Original articles

Effects of swimming training on aerobic capacity and exercise induced bronchoconstriction in children with bronchial asthma

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Abstract
Background—A study was undertaken to determine whether swimming training improved aerobic capacity, exercise induced bronchoconstriction (EIB), and bronchial responsiveness to inhaled histamine in children with asthma.
Methods—Eight children with mild or moderate asthma participated in swimming training every day for six weeks. The intensity of training was individually determined and set at 125% of the child's lactate threshold (LT), measured using a swimming ergometer. Another group of eight asthmatic children served as control subjects. Aerobic capacity and the degree of EIB were assessed by both cycle ergometer and swimming ergometer before and after swimming training.
Results—The mean (SD) aerobic capacity at LT increased by 0.26 (0.11) kp after training when assessed with the swimming ergometer and by 10.6 (4.5) W when assessed with the cycle ergometer, and these changes were significantly different from the control group. The mean (SD) maximum % fall in forced expiratory volume in one second (FEV_1) to an exercise challenge (cycle ergometer) set at 175% of LT decreased from 38.7 (15.4)% before training to 17.9 (17.6)% after training, but with no significant difference from the control group. There was, however, no difference in histamine responsiveness when compared before and after the training period.
Conclusion—A six week swimming training programme has a beneficial effect on aerobic capacity but not on histamine responsiveness in children with asthma.
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Keywords: asthma; swimming training; exercise training; children; lactate threshold; bronchial responsiveness

Several studies have shown that asthmatic patients can improve their exercise performance after participating in one of a number of physical conditioning programmes.[1–7] The role of swimming training is well accepted amongst the asthma community and is the form of exercise frequently prescribed for asthmatic children because it seems to precipitate asthma less than land based exercise.[7–9] Although training programmes have been advocated to improve the physical working capacity and clinical symptoms of patients, the effect on exercise induced bronchoconstriction (EIB) remains controversial.[10–13] The major problem with most previous studies has been the lack of individualisation of training,[1 2 5 10 11 13] the same training being prescribed for all subjects. Thus, some subjects may have been understressed while others may have been exhausted. In addition, the training effect of the exercise programme has generally been assessed using an exercise test of the same intensity (absolute load) as that used before training. An exercise challenge is usually graded to produce an increase in heart rate to approximately 80% of the subject's predicted maximum. If the training programme was successful and cardiorespiratory fitness was increased, one might expect that the same exercise load may have less effect on heart rate and on ventilation, which might translate into less EIB.[3] Thus, any true effect of exercise training on EIB may be masked.

The present study was undertaken to determine whether individualised swimming training improves aerobic capacity and whether this truly results in less EIB or whether the apparent protection from EIB is simply due to an increased exercise capacity. To individualise the training programme and to use the same load before and after training, each subject's aerobic capacity was defined by calculating the work load at which lactic acid production increased (lactate threshold; LT). This LT was used to individualise the training programme and to determine the work loads used in the exercise challenges. To determine the specificity of the type of training programme each subject's aerobic capacity was determined using both a swimming ergometer and a cycle ergometer before and after the swimming training programme. The effects of the swimming training programme were determined by exercise challenge tests using both the swim-

Table 1 Demographic data and baseline pulmonary function of 16 asthmatic children

