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Airway responsiveness to allergen is increased 24 hours after exercise challenge

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Although exercise is one of the most ubiquitous triggers of acute bouts of asthma, the changes in airway responsiveness before and after exercise are not well defined. Specifically, the effect of the changes in airway responsiveness induced by exercise has not been studied on subsequent allergen exposure. To test whether the reactivity to allergen is altered by preceding exercise and to define possible factors determining it, we subjected 24 children with atopic asthma to the relevant allergen challenge on two occasions: one as a control without a preceding procedure and the other 24 hours after exercise challenge. Mean postallergen maximal percent falls in forced expiratory volume in 1 second from baseline (ΔFEV_1) of the whole group were higher after the exercise challenge compared with those of control in both early (<1 hour) and late (3 to 10 hours) phases. The changes of postallergen maximal ΔFEV_1 between the control and post-exercise allergen challenges were not related to the early bronchial response to the preceding exercise challenge. Late asthmatic responses to exercise developed in six children, and the changes in both early and late phases were significantly higher in these children, compared with those without late asthmatic responses. Furthermore, the changes were well correlated with the magnitude of the late-phase response to preceding exercise in the group as a whole. It is concluded that an increased airway responsiveness to allergen occurs 24 hours after exercise in some patients with asthma. As the changes are related to a late bronchial response to exercise, late asthmatic response to exercise, when it occurs, may be associated with increased asthmatic symptoms for as long as 24 hours after exercise. (J ALLERGY CLIN IMMUNOL 1994;94:507-16.)

Key words: *airway responsiveness, exercise challenge, allergen challenge*

Several investigators have observed that natural seasonal exposure to allergens may increase airway responsiveness (AR).[1, 2] This increase in AR has been demonstrated also in the laboratory.[3-5] After the inhalation of relevant allergens by subjects with atopic asthma, bronchial hyperreactivity may be induced and may persist for days or even weeks.[6] The increased AR is closely associated with both the appearance and the magnitude of the late asthmatic response (LAR),[3, 7] which occurs between 3 and 8 hours after the initial contact with the allergen in the majority of sensitized subjects.[8]

In the last decade it has been suggested that exercise also produces phasic changes in lung function. LARs have been described as occurring after strenuous exercise in several studies,[9-12] although the prevalence is variable and some con-

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Abbreviations used
AC: Allergen challenge
AR: Airway responsiveness
EC: Exercise challenge
FEV_1: Forced expiratory volume in 1 second
ΔFEV_1: Percent fall in FEV_1 from baseline
LAR: Late asthmatic response
EAR: Early asthmatic response

troversies as to their specificity remain.[13-15] However, the increases in AR that usually follow the LAR as observed in allergen challenge (AC) do not uniformly apply to exercise challenge (EC). Thus some authors have reported an increase in AR after exercise,[10, 16] while others have found no significant changes of AR even after LAR to exercise.[11, 17, 18]

Increased AR induced by allergen is associated with increased symptoms of asthma and an increased need for treatment.[19] Recurrent nocturnal asthma also has been described after a severe LAR, which was associated with increased AR.[20] These phenomena led to a postulate that a vicious cycle may be established when allergen induces airway hyperresponsiveness, which, in turn, causes an increased response to subsequent exposure to allergen or bronchospastic triggering factors, such as exercise, cold air, smoke, and dust.[21] In this regard, the enhancing effect of allergen inhalation on the exercise-provoked asthmatic response has been reported.[4]

We have frequently seen asthmatic children whose complaint is that their symptoms worsen at night after strenuous daytime exercise. This might be an LAR to exercise or an increased reactivity to the exposed indoor allergen to which they are sensitive, or both. To the best of our knowledge, this hyperreactivity after exercise has not been studied for allergen. We can suppose that if the asthmatic responses to allergen inhalation are enhanced sometime after an EC, it may reflect an increased AR caused by exercise and have a clinical implication. Thus the aims of this study were to determine whether the reactivity to allergen is altered 24 hours after EC and to define possible factors determining it. To accomplish the latter, we tried to correlate exercise-induced changes of postallergen forced expiratory volume in 1 second (FEV_1) in the early (<1 hour) and late (3 to 10 hours) phases with the early or late-phase magnitude of bronchial response to a preceding EC.

