

Clinical Evaluation of Lumiward Immunoassay System for Detection of Specific IgE Associated with Allergic Rhinitis

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The detection of specific IgE is a critical prerequisite for both the definitive diagnosis and the therapeutic strategy of allergic rhinitis and other allergic disorders. The aim of the present study was thus to evaluate the clinical significance of the solid phase capture system (CAP) and the lumiward immunoassay system (LMD) in the diagnosis of allergic rhinitis due to *Dermatophagoides farinae* (*D. farinae*) and Japanese cedar (*Cryptomeria japonica*) pollens. The specificity of both the CAP and the LMD in the detection of *D. farinae*-specific IgE and Japanese cedar pollen-specific IgE was 100%. The sensitivity to detect *D. farinae*-specific IgE was 95.76% in the skin test, 86.53% in the CAP and 88.53% in the LMD, respectively. The combination of the nasal provocation test and the CAP substituted for the skin test resulted in correct diagnoses for 98.25% of the patients, and the combination of the nasal provocation test and the LMD substituted for the skin test resulted in correct diagnoses for 98.00% of the patients. Therefore, the diagnostic significance of the LMD for perennial allergic rhinitis is likely to be equal to that of the CAP. The sensitivity to detect Japanese cedar pollen-specific IgE was 94.50% in the skin test, 84.47% in the CAP, and 96.76% in the LMD, respectively. The sensitivity of the CAP in the detection of Japanese cedar pollen-specific IgE was inferior to that of the skin test, but the sensitivity of the LMD in the detection of pollen-specific IgE was somewhat superior to that of the skin test. In addition, the combination of the nasal provocation test and the CAP substituted for the skin test resulted in correct diagnoses for 98.38% of the patients, whereas the combination of the nasal provocation test and the LMD substituted for the skin test resulted in correct diagnoses for 100% of the patients. Therefore, the diagnostic significance of the LMD for seasonal allergic rhinitis due to Japanese cedar pollens is probably larger than that of the CAP. In conclusion, the LMD may be a better “gold standard” for the detection of Japanese cedar pollen-specific IgE than the skin test, and the combination of the nasal provocation test and the LMD is a better diagnostic tool for the detection of Japanese cedar pollen-induced seasonal allergic rhinitis than the combination of the nasal provocation test and the skin test or the CAP. **Key words:** allergic rhinitis, *Dermatophagoides farinae*, Japanese cedar pollen, lumiward immunoassay system, solid phase capture system, specific IgE.

INTRODUCTION

The detection of specific IgE is a critical prerequisite for both the definitive diagnosis and the therapeutic strategy of allergic rhinitis and other allergic disorders. To date, several diagnostic methods have been available for the detection of specific IgE to relevant allergens. Skin-prick testing (SPT) and nasal provocation testing remain the first-choice diagnostic methods in the detection of specific IgE in allergic rhinitis, if they are performed correctly. However, skin testing has several drawbacks, including the difficulty of evaluating many kinds of allergens at once and the possibility of systemic adverse reactions (1–3). In addition, it might be difficult to perform SPT correctly in some circumstances (e.g. interfering medication and non-compliant patients). In 1968, Wide et al. (4) introduced an *in vitro* method for the detection of specific IgE in serum, the radioallergosorbent test (RAST), where the allergen is bound to a particle and subsequently reacted with allergic serum and radiolabelled anti-IgE. The RAST offers some advantages over conventional skin tests, but the *in vitro* test has several drawbacks. The sensitivity and specificity of

the RAST is less than in SPT or nasal provocation tests (5–7), and it costs more than SPT. An additional disadvantage of the RAST is the several-day delay in obtaining results, whereas the results are immediately available with SPT. In addition, the RAST cannot test for specific IgE located exclusively in the nasal mucosa (8), because it is an *in vitro* test to determine specific IgE in serum.

Various great efforts have been made to improve on the RAST, and several modified methods have been introduced (9–12). In particular, the solid phase capture system (CAP) can bind up to three times more antibodies than the corresponding paper disc and increase the sensitivity of detection of specific IgE. The CAP may have replaced the RAST as the most prevalent *in vitro* test for detection of specific IgE.

Sanofi Diagnostics Pasteur has recently developed the lumiward immunoassay system (LMD) based on paramagnetic particles, haptenated liquid allergen and a chemiluminescent detection technology. The technology has been applied to a variety of different allergens and is expected to yield excellent results in terms of sensitivity and specificity. The LMD is cali-

brated to the WHO international reference for IgE, with an international unit (IU) corresponding to 2.4 ng.

