to 2500 grains/m^3 of JC pollen, which is equivalent to the amount of airborne pollen grains in the early stages of the pollen season. Although their allergic symptoms were reported to be mild, one of the subjects had to leave the room before the scheduled time since the subject was about to sneeze. The other 9 subjects were able to remain in the room for an hour without developing any allergic symptoms. We found that the average number of intranasal and intraocular pollen grains was 249.2 and 13.6, respectively. The subjects sat still during the study for up to 1 hour and did not move around, so their eyes simply received pollen grains, and their shedding tears and blinking cleared the pollen grains. On the other hand, subjects actively inhaled pollen grains through their noses, allowing more pollen to precipitate in the nose and they did neither sneeze nor blow their noses. These could be the possible reason why the number of intranasal pollen grains was much larger than that of the intraocular pollen grains. Gotoh *et al.*[12] conducted a study on the ratio of intranasal to intraocular pollen numbers, which were obtained from healthy volunteers walking in the open air at an ordinary speed for half an hour. Their study showed the almost same result with ours.

In the second part of the study, the concentration of pollen dispersed was increased to 4500 grains/m^3. This concentration is equivalent to the amount of airborne pollen grains during the midterm and late stages of the pollen season. Nasal and ocular symptoms gradually developed in a time dependent manner, but these symptoms were mild.

Okuda *et al.*[13] measured the number of intranasal grains of JC pollinosis patients during pollen seasons over several years. They showed that the average number of JC pollen found in a patient's nose was about 20, although the amount of pollen varies every year. They concluded that 90 to 150 pollen grains were considered to be sufficient to cause symptoms from the dynamic study of pollen in the nose.

In this study, we found that 90 to 500 pollen grains in the nose were not enough to develop nasal symptoms. The only exception was the subject who exited the room in 50 minutes due to sneezing, whose intranasal pollen counted 303. There is a difference in the number of pollen which develops nasal symptoms observed in our study and in the study conducted in a natural environment.[13] The following could be the reason for the difference; subjects in this study were mildly symptomatic patients with JC pollen; subjects had not received repetitive exposure to JC pollen, because the study was conducted 3 months ahead of the pollen season; and subjects were under psychological pressure since they had never experienced an environmental exposure study.

This is the first study to show the intranasal and intraocular pollen grains and allergic symptoms using the OHIO Chamber. As far as pollinosis is concerned, however, our data cannot be immediately generalized since the results depend on the amount of pollen, the priming effects of the nasal mucosa, and the severity of the patients' symptoms. We need to evaluate the results of our data carefully. Therefore, further investigations are required to decide an appropriate amount of pollen and exposure time to obtain reproducible results and to secure the safety of the subjects.

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Increasing the dose of cetirizine may lead to better control of chronic idiopathic urticaria: an open study of 21 patients

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Sir, Chronic idiopathic urticaria (CIU) is characterized by the occurrence of spontaneous pruritic weals on most days. It is common, but often disabling because of persistent clinical symptoms which negatively influence the quality of life. Antihistamines have been the mainstay of treatment and they produce a good response in most patients, but not in all. For those patients who derive only limited benefit from the initial treatment, therapeutic guidelines advocate the use of antihistamines above the licensed or manufacturers' recommended doses.[1,2] However, there is scant evidence regarding the effectiveness of dose increases of the same antihistamine in the patients who responded poorly to the first dosage of the agent.

Cetirizine is a second-generation antihistamine effective in treating patients with CIU.[3] The manufacturer's recommended dosage is 10 mg daily and it is permissible to increase the dose up to 20 mg daily. As cetirizine inhibits histamine-induced weal and flare reactions dose-dependently,[4] it is plausible that higher doses of the drug will be more effective in controlling urticarial symptoms. However, the clinical effect of such dose increases has not been evaluated in patients with CIU. In some previous studies, patients with CIU were initially treated with cetirizine 5 mg, and they were allowed to increase the dose to 10 or 20 mg if no benefit was obtained at the starting dose.[5,6] However, neither urticarial activity at each dose nor clinical effects of the dose increase were assessed in these studies. In the present open study, we evaluated the effect of increasing the dose of cetirizine in order to control the disease activity in patients with CIU, who had derived only limited benefit from 10 mg daily of the same drug.

Patients with CIU (> 1 month duration) were recruited from secondary care hospitals. Patients with physical urticaria, or urticaria caused by medications, foods or other known causes were excluded. Prior to the dose-increasing study, patients were treated with cetirizine 10 mg daily for 1 or 2 weeks as a screening period. Twenty-one patients who responded poorly to the treatment, i.e. the change of the total daily score of urticarial symptoms (see below) was less than 1, during the screening period, were enrolled in the study. Approximately one-third of patients who entered the screening period were eligible. At the beginning of the study, patients were randomly assigned to group A (11 patients) or group B (10 patients), after obtaining informed consent, and all patients were given an increased dose of cetirizine, 20 mg daily (10 mg twice daily), for 1 or 2 weeks (period 1). Thereafter, patients in group A continued the daily dosage of cetirizine 20 mg, whereas the patients in group B received the decreased dosage of 10 mg, for an additional 1 to 2 weeks (period 2). Patients were instructed to record daily urticarial activity scores throughout the study period including the screening period. The urticarial activity was assessed by using the scoring system as previously described.[7] Namely, each of the number of weals, the duration of the weals, and the severity of itch, was scored from 0 to 3. The total daily score of the urticarial symptoms, therefore, ranged from 0 to 9. For the assessment of the clinical effect of increase/decrease in the dosage, the data were analysed by the Friedman test and the Steel–Dwass test.