METHODS

Patients

Twenty-four children with asthma (15 boys and 9 girls), aged 7.2 to 14.7 years (mean ± SD, 10.8 ± 1.9 years), completed this study (Table I). Initially 30 children with asthma took part in the study, but six were eliminated: three subjects had such severe late phase reactions as to need medications, and three other subjects did not show asthmatic responses to the control AC. All children had atopic asthma and had positive prick test results to house dust mite *(Dermatophagoides pteronyssinus)* and some other common airborne allergens. At the time of study all patients were free of symptoms of acute respiratory infections, and baseline lung functions were 70% of the predicted value or more in every case. Asthma was mild to moderate, stable, and controlled by β_2-agonist on an as-needed basis, added to a theophylline in six subjects and to inhaled beclomethasone in seven subjects. Throughout the study period, all patients had to submit to concomitant medication rules. The patients had to stop using inhaled bronchodilators, or other medications 24 hours, oral theophylline 48 hours, and inhaled steroid 7 days, respectively, before the study days. The parents of the patients gave informed consent for the study, and the protocol was approved by the hospital ethics committee.

Study design

Subjects attended the laboratory on 4 days, divided into two study periods. Each subject arrived at the laboratory at 8 AM. On each day of the study lung function was measured with a computerized spirometer (Microspiro-HI 298, Chest, Tokyo, Japan) after a rest of 30 minutes, and the study was continued only if the baseline forced expiratory volume in 1 second (FEV_1) before each test was at least 70% of the predicted value.[22] The largest value of the triplicate FEV_1 at each time was used for analysis. During the whole day, subjects stayed in the laboratory and did not take any medication or caffeine.

The first (control) period was used to examine the diurnal pattern of the FEV_1 changes at hourly intervals for 10 hours on the first day, and to document the airway response to AC (control) on the second day. Only the subjects with a definite early (<1 hour) or late (3 to 10 hours) asthmatic response to allergen ($\Delta FEV_1 \geq 20\%$ from baseline) continued to the second period of study.

In the second period, at least 2 months after the first period, an exercise test was performed on the first day. FEV_1 was measured at graduated intervals, 3 to 10 minutes apart, until 60 minutes after exercise, and then hourly up to 10 hours. The subjects were asked to return the next morning, and, 24 hours after the exercise, the second (post-exercise) AC was performed.

Allergen challenge test

Allergen challenge tests were performed with a simple modification of the method described by Chai et al.[23]

TABLE I. Results of exercise and allergen challenge tests

Subject No.	Sex	Age (yr) (mo)	Exercise challenge Baseline FEV_1	Exercise challenge Early phase*	Exercise challenge Late phase†	Control allergen challenge Baseline FEV_1	Control allergen challenge Early phase‡	Control allergen challenge Late phase†	Postexercise allergen challenge Baseline FEV_1	Postexercise allergen challenge Early phase‡	Postexercise allergen challenge Late phase†
1	M	10 3/12	1640§ (84.8)‖	51¶	97¶	1620§ (83.8)‖	72¶	71¶	1640§ (84.8)‖	69¶	62¶
2	M	9 7/12	1560 (87.5)	67	88	1580 (88.7)	75	68	1550 (87.0)	66	60
3	F	11 6/12	1600 (82.3)	80	90	1580 (81.2)	81	74	1600 (82.3)	69	69
4	M	11 3/12	1760 (81.2)	63	97	1760 (81.2)	80	64	1780 (82.2)	88	63
5	F	14 8/12	2680 (105.2)	62	95	2680 (105.2)	73	75	2660 (104.4)	84	70
6	F	7 2/12	1080 (95.3)	83	97	1060 (93.5)	94	69	1100 (97.0)	87	73
7	M	10	1600 (85.3)	92	90	1610 (85.9)	59	70	1580 (84.3)	53	57
8	F	13 9/12	1800 (76.0)	84	95	1800 (76.0)	73	75	1840 (77.7)	59	70
9	M	8 4/12	1400 (94.7)	82	97	1410 (95.3)	70	84	1420 (96.0)	71	79
10	M	9 2/12	1440 (85.3)	86	100	1420 (84.1)	57	68	1480 (87.6)	49	63
11	M	9 11/12	1480 (80.0)	79	94	1440 (77.8)	66	62	1500 (81.0)	58	60
12	M	11 9/12	1960 (85.9)	59	83	1920 (84.1)	65	70	1900 (83.2)	59	63
13	F	12 3/12	2000 (95.8)	50	100	1940 (93.2)	62	59	2040 (97.7)	64	55
14	M	12	2200 (94.0)	49	75	2020 (86.3)	57	59	2080 (88.8)	42	42
15	M	12 8/12	2040 (81.5)	96	94	2000 (79.9)	68	69	1980 (79.1)	69	66
16	F	13 1/12	2240 (99.7)	50	89	2220 (98.8)	71	65	2180 (97.1)	61	53
17	M	11 6/12	2000 (89.9)	49	92	1980 (89.0)	55	49	2020 (90.8)	62	54
18	M	10 3/12	1720 (88.9)	62	93	1680 (86.9)	64	57	1760 (91.0)	56	56
19	F	9 4/12	1680 (109.5)	78	88	1680 (109.5)	61	59	1640 (106.9)	49	46
20	M	10 9/12	1760 (85.8)	48	69	1770 (86.3)	69	66	1680 (81.9)	50	34
21	F	7 5/12	1200 (102.4)	56	80	1180 (100.7)	70	63	1140 (97.3)	46	52
22	F	11 5/12	2160 (112.2)	61	76	2120 (110.1)	75	67	2020 (104.9)	62	47
23	M	9 4/12	1560 (91.1)	58	77	1530 (89.4)	84	59	1540 (90.0)	64	47
24	M	8 10/12	1360 (85.2)	64	94	1340 (84.0)	73	85	1340 (84.0)	77	74
Mean		10.8	90.8	67.0	89.6	89.6	69.8	67.0	89.9	63.1	59.0
±SD		±1.9	+9.5	±15.1	±8.6	±9.5	±9.3	±8.3	±8.5	±12.4	±11.0