Subject no	Sex	Age (y)	Height (cm)	Weight (kg)	Medication	FVC (l)	FVC (% pred)	FEV_1 (l)	FEV_1 (% pred)	MMF (l/s)	MMF (% pred)	PEF (l/s)	PEF (% pred)
Training group													
1	M	10	126.5	25.4	T,B,C,β	2.06	(105)	1.28	(75)	0.87	(40)	3.31	(96)
2	F	10	126.0	25.0	T	1.63	(89)	1.33	(83)	1.29	(63)	3.67	(125)
3	M	10	137.0	34.0	T,B,β	2.44	(101)	1.88	(90)	1.66	(66)	4.34	(103)
4	M	9	129.5	28.0	T,B,C,β	1.99	(99)	1.34	(77)	0.96	(44)	3.03	(86)
5	M	12	159.0	47.0	T,C	1.93	(87)	1.57	(81)	1.45	(61)	5.66	(146)
6	M	11	133.5	28.8	T,B,C,β	2.28	(89)	1.76	(79)	1.46	(56)	5.76	(129)
7	M	11	142.0	38.0	—	3.37	(99)	2.41	(82)	1.92	(59)	5.34	(91)
8	M	11	124.0	21.2	T	2.01	(115)	1.59	(105)	1.47	(74)	4.17	(136)
Mean		10.5	134.7	30.9		2.21	(98.0)	1.65	(84.0)	1.39	(57.8)	4.41	(114.0)
SD		0.9	11.6	8.4		0.52	(9.5)	0.38	(9.6)	0.35	(11.2)	1.07	(22.7)
Control group													
1	M	10	146.0	37.0	—	2.28	(71)	1.8	(65)	1.58	(51)	4.3	(78)
2	M	11	133.0	26.2	T,B,β	1.87	(85)	1.26	(66)	0.84	(36)	3.18	(83)
3	M	10	137.0	32.8	T,B,C,β	1.66	(71)	1.15	(57)	0.85	(35)	2.84	(69)
4	M	8	119.0	26.7	T,B,C,β	1.77	(123)	1.54	(124)	1.62	(92)	3.34	(131)
5	M	9	133.0	28.0	T	1.87	(87)	1.34	(72)	1.09	(47)	2.94	(78)
6	M	11	137.0	24.0	T,β	1.66	(89)	1.49	(92)	0.92	(44)	3.04	(93)
7	M	10	133.5	27.0	—	2.15	(96)	1.71	(89)	1.58	(67)	3.71	(96)
8	F	10	129.0	25.0	B	1.78	(97)	1.63	(101)	2.21	(108)	3.56	(121)
Mean		9.9	133.4	28.3		1.88	(89.8)	1.49	(83.2)	1.34	(60.0)	3.36	(93.6)
SD		1.0	7.7	4.4		0.22	(16.6)	0.23	(22.4)	0.49	(26.9)	0.48	(21.9)
Difference between groups	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS	NS	NS

FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; MMF = maximal mid-expiratory flow rate; PEF = peak expiratory flow rate; NS = not significant; T = theophylline; B = beclomethasone dipropionate; C = disodium cromoglycate; β = $β_2$ agonist.

ming and cyclic ergometers and a histamine challenge test.

Methods

SUBJECTS

Sixteen children with asthma diagnosed according to the ATS criteria[14] who had been admitted to hospital for treatment participated in the study. All had severe asthma when admitted and the asthma attacks were controlled by treatment as an inpatient. None were prescribed oral steroids. The characteristics of the children are shown in table 1. They were randomly allocated to either a training group (n = 8) or a control group (n = 8). The two groups did not differ with respect to age, height, pulmonary function, or frequency of acute attacks of asthma. Asthma medication (disodium cromoglycate, $β_2$ agonists, theophylline, beclomethasone dipropionate) was not modified during the study period. The study was performed during late autumn when allergic stimuli were minimal. All studies were performed when the children were free from symptoms of asthma or respiratory infections.

BASELINE ASSESSMENTS
Determination of aerobic capacity
To determine each child's aerobic capacity, exercise tests were performed using a cyclic ergometer (Bosch Co.) and swimming ergometer (Ezaki Co. Japan) with an interval of one day between the tests. The incremental cyclic ergometer test started with 10–15 W for four minutes. The work load was then increased by 5–10 W every four minutes until exhaustion. The incremental swimming ergometer test was performed using a tethered swimming method in a heated (30°C) indoor pool. Subjects swam "crawl" for two minutes while their position was kept constant and a load was applied with a rope attached around their waist (fig 1). The work load was 0.1–0.2 kp initially and was increased gradually by 0.2 kp every two minutes until exhaustion. During both exercise tests the heart rate was monitored continuously by radiotelemetry.