There were no statistically significant differences between the two groups in age (42·5 ± 14·1 vs. 36·9 ± 16·7 years, mean ± SD, for groups A and B, respectively) or mean urticarial activity scores during the screening period [weal scores 1·09 ± 0·78 vs. 1·11 ± 0·64, itch scores 1·53 ± 0·89 vs.

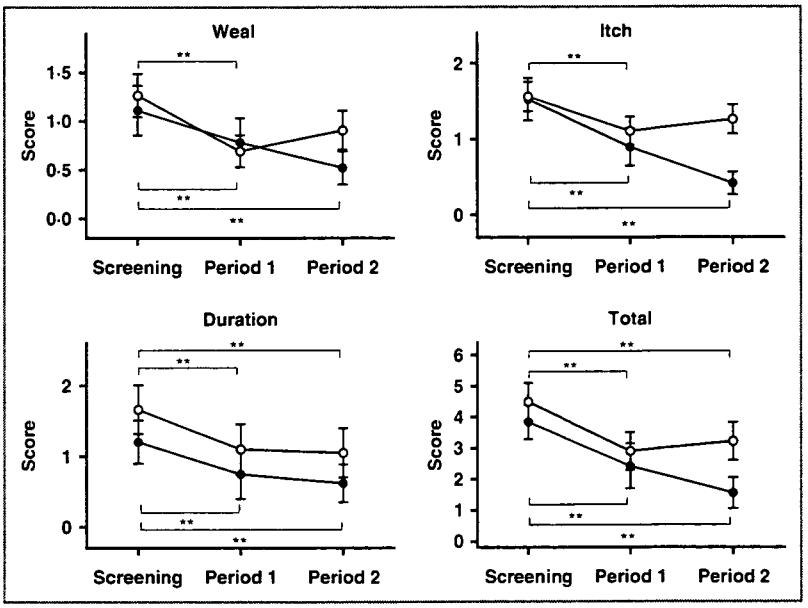

Fig 1. Mean urticarial activity scores during each observation period. Mean urticarial activity scores for weal, itch, duration and total scores for group A (closed circle) and group B (open circle) during each observation period are shown. **$P < 0.01$.

1·56 ± 0·64, duration scores 1·21 ± 0·96 vs. 1·66 ± 1·14 and total scores 3·84 ± 1·76 vs. 4·49 ± 2·02 (Mann–Whitney test)]. All patients had been unsatisfactorily treated with H_1-receptor antagonists, such as loratadine, fexofenadine, olopatadine or hydroxyzine, with or without corticosteroids. The numbers of previously used drugs were also not significantly different (2·90 ± 1·37 vs. 3·09 ± 1·92). These medications were ceased before the screening period in each patient. Two patients in group A had received montelukast 10 mg daily before the study, and they received the same dose of the agent throughout the study. As shown in Figure 1, urticarial activity scores in period 1 were significantly lower than those in the screening period in both groups, indicating the effect of dose increases in controlling the symptoms. In group A, urticarial activity scores improved further in period 2. On the other hand, in group B, urticarial activity scores of weal, itch and total in period 2 were higher than those in period 1 and weal and itch scores in period 2 were not significantly different from those in the screening period.

It is known that urticarial activity is usually higher during the early stages in each patient and tends to remit with time. It is thus possible that spontaneous resolution of the disease may affect the study. However, the exacerbation after the decrease of cetirizine observed in group B indicates that the improvement observed in this study is due to dose increment rather than spontaneous resolution. In addition, our results indicate that the continuation of effective doses of cetirizine may lead to further improvement as shown in group A. Concerning adverse effects, two patients in group B complained of drowsiness in period 1, but their complaints disappeared after the decrease of dosage of cetirizine in period 2. Otherwise adverse effects were not observed throughout the study period in all subjects. Although the observation periods of 1–2 weeks could be short for evaluating this fluctuating disease and we could not deny the possible involvement of placebo effect in this study, our results indicate the clinical usefulness of a dose increase of cetirizine.

In conclusion, our results support the clinical impressions[8] that dose increases of antihistamines may lead to better control of urticarial activity in patients who have not responded well to initial doses of the same drug, and that the continuation of the effective dose leads to further improvement of the disease severity. For more robust evidence, a longer double-blinded study is indicated and other H_1 antagonists should be studied in a similar fashion.

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Circumscribed palmar hypokeratosis: partial remission by photodynamic therapy

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SIR, A 73-year-old man presented a solitary, well-circumscribed erythematous lesion located on the thenar region of his right palm. The lesion had developed at the site of a previous minor injury and had slowly increased for the last 2·5 years (Fig. 1a). The lesion felt fragile and delicate by the patient. Topical treatment with corticosteroids was of no benefit. Past medical history and physical examination were unremarkable.

Skin biopsy taken from the edge of the lesion showed a moderately depressed epidermis of the affected area due to a sharp difference between the thickness of the cornified layer of involved and uninvolved skin. The affected area displayed slight parakeratosis, discrete acanthosis with hypogranulosis and a sparse dermal lymphocytic infiltrate. No cornoid lamellation was found in serial sections. Immunohistochemical staining showed an accumulation of the tumour suppressor gene p53 as well as the cell proliferation marker MIB-1 in involved skin. Based on these findings, the diagnosis of circumscribed palmar hypokeratosis was established.

Because of the increased expression of p53 and MIB-1 in the altered keratinocytes of the involved skin, treatment with 5-aminolaevulinic acid-mediated photodynamic therapy (PDT) was initiated. After a 5-h incubation with 20% 5-aminolaevulinic acid covered by a plastic foil to allow better penetration,