 2nd day and the 7th day after vaccination. Their bronchial response decreased to the level of prevaccination on the 14th day, then increased.

Received for publication December 27, 1982.
again on the 21st day after vaccination. In 2 out of 3 monkeys without an increased antibody titer, an increase of bronchial response was also observed similarly to the monkeys with increased titer. Fig. 2 shows the dose response curves to histamine before and on the 2nd day after vaccination. The bronchial response to histamine significantly increased after the vaccination. Fig. 3 shows the dose response curves to methacholine before and on the 21st day after vaccination. The bronchial response to methacholine also significantly increased after vaccination.

The mechanism of the influenza virus vaccination is unknown yet. Empey et al. (1976), however, suggested that airway epithelial damage by infection exposes and thus sensitizes the rapidly adapting airway receptors to inhaled irritants, resulting in an increased bronchoconstriction via a vagal reflex. In other study, Schreurs et al. (1980) indicated that vaccination of experimental animals with Haemophilus influenzae decreased B-adrenergic receptors of airways. We could not conclude that the increased bronchial response might be related to the increase of the titer of neutralizing antibody.

References