*Time of the maximal response during the first hour after exercise challenge.
†Time of the maximal response between 3 and 10 hours after exercise or allergen challenge.
‡Ten minutes after inhalation of the last concentration of allergen.
§Milliliters per second.
‖Values in parentheses are percents predicted.[22]
¶% Baseline.

The extracts of house dust mite *(D. pteronyssinus)* were obtained from Bencard, U. K., and diluted with buffer phosphate. Serial alternative fivefold and twofold dilutions were prepared, as described,[23] from a 10^{-3} wt/vol concentration, and inhaled after a control inhalation of buffer phosphate, starting with the dilution producing a 2 mm wheal reaction in the skin prick test. The baseline values of each allergen test were FEV_1 values obtained after inhaling buffer solutions just before allergen exposure.

Aerosols were generated by a nebulizer operated by compressed air at 20 psi (AP-50, model 646; DeVilbiss, Somerset, Pa.) and an inhalation-triggered dosimeter (Rosenthal-French, model 2A, Laboratory for Applied Immunology, Fairfax, Va.). Volume history was standardized by having each participant perform five maximal inhalations from functional residual capacity to total lung capacity at each concentration of allergen. For the control AC, inhalations were continued at 10-minute intervals until there was a 20% fall or more from baseline FEV_1 or the maximal concentration was reached. The response was measured spirometrically. After the last concentration, FEV_1 was measured at hourly intervals for 10 hours. Response was expressed as ΔFEV_1, measured at 10 minutes after the last concentration of allergen (magnitude of the early response) and the maximal ΔFEV_1 between 3 and 10 hours after the allergen inhalation (magnitude of the late response). The early asthmatic response (EAR) or LAR was defined as when the magnitude of the early or late response exceeded 20%.

For the second allergen challenge test, we used the same series of concentration of allergen as determined at the control AC in each subject. The response was measured and expressed by the same method as the control AC.

Exercise challenge test

Exercise tests were performed, as previously described,[24] through a 6-minute period of treadmill run-