The aim of the present study was to evaluate the clinical significance of the LMD in the diagnosis of allergic rhinitis, especially in comparison to the CAP. The most important allergens associated with allergic rhinitis in Japan are *Dermatophagoides farinae* (*D. farinae*) and Japanese cedar (*Cryptomeria japonica*) pollens. The former is the most important allergen associated with perennial allergic rhinitis in many countries as well as in Japan, and the latter is the most important seasonal allergen associated with seasonal allergic rhinitis during the early spring in Japan. Thus, our study focused on the detection of *D. farinae*-specific IgE and Japanese cedar pollen-specific IgE.

MATERIALS AND METHODS

Detection of D. farinae-specific IgE

Subjects. Fifty-three patients without perennial allergic rhinitis (non-perennial rhinitis group) and 401 patients with perennial allergic rhinitis due to *D. farinae* (perennial rhinitis group) were enrolled in the study. All 50 patients in the control group had seasonal allergic rhinitis due to Japanese cedar pollens. They were chosen on the basis of the following criteria: *i*) no symptomatic episodes of perennial allergic rhinitis, *ii*) a well-documented history of typical seasonal allergic rhinitis during the cedar pollen season, *iii*) no physical findings indicative of perennial allergic rhinitis, *iv*) negative skin test reaction to *D. farinae*, *v*) negative nasal provocation reaction to *D. farinae*, *vi*) positive skin test reaction to cedar pollen extracts and *vii*) positive nasal provocation reaction to cedar pollen extracts. All 401 patients with perennial allergic rhinitis satisfied the following criteria: they had both a well-documented history of typical perennial allergic rhinitis, and they fulfilled the criteria for Okuda's diagnosis (positive skin test result and/or positive provocation test result) for perennial allergic rhinitis (13).

Study design. This study design followed the principles outlined in the Declaration of Helsinki (14). All patients in the perennial rhinitis group were examined via skin and nasal provocation tests for sensitivity to *D. farinae*. Skin tests were performed with an intracutaneous injection of *D. farinae* (6 allergen units [AU], Miles Inc., Spokane, WA, USA), and the results were evaluated using Okuda's criteria (13). Nasal provocations were performed using our disk method, and the results were also evaluated according to Okuda's criteria (13).

Venous blood was collected from each patient, and all the serum samples were separated and stored at -80°C until determination of serum concentrations of *D. farinae*-specific IgE. *D. farinae*-specific IgE in each sample was simultaneously determined with both the CAP and the LMD.

Detection of Japanese cedar pollen-specific IgE

Subjects. Fifty individuals without seasonal allergic rhinitis and 309 patients with seasonal allergic rhinitis due to Japanese cedar pollens were enrolled in the study. The 50 individuals without seasonal allergic rhinitis (non-pollinosis group) were chosen on the basis of the following criteria: *i*) no symptomatic episodes of seasonal allergic rhinitis during the cedar pollen season, *ii*) no physical findings indicative of seasonal allergic rhinitis during the cedar pollen season, *iii*) negative skin test reaction to cedar pollen extracts and *iv*) negative nasal provocation reaction to cedar pollen extracts. All 309 patients with seasonal allergic rhinitis due to cedar pollen (pollinosis group) satisfied the following criteria: they had both a well-documented history of typical seasonal allergic rhinitis during the cedar pollen season, and they fulfilled the criteria for Okuda's diagnosis (positive skin test result and/or positive provocation test result) for seasonal allergic rhinitis due to cedar pollen (13).

Study design. The study design followed the principles outlined in the Declaration of Helsinki (14). All the patients in the pollinosis group were examined via skin and nasal provocation tests for sensitivity to cedar pollen extracts. Skin tests were performed with an intracutaneous injection of pollen extracts (0.02 ml of 1:10,000 wt/vol, Torii Co., Ltd., Tokyo, Japan), and the results were evaluated according to Okuda's criteria (13). Nasal provocations were performed using our disk method, and the results were also evaluated according to Okuda's criteria (13). Venous blood was collected from each patient, and all serum samples were separated and stored at -80°C until determination of serum concentrations of Japanese cedar pollen-specific IgE. Japanese cedar pollen-specific IgE in each sample was simultaneously determined with both the CAP and the LMD.

Statistical analysis. The lowest detectable levels were 0.34 U/ml for the CAP and 0.06 IU/ml for the LMD, respectively. If the level was below the sensitivity of the respective assay, 0.0 U/ml for the CAP and 0.0 IU/ml for the LMD were arbitrarily used for the statistical analysis, respectively. For comparisons of paired values within a group, Wilcoxon's signed-rank test was used. Differences were considered significant when $p < 0.05$. Spearman's correlation coefficient (r_s) was calculated to determine the degree

of correlation between parameters, and significant correlation was accepted when $p < 0.05$ on Spearman's rank correlation analysis.

