

# Synergistic Effect of Vitamin E and $\beta$ -Carotene on the Suppression of Ovalbumin-Specific Immunoglobulin E Production in Mice

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Vitamin E and other antioxidants such as carotenoids and flavonoids are suggested to be responsible for the anti-allergic effect of fruits and vegetables in epidemiologic studies.<sup>1</sup> Therefore, the effect of vitamin E on immunoglobulin E (IgE) production *in vivo* seems to be of much interest, as IgE antibody is well known to participate in the type I allergic reaction. We sought to determine whether or not supplementation with vitamin E and  $\beta$ -carotene, a typical carotenoid from plant foods, affects IgE production in the allergic model mice. The results strongly suggest that the combination of both antioxidants suppresses allergen-specific IgE production and total IgE production.

## METHODS

BALB/c mice (female; 6 weeks of age) were given a diet supplemented with vitamin E and/or  $\beta$ -carotene for 3 weeks. These mice were then subcutaneously immunized twice with ovalbumin (OVA) without adjuvant. After 6 weeks, antiserum was obtained by decapitation with the mice under anesthesia. OVA-specific IgE production was evaluated with passive cutaneous anaphylaxis analysis. Total IgE and antigen-specific-IgG<sub>1</sub> concentrations in the serum were measured by the sandwich ELISA method.

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## RESULTS

### *Diets with Vitamin E*

Some mice were fed diets containing different amounts of vitamin E ( $\alpha$ -tocopherol). The amounts included 0.5, 5, 10, and 50 mg of vitamin E per 100-g diet. The diet containing 5 mg of vitamin E was usually given to mice as a control diet. Passive cutaneous anaphylaxis analysis demonstrated that the mice fed the diet containing 5 mg of vitamin E produced OVA-specific IgE antibody. The lower level of antigen-specific IgE antibody was found in the mice fed the diet supplemented with 0.5, 10, and 50 mg of vitamin E. Lower IgE production in the case of the low vitamin E diet (0.5 mg per 100-g diet) may be explained by impairment of the immunological function due to vitamin E deficiency.

### *Diets with Basal Vitamin E Plus $\beta$ -Carotene*

Some mice received the basal diet (containing 5 mg of  $\alpha$ -tocopherol acetate as vitamin E) with different amounts of  $\beta$ -carotene. The amounts included 2, 10, 50, and 250 mg of  $\beta$ -carotene. IgE production increased in the mice with 10 mg of  $\beta$ -carotene supplementation and decreased in the mice with 250 mg of  $\beta$ -carotene supplementation. Fifty milligrams of  $\beta$ -carotene supplementation had little effect on the

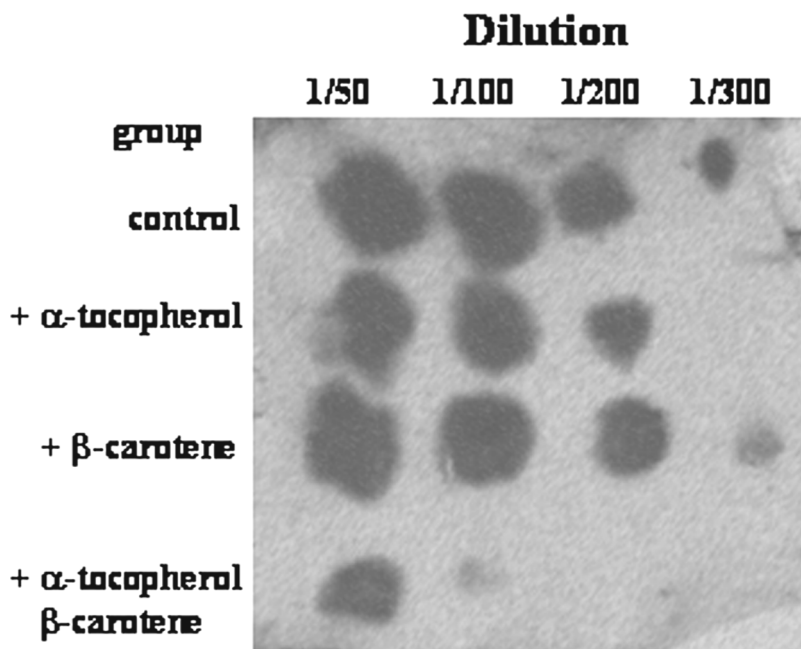


**FIGURE 1.** Passive cutaneous anaphylaxis analysis of allergen-specific IgE production in experimental animals. (From Bando *et al.*<sup>3</sup> Reproduced by permission.)

IgE elevation.  $\beta$ -Carotene added to the diet might have been oxidized through the feeding period at 25°C, and this process might have resulted in the enhancement of IgE production by a pro-oxidant function of  $\beta$ -carotene oxidation products.

### *Combination Diets*

The basal diet contained 5 mg of  $\alpha$ -tocopherol acetate. In the combination diet, 5 mg of vitamin E and/or 50 mg of  $\beta$ -carotene were added to the basal diet in order to evaluate the effect of their combination. Vitamin E plus  $\beta$ -carotene effectively suppressed the allergen-specific IgE antibody as compared with either the case of vitamin E alone or the case of  $\beta$ -carotene alone (FIG. 1).<sup>2</sup> A similar effect was observed by addition of vitamin E and  $\beta$ -carotene on the level of total IgE and allergen-specific IgG<sub>1</sub>, both Th2 immunoglobulins. Vitamin E and  $\beta$ -carotene were accumulated in the serum by supplementation with the respective compounds.

This phenomenon may reflect the synergistic antioxidative activity of vitamin E and  $\beta$ -carotene. It has been reported that vitamin E protects  $\beta$ -carotene from free radical-induced oxidation when the both compounds coexist. The provitamin A activity of  $\beta$ -carotene, as well as its antioxidative action, may be related to the combined effect of vitamin E and  $\beta$ -carotene on IgE production. Nevertheless, the literature shows that retinoic acid affects IgE production *in vitro* and *in vivo* through different functions.<sup>3,4</sup>

It is still unclear whether or not dietary  $\beta$ -carotene acts as a provitamin A for inhibiting IgE production. A high intake of  $\beta$ -carotene may induce a harmful effect by acting as a pro-oxidant through an unknown mechanism. It is unlikely, however, that a high dose of vitamin E and/or  $\beta$ -carotene exerts any undesirable effect, because the growth curve was not affected by a higher administration in this study. Therefore, intake of vitamin E together with  $\beta$ -carotene is helpful in the prevention of allergic IgE production.

## CONCLUSION

The combination of dietary vitamin E and  $\beta$ -carotene suppresses IgE production dramatically in allergic model mice and would therefore help to attenuate the type I allergy syndrome.

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