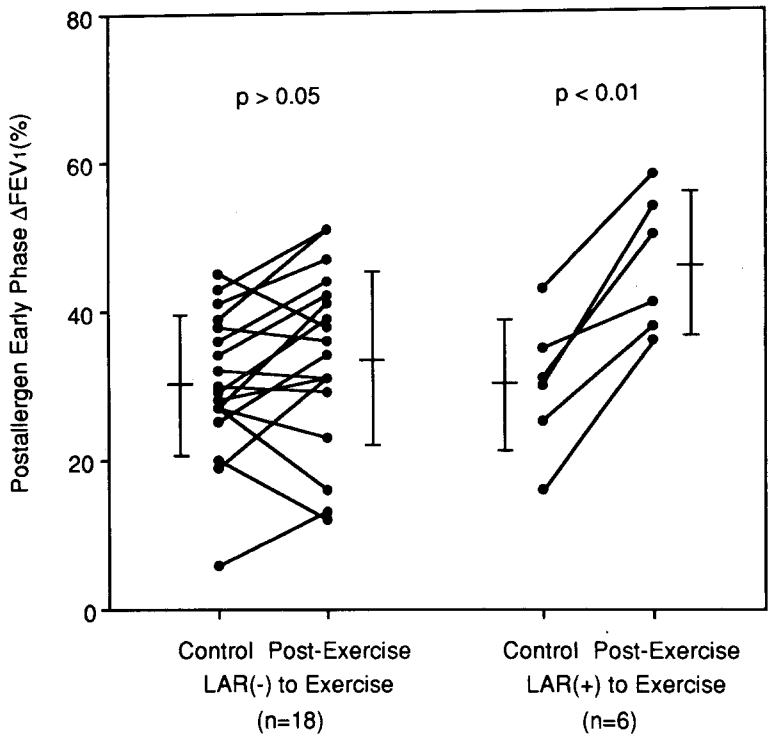

FIG. 1. Changes of postallergen early phase ΔFEV_1 between the control and the post-exercise allergen challenges in the patients without late asthmatic response *(LAR)* to exercise *(left)* and in the patients with LAR to exercise *(right)*. The *bars* show mean and ±1 SD. The change was significant in the group with LAR, whereas the change was not significant in the group without LAR.

ning, with speed and slope adjusted to give a heart rate of approximately 160 to 180 beats/min. Tests were performed in an air-conditioned laboratory, and there were no significant variations in environmental temperature or humidity throughout the series of experiments. FEV_1 was measured at the time intervals described above. Response was expressed as the maximal ΔFEV_1 from the pre-exercise value, occurring in the first hour (magnitude of the early response), and between 3 and 10 hours (magnitude of the late response) after the achievement of the target workload. The EAR or LAR was defined as when the magnitude of the early or late response exceeds 15%.[17, 18]

Statistical analysis

Statistical analysis was performed by using the Student's *t* test for paired observations. Comparison between the groups with or without LAR was made by the unpaired Student's *t* test. Correlation between the values was assessed with the use of simple or multiple regression equation. All the analyses were done by using StatView II (Abacus Concepts, Inc., Berkeley, Calif.) on a Macintosh computer (Apple Computer, Inc., Cupertino, Calif.). A difference between groups with a p value < 0.05 was accepted as being statistically significant.

RESULTS

There was no significant diurnal change of FEV_1 on day 1 in the first period, although some patients showed the trend of increase in the afternoon (not shown). The bronchial response to exercise for each patient is illustrated in Table I. Most patients showed the early response at 5 or 8 minutes after exercise, but the time of the late response was variable. The mean (±SD) magnitude of early responses in the whole group was 33.0% (±15.1%), and that of late responses was 10.1% (±8.6%). The correlation between the early and late-phase responses to exercise was significant, with $r = 0.433$ ($p = 0.03$). It may be observed that EAR to exercise developed in all but three patients. A definite LAR developed in six patients. The subjects with LAR showed higher early responses than those without LAR (44.8% ± 5.4% vs 29.0% ± 15.3%; $p < 0.01$). The late response of the latter group was 6.1% ± 3.8%, whereas that of the former group was 23.3% ± 4.8%.

The results of two AC tests are illustrated also in Table I. After the control AC, three subjects had a ΔFEV_1 <20% in the early phase, although they had inhaled the top concentrations of the allergen extracts, but they demonstrated a definite LAR. Two subjects demonstrated only an EAR. The other 19 subjects demonstrated dual asthmatic responses to allergen inhalation. After the