RESULTS

Detection of *D. farinae*-specific IgE

Non-perennial rhinitis group. The serum concentration of *D. farinae*-specific IgE determined with the CAP was below the sensitivity level of the assay in each individual. Similarly, the serum concentration of *D. farinae*-specific IgE determined with the LMD was below the sensitivity level of the assay in each individual.

Perennial rhinitis group. Statistical analysis for 401 patients. Skin and nasal provocation tests were positive in 384 (95.76%) patients and 348 (86.78%) patients, respectively. However, skin and nasal provocation tests were negative in 17 (4.24%) patients and 53 (13.22%) patients, respectively.

Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the CAP in 347 (86.53%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the CAP in the remaining 54 patients (13.47%) because the values were beneath the lower limit of the CAP. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the LMD in 355 (88.53%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the LMD in the remaining 46 patients (11.47%) because the values were beneath the lower limit of the LMD.

The serum concentrations (mean $\pm$ SD) of *D. farinae*-specific IgE determined with the CAP and the LMD were 26.36 ± 31.95 U/ml and 25.79 ± 33.85 IU/ml, respectively. The levels of *D. farinae*-specific IgE determined with the LMD were significantly lower than those determined with the CAP ($p < 0.0001$, Fig. 1). The concentrations of *D. farinae*-specific IgE determined with the CAP were significantly correlated with the concentrations determined with the LMD ($r_s = 0.980$, $p < 0.0001$, Fig. 2).

Statistical analysis for 384 patients with positive skin test results. Nasal provocation tests were positive in 331 (86.20%) patients and negative in the remaining 53 (13.80%) patients. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the CAP in 342 (89.06%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the CAP in the remaining 42 patients (10.94%) because the values were beneath the lower limit of the CAP. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the LMD in 347 (90.36%) patients,

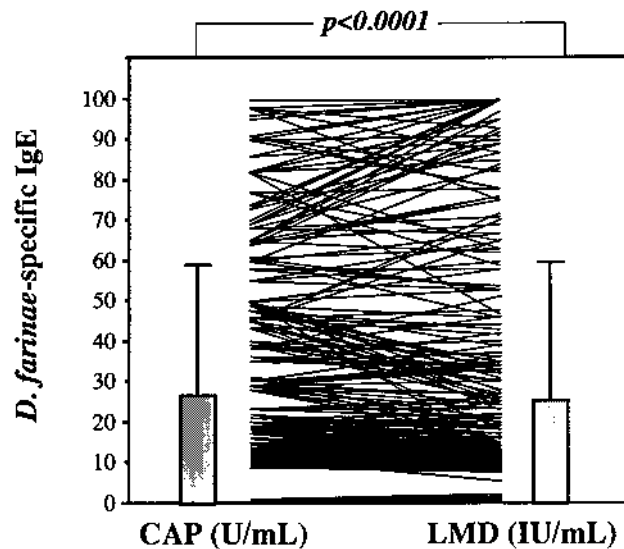


Fig. 1. Comparison between the levels of *D. farinae*-specific IgE determined by the CAP and those by the LMD in the 401 patients in the rhinitis group. The levels of *D. farinae*-specific IgE determined by the LMD were significantly lower than those determined by the CAP.

but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the LMD in the remaining 37 patients (9.64%) because the values were beneath the lower limit of the LMD.

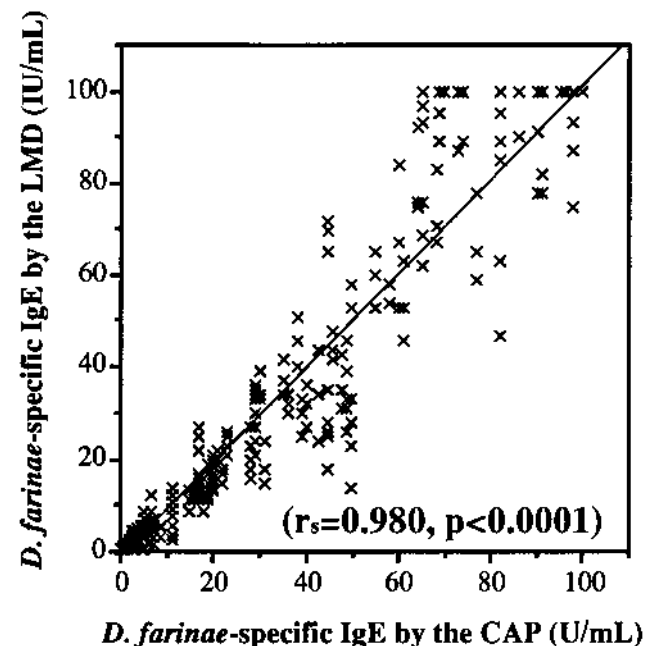


Fig. 2. Correlation between the levels of *D. farinae*-specific IgE determined by the CAP and those determined by the LMD in the 401 patients in the rhinitis group. The levels of *D. farinae*-specific IgE determined by the LMD correlated significantly with those determined by the CAP.