To measure blood lactate concentrations 20 μl blood samples were obtained from an ear lobe at rest and immediately after each exercise increment. Blood was immediately haemolysed, diluted 10 times with 0.1 mM phosphate buffer (pH 7.3), and frozen. The concentration
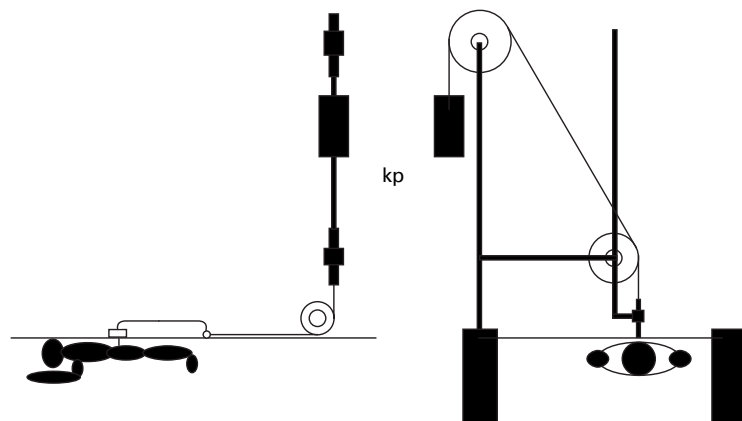

Figure 1 Scheme of the swimming ergometer. Subjects swam "crawl" for two minutes while their position was kept constant and a load was applied with a rope attached around their waist.
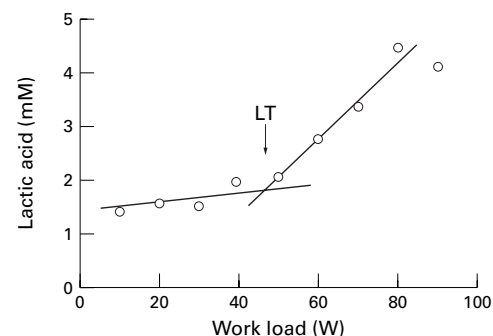

Figure 2 Determination of lactate threshold (LT) in a single subject from a plot of blood lactate levels against work load (in watts). The initial break point in blood lactate concentration was determined by visual inspection. The mean value of the points determined by three observers was defined as the LT.

Table 2 Duration of swimming training and distance achieved by subjects in the training group

Subject no	Days	Achieved distance (m)	Mean distance (m/day)
1	34	29 100	855.9
2	25	23 075	923.0
3	34	28 125	827.2
4	34	29 100	855.9
5	32	24 975	780.5
6	29	22 750	784.5
7	33	29 950	907.6
8	30	26 325	877.5
Mean	31.4	26 675.0	851.5
SD	3.2	2827.6	52.2
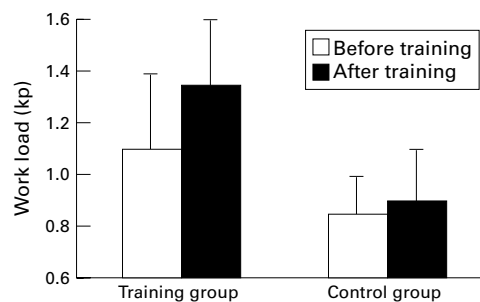
Figure 3 Mean (SD) changes in work load by swimming ergometer before and after training in training group (n = 8) and control group (n = 8).

of lactate in these samples was determined using a commercial lactate analyser (Roche 646). The lactate threshold (LT) was calculated for each subject from a plot of blood lactate against work load (in watts). The initial break point in blood lactate concentration was determined by visual inspection. The mean value of the points determined by three observers was defined as the lactate threshold (fig 2). Aerobic capacity was defined as the work load at LT.