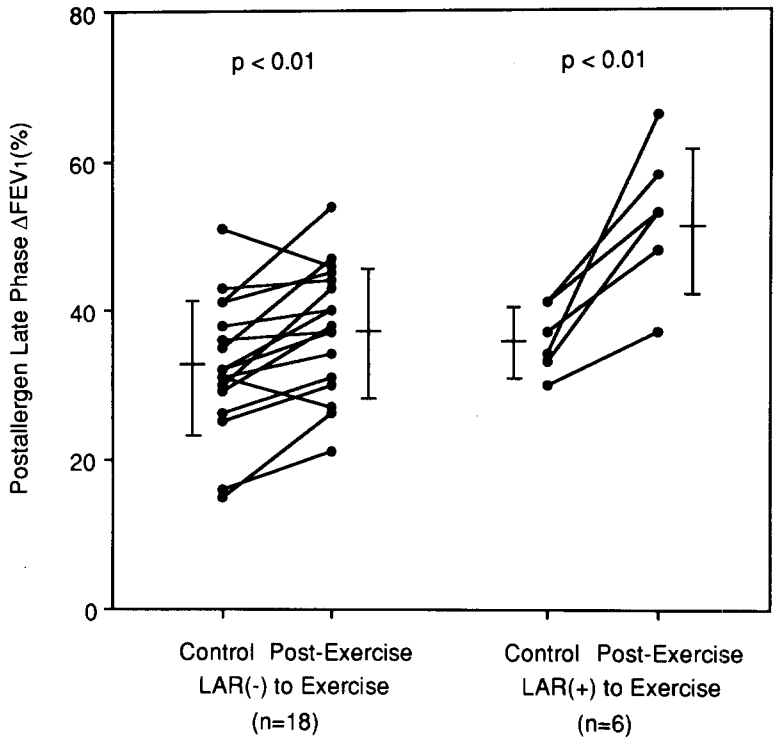

FIG. 2. Changes of postallergen late phase ΔFEV_1 between the control and the post-exercise allergen challenges in the patients without late asthmatic response *(LAR)* to exercise *(left)* and in the patients with LAR to exercise *(right)*. The *bars* show mean and ±1 SD. The change was significant not only in the group with LAR, but also in the group without LAR. However, the former group showed a significantly greater increment than the latter group ($p < 0.05$).

AC following exercise, three subjects showed no EAR, but all the subjects showed an LAR.

The changes of postallergen ΔFEV_1 between the control and post-exercise ACs are shown in Fig. 1 (early phase) and Fig. 2 (late phase). In the early phase, postallergen ΔFEV_1 increased significantly from the control AC to the post-exercise AC in the whole group (from 30.2% ± 9.3% to 36.9% ± 12.4%; $p < 0.01$). However, when the data are analyzed according to whether LAR to exercise occurs (Fig. 1), the change of postallergen ΔFEV_1 between the control and post-exercise ACs was not significant in the group without LAR (30.3% ± 9.6% vs 33.8% ± 11.9%; $p > 0.05$), but the change was significant in the group with LAR (30.0% ± 9.1% vs 46.2% ± 9.1%; $p < 0.01$). In the late phase, too, postallergen ΔFEV_1 increased significantly from the control AC to the post-exercise AC in the whole group (from 33.0% ± 8.3% to 41.0% ± 11.0%; $p < 0.01$). When the data are analyzed in the similar way (Fig. 2), the changes of postallergen FEV_1 between the control and post-exercise ACs were significant in the group without LAR to exercise (32.1% ± 9.1% vs 37.2% ± 8.6%; $p < 0.01$), as well as in the group with LAR (36.0% ± 4.5% vs 51.5% ± 10.0%; $p < 0.01$). The magnitudes of the changes, however, differed markedly between the two groups. To compare the dimensions of the changes, the group with LAR showed a greater increment than the group without LAR (15.5% ± 8.7% vs 5.1% ± 5.2%; $p < 0.05$).

To substantiate the change of postallergen ΔFEV_1 between the control and post-exercise ACs according to EAR or LAR to preceding exercise, we tried to correlate the changes (Postallergen ΔFEV_1 of post-exercise AC − Postallergen ΔFEV_1 of control AC) to the magnitudes of early response or late response to exercise. The correlations of the early and late-phase changes to the magnitude of early response to exercise are illustrated in Fig. 3. There was no correlation of either the early phase or the late-phase change of postallergen ΔFEV_1 to the magnitude of the early response to exercise (early phase, $r = 0.067$, $p > 0.05$; late phase, $r = 0.322$, $p > 0.05$). When the early phase change was correlated to the magnitude of late response to exercise (Fig. 4), there was a good positive correlation ($r = 0.685$, $p < 0.01$). The same figures were obtained when the late-phase changes were plotted with the magnitude of the late response to exercise ($r = 0.762$, $p < 0.01$) (Fig. 5).