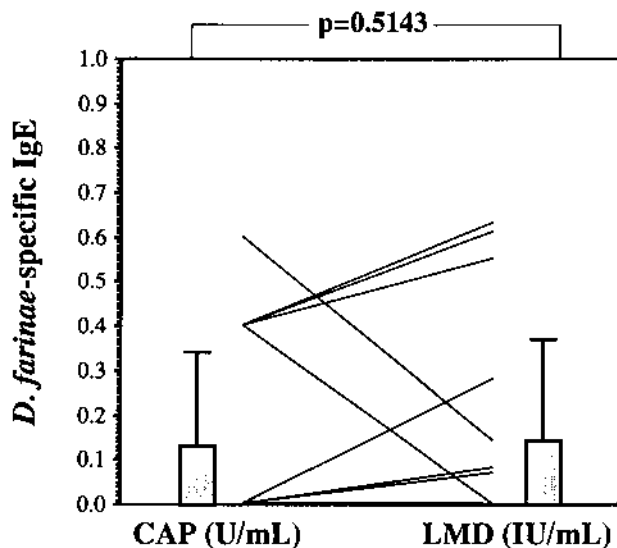


Fig. 3. Comparison between the levels of *D. farinae*-specific IgE determined by the CAP and those determined by the LMD in the 17 patients with negative skin test results in the rhinitis group. The levels of *D. farinae*-specific IgE determined by the LMD were not significantly different from those determined by the CAP.

The serum concentrations of *D. farinae*-specific IgE determined with the CAP and the LMD were 27.52 ± 32.15 U/ml and 26.93 ± 34.15 IU/ml, respectively. The levels of *D. farinae*-specific IgE determined with the LMD were significantly lower than those determined with the CAP ($p < 0.0001$). The concentrations of *D. farinae*-specific IgE determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.980$, $p < 0.0001$).

Statistical analysis for 17 patients with negative skin test results. Nasal provocation tests were positive in all patients. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the CAP in 5 (29.41%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the CAP in the remaining 12 patients (70.59%) because the values were beneath the lower limit of the CAP. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the LMD in 8 (47.06%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the LMD in the remaining 9 patients (52.94%) because the values were beneath the lower limit of the LMD. The serum concentrations of *D. farinae*-specific IgE determined with the CAP and the LMD were 0.13 ± 0.21 U/ml and 0.14 ± 0.23 IU/ml, respectively. The levels determined with the LMD were not significantly different from those determined with the CAP ($p = 0.5143$, Fig. 3). The concentrations

determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.962$, $p = 0.0178$).

Statistical analysis for 348 patients with positive provocation test results. Skin tests were positive in 331 (95.11%) patients and negative in the remaining 17 (4.89%). Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the CAP in 301 (86.49%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the CAP in the remaining 47 patients (13.51%) because the values were beneath the lower limit of the CAP. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the LMD in 310 (89.08%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the LMD in the remaining 38 patients (10.92%) because the values were beneath the lower limit of the LMD.

The serum concentrations of *D. farinae*-specific IgE determined with the CAP and the LMD were 26.43 ± 31.37 U/ml and 25.71 ± 33.33 IU/ml, respectively. The levels determined with the LMD were significantly lower than those determined with the CAP ($p = 0.0002$). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.980$, $p < 0.0001$).

Statistical analysis for 53 patients with negative provocation test results. Skin tests were positive in every patient. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the CAP in 46 (86.79%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the CAP in the remaining 7 patients (13.21%) because the values were beneath the lower limit of the CAP. Serum concentrations of *D. farinae*-specific IgE were quantitatively determined with the LMD in 45 (84.91%) patients, but the concentrations of *D. farinae*-specific IgE were not quantitatively determined with the LMD in the remaining 8 patients (15.09%) because the values were beneath the lower limit of the LMD.

The serum concentrations of *D. farinae*-specific IgE determined with the CAP and the LMD were 25.89 ± 35.81 U/ml and 26.32 ± 37.40 IU/ml, respectively. The levels determined with the LMD were not significantly different from those determined with the CAP ($p = 0.1503$). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.961$, $p < 0.0001$, Fig. 4).