Evaluation of exercise induced bronchoconstriction (EIB)
Exercise challenge tests were performed on consecutive days on both the cycle ergometer and the swimming ergometer using six minute challenge protocols. Work loads were set at 100% and 175% of the LT, determined as described above. There was an interval of at least 24 hours between each exercise test so as not to influence the refractory period of EIB. With the cycle ergometer subjects inhaled dry air at room temperature through a two way valve and mask. Challenge tests using the swimming ergometer were performed in a heated (30°C) indoor pool. Forced expiratory volume in one second (FEV_1) was measured with an AS 300 spirometer (Minato Medical Science Co.) immediately before exercise and five and 15 minutes afterwards. EIB was expressed as the percentage fall from the pre-exercise value ((pre-exercise—lowest post-exercise/pre-exercise) × 100). Heart rate was monitored throughout the study. All medication was withheld for 12 hours before the investigation.

Histamine challenge test
To evaluate bronchial responsiveness a histamine challenge test was performed. Histamine aerosols were generated using a DeVilbiss 646

nebuliser. Following inhalation of phosphate buffer saline, doubling concentrations of histamine (from 20 μg/ml to 10 000 μg/ml) were inhaled. The challenge test was discontinued when FEV_1 had fallen to 20% or more below the initial value. The provocative concentration (PC_{20}) was calculated from the log concentration-response curve by linear interpolation of the last two points.

SWIMMING TRAINING PROGRAMME
Before commencing the training programme the work rate and corresponding heart rate at 125% of LT were assessed in each subject using the swimming ergometer. The heart rate was continuously monitored by radiometry and the swimming speed was regularly noted at this intensity in a series of 25 m "crawls". It was therefore possible for subjects to control their swimming speed by being informed of the time taken to swim every 25 m. The training intensity was thus set to 125% of LT for each subject individually. During the six week training period the training group swam in a heated indoor pool (30°C) for two 15 minute periods on six days of the week. A 10 minute break was taken between the two periods. Once a week blood lactate concentrations and heart rate were measured in each subject after the first 15 minute period to ensure that the training intensity remained at 125% of the subject's LT. The training intensity was increased where necessary.

POST-TRAINING EVALUATION
After the training period the aerobic capacity of the subjects in both the training and control groups was reassessed with both the cycle and swimming ergometers and LT was recalculated. Exercise challenge tests were then performed with loads of 100% and 175% of the original LT (designated as absolute load) and at 100% and 175% of the new LT (designated as relative load) using both the cycle and swimming ergometers. As there were no changes in the aerobic capacity of the subjects in the control group (see later), they performed tests at 100% and 175% of the original LT (absolute load) only. Histamine responsiveness was reassessed using a protocol identical to that used at baseline.

STATISTICAL ANALYSIS
All values are reported as group mean (SD). Paired *t* tests were used to detect differences within a group—for example, pre-training and
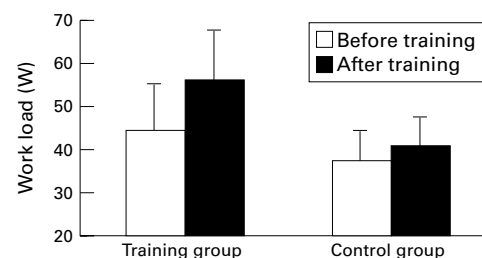