Multivariate analysis was performed to ascertain that the late response to exercise is the most

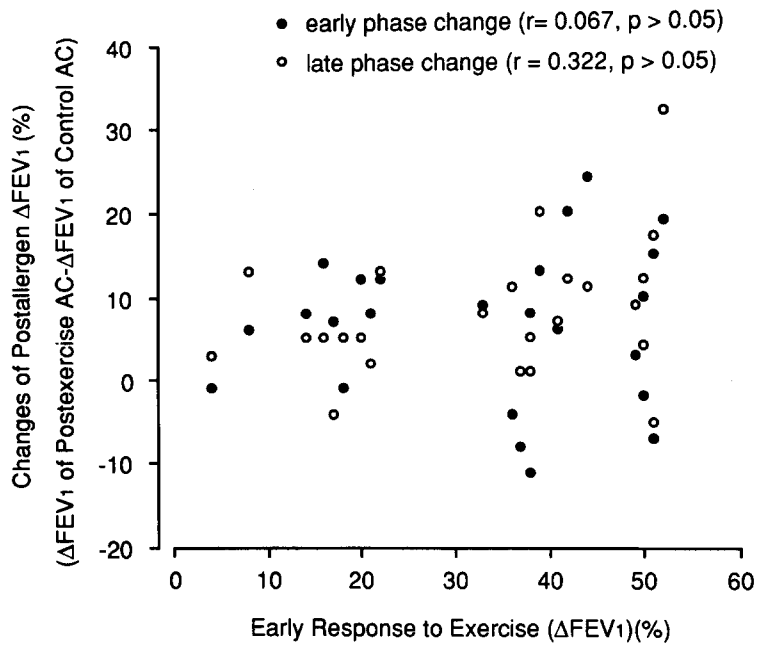

FIG. 3. Changes of postallergen early phase and late phase ΔFEV_1 from the control to the post-exercise allergen challenge according to the magnitude of early response to exercise. Neither the early phase nor the late-phase change showed a significant correlation with the early response to exercise.

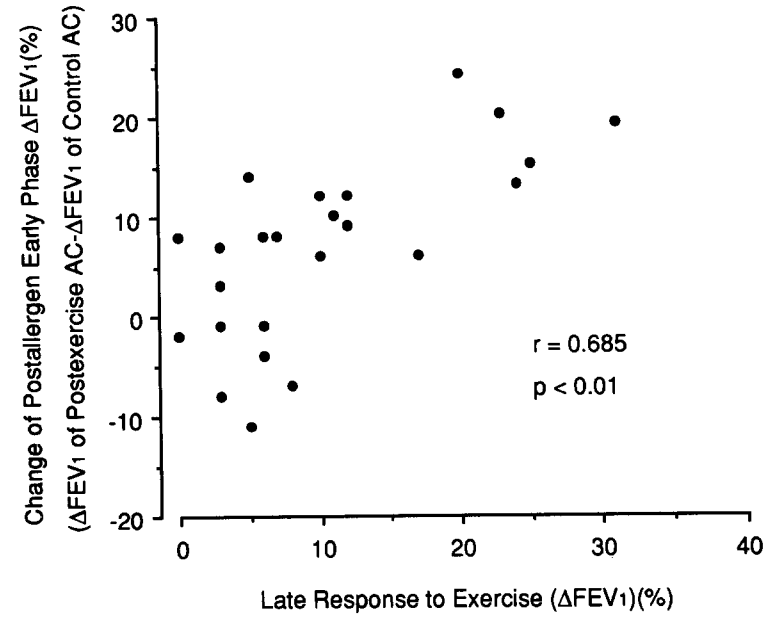

FIG. 4. Change of postallergen early phase ΔFEV_1 from the control to the post-exercise allergen challenge according to the magnitude of late response to exercise. The early phase change showed a good positive correlation with the late response to exercise.

influential in increasing the reactivity to allergen. When the dependent variable was the early phase change of ΔFEV_1 between the control and post-exercise ACs, the late response to exercise was the only significant factor among the independent variables considered (the early response to exercise, the late response to exercise, and the late response to control AC). Similarly, when the dependent variable was the late phase change, the late response to exercise, too, was the only signifi-