Rate of correct diagnosis by combination of CAP and provocation test. The combination of the CAP and the nasal provocation test substituted for the

combination of the skin test and the nasal provocation test resulted in correct diagnoses for the 394 patients (98.25%) of the perennial rhinitis group. However, the combination of the CAP and the nasal provocation test failed to result in correct diagnoses for the remaining 7 patients (1.75%) of the perennial rhinitis group.

Rate of correct diagnosis by combination of LMD and provocation test. The combination of the LMD and the nasal provocation test substituted for the combination of the skin test and the nasal provocation test resulted in correct diagnoses for the 393 (98.00%) patients of the perennial rhinitis group. However, the combination of the LMD and the nasal provocation test failed to make a correct diagnosis for the remaining 8 (2.00%) of the perennial rhinitis group.

Detection of Japanese cedar pollen-specific IgE

Non-pollinosis group. The serum concentration of Japanese cedar pollen-specific IgE determined with the CAP was below the sensitivity level of the assay in each individual. Similarly, the serum concentration of pollen-specific IgE determined with the LMD was below the sensitivity level of the assay in each individual.

Pollinosis group. Statistical analysis for 309 patients. Skin tests and nasal provocation tests were

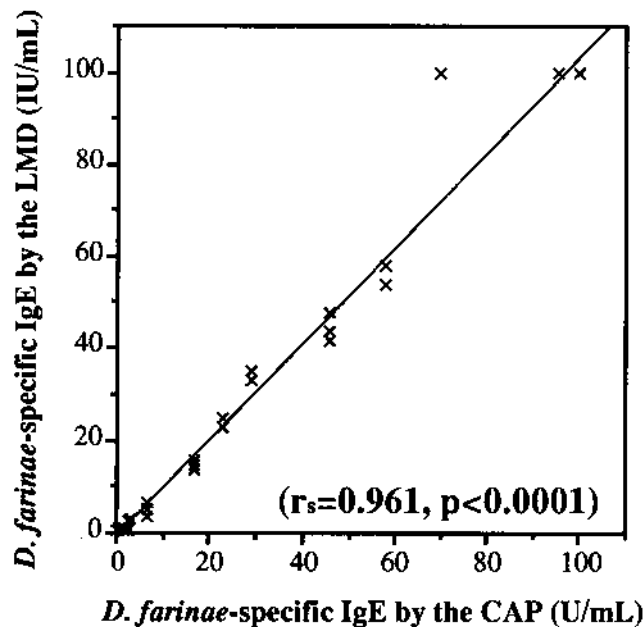


Fig. 4. Correlation between the levels of *D. farinae*-specific IgE determined by the CAP and those determined by the LMD in the 53 patients with negative provocation test results in the rhinitis group. The levels of *D. farinae*-specific IgE determined by the LMD correlated significantly with those determined by the CAP.

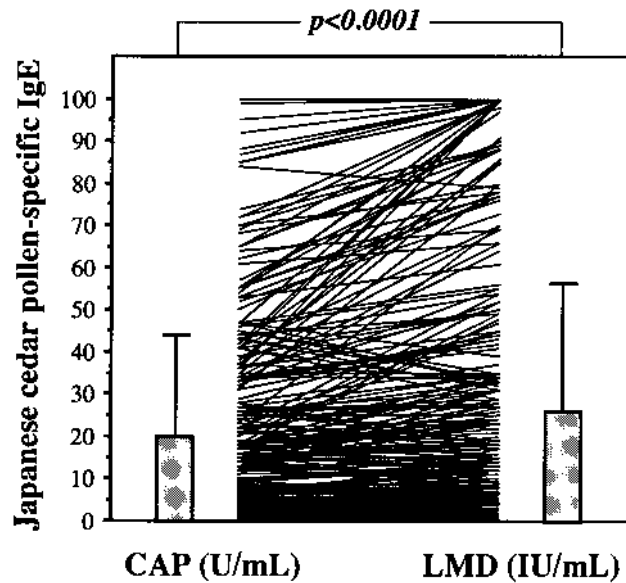


Fig. 5. Comparison between the levels of Japanese cedar pollen-specific IgE determined by the CAP and those determined by the LMD in the 309 patients in the pollinosis group. The levels of Japanese cedar pollen-specific IgE determined by the LMD were significantly higher than those determined by the CAP.

positive in 292 (94.50%) patients and 249 (80.58%) patients, respectively. On the other hand, skin tests and nasal provocation tests were negative in 17 (5.50%) patients and 60 (19.42%) patients, respectively.