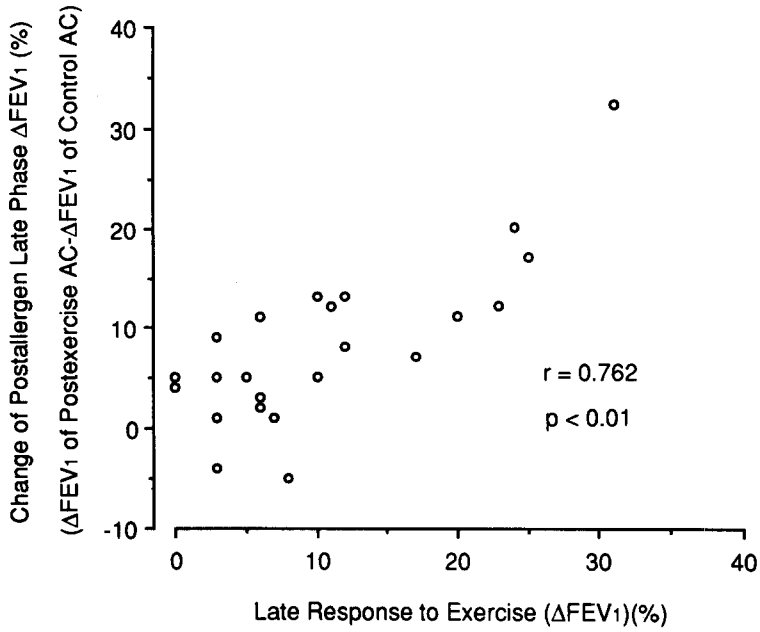

FIG. 5. Change of postallergen late phase ΔFEV_1 from the control to the post-exercise allergen challenge according to the magnitude of late response to exercise. The late phase change showed a good positive correlation with the late response to exercise.

cant factor among the independent variables (the early response to exercise, the late response to exercise, the early response to control AC, and the early response to post-exercise AC) (not shown).

DISCUSSION

An AC is frequently associated with a late response that may be prolonged, severe, or recurrent,[9] and it has consequences of increased AR not only to a variety of chemical bronchoconstrictors, such as histamine or methacholine,[25] but also to naturally occurring stimuli, such as exercise or subsequent allergen exposure.[1, 4]

Exercise also may cause an LAR,[9-12] although its prevalence seems to be somewhat lower than that of allergen.[9, 26, 27] The pattern of response is reported to be very similar to the pattern observed after allergen, and a release of mediators has been described during LAR to exercise,[27] as in allergen-induced asthma. However, data on the changes of AR after exercise are still incomplete. Suzuki et al.[16] have suggested that physical exertion uniformly makes the airways more sensitive to methacholine. Other investigators could not find the changes in AR to nonspecific stimuli, including methacholine, after exercise.[11, 17, 18] But most studies mentioned above have dealt with the cases without LAR to exercise. Moreover, data as to its consequences on AR to other stimuli or its clinical relevance are tenuous. Iikura et al.[28] have reported a notable increase in children's asthmatic symptoms for several days after the development of late-phase reactions caused by exercise. Although some other investigators could not confirm this finding,[11] our observations indicated that many parents of asthmatic children complain about the nocturnal worsening of asthma on the night after daytime physical exertion. This might be increased reactivity to indoor allergen exposure to which the children are sensitive. Therefore our hypotheses were that the reactivity to allergen may be increased for some time after exercise and that the factor determining it might be the LAR to exercise, as is observed after allergen inhalation.

In this study we have demonstrated that AR to allergen is increased 24 hours after exercise and that the increased AR is related to the late-phase reaction to the preceding EC. Although there are some limitations in looking at a single time point to examine the effect of preceding exercise, 24 hours was chosen as the period after the EC for the AC because it is a time point that is feasible to perform and that reasonably reflects the increase in AR after exercise.[10] It is not the case that the change of responses to allergen may be accounted for by the difference in airway caliber,[3, 29] because the baseline FEV_1 was almost same in each individual on both AC days; thus the mean percents of predicted values were not different (Table I). The season of the study also

seems to have had no effect on the change of responses to allergen. Our study was performed from December to February, months during which the indoor level of the relevant allergen, the house dust mite *(D. pteronyssinus),* has been found to be lowest and not changed in our country.[30] And we do not think that other concomitant environmental factors influenced the results of this study. One point to be considered in the documentation of changes of AR to allergen is the reproducibility of the response. For ethical reasons we were not able to repeat the control AC or the post-exercise AC. A few studies have included some form of check on the reproducibility of the responses induced by allergen inhalation, which demonstrated that allergen inhalation gives a fairly reproducible response not only in the early phase,[31, 32] but also in the late phase.[33]