Serum concentrations of pollen-specific IgE were quantitatively determined with the CAP in 261 (84.47%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the CAP in the remaining 48 patients (15.53%) because the values were beneath the lower limit of the CAP. Serum concentrations of pollen-specific IgE were quantitatively determined with the LMD in 299 (96.76%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the LMD in the remaining 10 patients (3.24%) because the values were beneath the lower limit of the LMD.

The serum concentrations (mean $\pm$ SD) of pollen-specific IgE determined with the CAP and the LMD were 19.55 ± 23.37 U/ml and 25.50 ± 30.61 IU/ml, respectively. The levels determined with the LMD were significantly higher than those determined with the CAP ($p < 0.0001$, Fig. 5). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.965$, $p < 0.0001$, Fig. 6).

Statistical analysis for 292 patients with positive skin test results. Nasal provocation tests were positive in

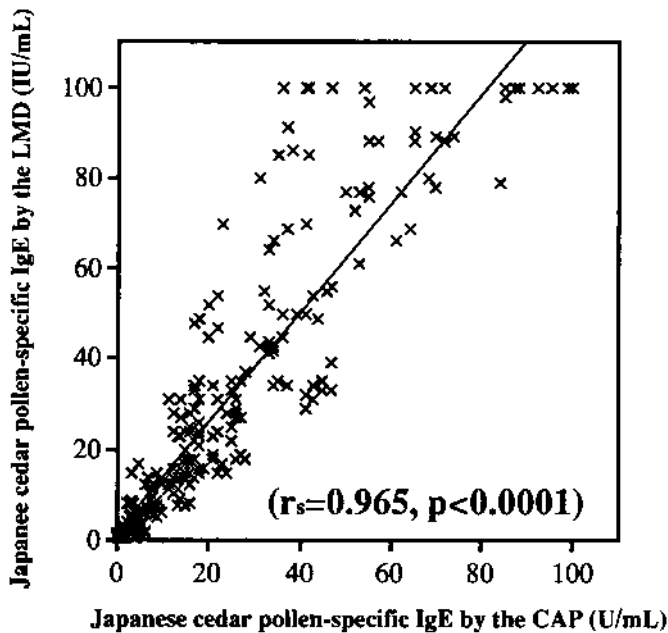


Fig. 6. Correlation between the levels of Japanese cedar pollen-specific IgE determined by the CAP and those determined by the LMD in the 309 patients in the pollinosis group. The levels of Japanese cedar pollen-specific IgE determined by the LMD correlated significantly with those determined by the CAP.

232 (79.45%) patients and negative in the remaining 60 (20.55%). Serum concentrations of pollen-specific IgE were quantitatively determined with the CAP in 249 (85.27%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the CAP in the remaining 43 patients (14.73%) because the values were beneath the lower limit of the CAP. Serum concentrations of pollen-specific IgE were quantitatively determined with the LMD in 282 (96.58%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the LMD in the remaining 10 patients (3.42%) because the values were beneath the lower limit of the LMD.

The serum concentrations of pollen-specific IgE determined with the CAP and the LMD were 20.14 ± 23.70 U/ml and 26.17 ± 30.88 IU/ml, respectively. The levels determined with the LMD were significantly higher than those determined with the CAP ($p < 0.0001$). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.965$, $p < 0.0001$).

Statistical analysis for 17 patients with negative skin test results. Nasal provocation tests were positive in every patient. Serum concentrations of pollen-specific IgE were quantitatively determined with the CAP in 12 (70.59%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the CAP in the remaining 5 patients (29.41%) because the values were beneath the lower limit of the CAP. By contrast, serum concentrations of pollen-specific IgE were quantitatively determined with the LMD in all patients.

The serum concentrations of pollen-specific IgE determined with the CAP and the LMD were 9.47 ± 13.81 U/ml and 14.00 ± 23.31 IU/ml, respectively. The levels determined with the LMD were significantly higher than those determined with the CAP ($p = 0.0216$). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.963$, $p = 0.0001$, Fig. 7).