The way that the control AC was executed allows the following question to be raised: Was the exercise *per se* or the exercise-induced bronchial reaction responsible for the increase in AR to allergen? We realize that the control AC may have been preceded preferably by an exercise protocol, in which the subjects breathe warm, moist air instead of room air. However, there is now some doubt regarding aspects of respiratory heat or water loss hypothesis. For example, in a study by Anderson et al.[34] more than half a group of severe asthmatic subjects had exercise-induced asthma after exercising while breathing air conditioned to body temperature and humidity. The strong relationship between the development of LARs after exercise and the increase in AR to allergen in the present study supports the argument that the etiologic event was the bronchial reaction to exercise, rather than exercise *per se.*

The question of how to define the LAR to EC and its specificities remains controversial.[35, 36] Because of diurnal variation of pulmonary function, some studies have advocated the use of clock-time comparison on a control day without exercise instead of pre-exercise baseline comparison.[35, 37] But on a control day in our study, no significant change of FEV_1 over the 10-hour measurement period was found. Furthermore, FEV_1 tended to increase at the time of LAR to be elicited from the baseline values in some patients. Thus the comparison with the baseline values for defining LAR in this study should not change the figure. This result also argues strongly against the fact that LAR after EC could be a nonspecific phenomenon, for example, such as that due to medication withdrawal.[14] The prevalence of LARs to exercise in the present study was consistent with the observations of other investigators in which such reactions were noted in 30.4% and 32.6% of subjects.[11, 27]

The short-term effect of repeated exercise at short intervals on subsequent allergen exposure was reported by Weiler-Ravell and Godfrey.[32] After an average of three runs, all subjects were rendered refractory to subsequent exercise, but allergen-induced asthma of the same or greater severity developed in half the subjects. The relative long-term effect (as long as 24 hours) of exercise on the AC has not been reported yet.

Our present data indicated that, occasionally, an EC may lead to priming on subsequent allergen exposure at 24 hours. Previous investigations have focused primarily on the priming induced by AC. Thus allergen-induced increase in nonallergic AR will result in enhanced response to any bronchoconstrictor stimuli, including the early response to exercise or inhaled allergen.[4, 38] We realize that exercise- and allergen-induced asthma may utilize a different pathway, the prevalence and the severity of LAR are lower in exercise-induced asthma than in allergen-induced asthma, and late effect on the AR to nonspecific agents is somewhat different. However, our results indicate that exercise also primes the airway to subsequent allergen exposure in the case when late response to exercise is considerable. Although we did not compare the nonspecific AR before and after exercise, most studies report that nonspecific AR does not increase after exercise.[11, 17, 39] Nonetheless, it could be that allergen exposure is a greater stimulus than nonspecific agents to invoke the changes of AR between before and after exercise.[40]

The mechanism of the priming by exercise is not clear. There have been few studies investigating the possible link between LAR after exercise and airway inflammation. Crimi et al.[41] reported that bronchoalveolar lavage performed 3 hours after an EC revealed mast cell degranulation and eosinophil inflammation in dual responders. Jarjour et al.[42] observed no changes in bronchoalveolar cell counts, differentials, or reactive oxygen species metabolism 24 hours after an EC, but they could not rule out the possibility of airway inflammation after an EC, because LAR did not occur in any of the subjects studied. Therefore if airway inflammation is also an important etiologic factor in LAR after EC and it fails to resolve completely despite return of airway caliber at the time of 24 hours after EC, the responses to AC may be enhanced in the same way as that the responses to EC were augmented after AC.[4] Another possibil-

ity is that exercise may have resulted in infiltration of the bronchial mucosa by cells from the circulation that carry *D. pteronyssinus*–specific IgE, namely, basophils. If that was the case, the number of target cells for the allergen inhalation challenge was increased, leading to the release of large amounts of inflammatory mediators and the induction of a stronger early and subsequently late reaction to allergen.

In conclusion, increased AR to allergen occurs in some patients with asthma after exercise, and it is related to the late bronchial response to exercise. From these observations it is to be expected that the severity of AR to allergen will vary, depending on the recent performance of exercise and the development of LAR, even for the same doses of allergen. This suggests that LAR to exercise, when it occurs, may be associated with increased asthmatic symptoms for as long as 24 hours after exercise.

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