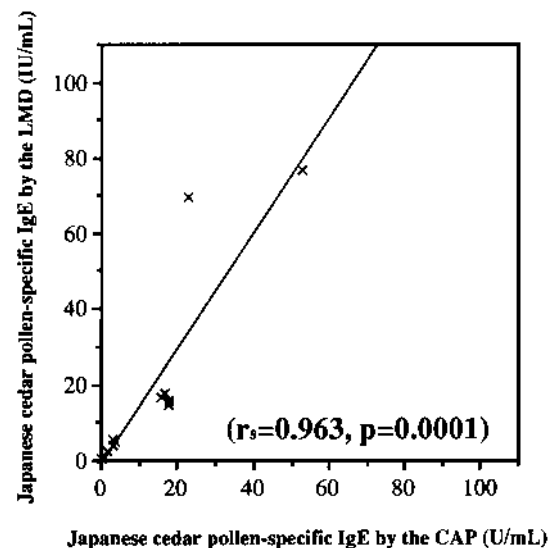


Fig. 7. Correlation between the levels of Japanese cedar pollen-specific IgE determined by the CAP and those determined by the LMD in the 17 patients with negative skin test results in the pollinosis group. The levels of Japanese cedar pollen-specific IgE determined by the LMD correlated significantly with those determined by the CAP.

Statistical analysis for 249 patients with positive provocation test results. Skin tests were positive in 232 (93.17%) patients and negative in the remaining 17 (6.83%). Serum concentrations of pollen-specific IgE were quantitatively determined with the CAP in 206 (82.73%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the CAP in the remaining 43 patients (17.27%) because the values were beneath the lower limit of the CAP. Serum concentrations of pollen-specific IgE were quantitatively determined with the LMD in 239 (95.98%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the LMD in the remaining 10 patients (4.02%) because the values were beneath the lower limit of the LMD.

The serum concentrations of pollen-specific IgE determined with the CAP and the LMD were 19.72 ± 24.40 U/ml and 25.91 ± 31.75 IU/ml, respectively. The levels determined with the LMD were significantly higher than those determined with the CAP ($p < 0.0001$). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.976$, $p < 0.0001$).

Statistical analysis for 60 patients with negative provocation test results. Skin tests were positive in every patient. Serum concentrations of pollen-specific IgE were quantitatively determined with the CAP in 55 (91.67%) patients, but the concentrations of pollen-specific IgE were not quantitatively determined with the CAP in the remaining 5 patients (8.33%) because the values were beneath the lower limit of the CAP. By contrast, serum concentrations of pollen-specific IgE were quantitatively determined with the LMD in all patients.

The serum concentrations of pollen-specific IgE determined with the CAP and the LMD were 18.83 ± 18.65 U/ml and 23.80 ± 25.48 IU/ml, respectively. The levels determined with the LMD were significantly higher than those determined with the CAP ($p = 0.0025$, Fig. 8). The concentrations determined with the CAP correlated significantly with the concentrations determined with the LMD ($r_s = 0.932$, $p < 0.0001$, Fig. 9).

Rate of correct diagnosis by combination of CAP and provocation test. The combination of the CAP and the nasal provocation test substituted for the combination of the skin test and the nasal provocation test resulted in correct diagnoses for the 304 patients (98.38%) of the pollinosis group. However, the combination of the CAP and the nasal provocation test failed to result in correct diagnoses for the remaining 5 patients (1.62%) of the pollinosis group.

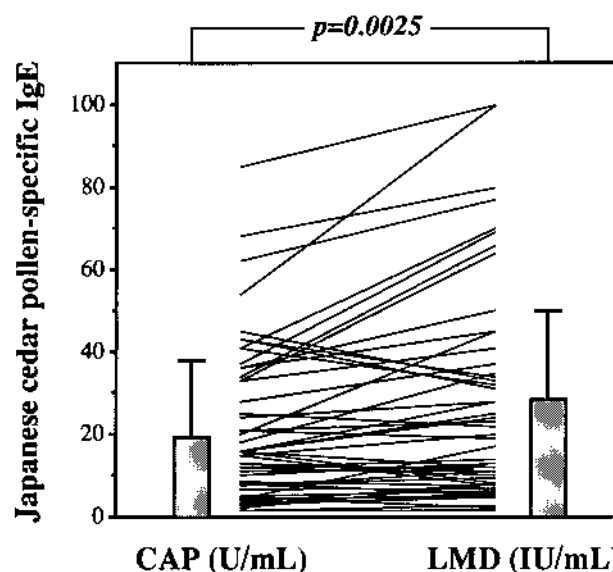


Fig. 8. Comparison between the levels of Japanese cedar pollen-specific IgE determined by the CAP and those determined by the LMD in the 60 patients with negative provocation test results in the pollinosis group. The levels of Japanese cedar pollen-specific IgE determined by the LMD were significantly higher than those determined by the CAP.

Rate of correct diagnosis by combination of LMD and provocation test. The combination of the LMD and the nasal provocation test substituted for the combination of the skin test and the nasal provocation test resulted in correct diagnoses for all patients of the pollinosis group.

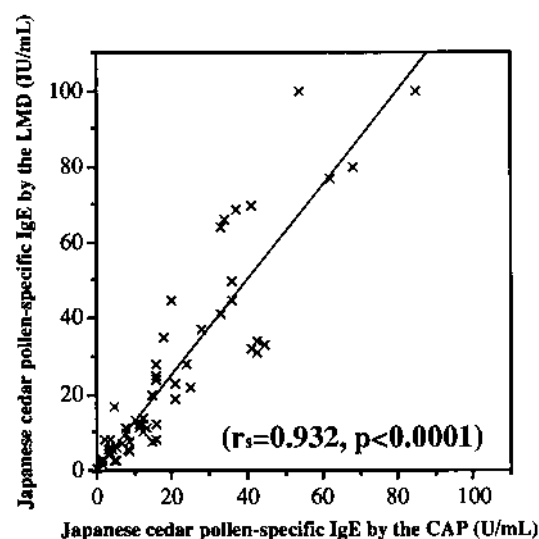


Fig. 9. Correlation between the levels of Japanese cedar pollen-specific IgE determined by the CAP and those determined by the LMD in the 60 patients with negative provocation test results in the pollinosis group. The levels of Japanese cedar pollen-specific IgE determined by the LMD correlated significantly with those determined by the CAP.

DISCUSSION

The CAP is the most widely utilized methodology in testing for specific IgE. While its specificity is excellent, its sensitivity is relatively lower when compared with SPT (15–17). The new *in vitro* assay for specific IgE, the LMD (chemiluminescent enzyme immunoassay), has recently (since 1996) been introduced in the clinical practice of allergic rhinitis in Japan. The sensitivity and specificity of the CAP and the LMD were compared in 406 patients with various atopic diseases due to a variety of allergens, and the LMD was superior to the CAP on both parameters (18).

Since the most relevant allergens in allergic rhinitis are *D. farinae* and Japanese cedar pollen in Japan, our present study focused on the diagnostic usefulness of the CAP and the LMD in the detection of *D. farinae*-specific and Japanese cedar pollen-specific IgE. The specificity of both the CAP and the LMD in the detection of *D. farinae*-specific IgE and Japanese cedar pollen-specific IgE was 100%. The specificity of both methods in our study was considerably better than that in previous studies (7, 18). Our strict selection of the subjects is likely to be the major reason for this high specificity.

The sensitivity to detect *D. farinae*-specific IgE was 95.76% in the skin test, 86.53% in the CAP and 88.53% in the LMD, respectively. Thus, the highest sensitivity was observed in the skin test, and the CAP and the LMD were inferior to the skin test in their sensitivity to detect *D. farinae*-specific IgE, a result in agreement with previous reports (15–18). A total of 17 patients with perennial allergic rhinitis associated with *D. farinae* demonstrated negative results to the skin test. Five and eight of them demonstrated positive results to the CAP and the LMD, respectively. In addition, the combination of the nasal provocation test and the CAP substituted for the skin test resulted in correct diagnoses for 98.25% of the patients, whereas the combination of the nasal provocation test and the LMD substituted for the skin test resulted in correct diagnoses for 98.00% of the patients. Therefore, the diagnostic significance of the LMD is likely to be equal to that of the CAP.

Similarly, the sensitivity to detect Japanese cedar pollen-specific IgE was 94.50% in the skin test, 84.47% in the CAP and 96.76% in the LMD, respectively. The sensitivity of the CAP in the detection of Japanese cedar pollen-specific IgE was inferior to that of the skin test, a result also in line with previous studies (7, 10, 18, 19). By contrast, the sensitivity of the LMD in the detection of pollen-specific IgE was somewhat superior to that of the skin test. The skin test has been considered the “gold standard” for the

detection of specific IgE, but our data demonstrate that the LMD might be a better standard. In addition, the combination of the nasal provocation test and the CAP substituted for the skin test resulted in correct diagnoses for 98.38% of the patients, whereas the combination of the nasal provocation test and the LMD substituted for the skin test resulted in correct diagnoses for 100% of the patients. Therefore, the diagnostic significance of the LMD is probably larger than that of the CAP.

In conclusion, our study has demonstrated that the LMD is not inferior to the CAP in diagnostic significance of perennial allergic rhinitis due to *D. farinae*, that the LMD may be a better “gold standard” for the detection of Japanese cedar pollen-specific IgE than the skin test, and that the combination of the nasal provocation test and the LMD is a better diagnostic tool for the detection of Japanese cedar pollen-induced seasonal allergic rhinitis than the combination of the nasal provocation test and the skin test or the CAP.

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