Figure 4 Mean (SD) changes in work load by cycle ergometer before and after training in training group (n = 8) and control group (n = 8).
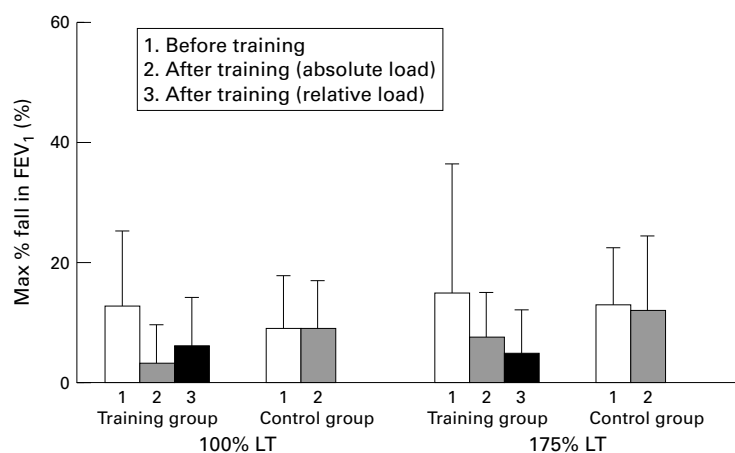
Figure 5   Mean (SD) changes in maximum % fall in forced expiratory volume in one second (FEV$_1$) at 100% and 175% of lactate threshold (LT) by swimming ergometer before and after training in the training group (n = 8) and control group (n = 8).
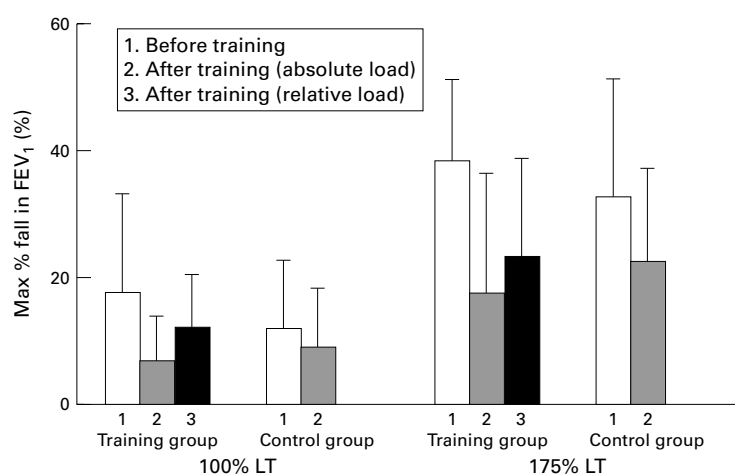

Figure 6   Mean (SD) changes in maximum % fall in forced expiratory volume in one second (FEV$_1$) at 100% and 175% of lactate threshold (LT) by cycle ergometer before and after training in the training group (n = 8) and control group (n = 8).
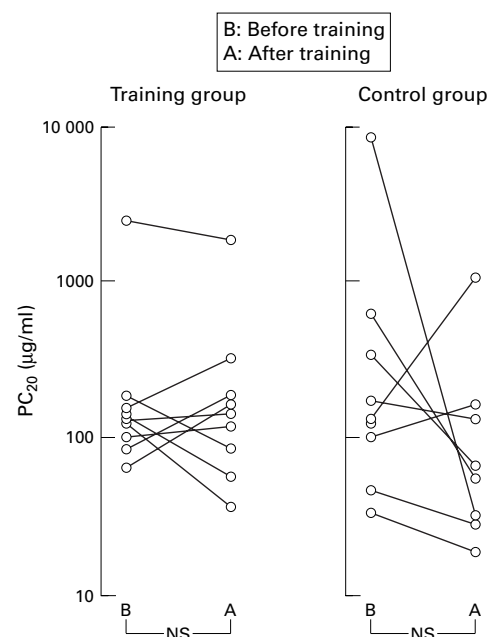

Figure 7   Changes in individual concentrations of histamine required to provoke a fall in forced expiratory volume in one second of 20% or more (PC$_{20}$) before and after training in training and control groups. No significant differences were found before and after training in the two groups.

post-training effects. Unpaired *t* tests were used to detect differences between groups. Statistical significance was accepted at p<0.05.

Results

The duration of swimming training, the total distance achieved during swimming training, and the mean swimming distance per day for each subject in the training group are shown in table 2.

EFFECT OF SWIMMING TRAINING ON AEROBIC CAPACITY

The swimming training programmes improved the aerobic capacity significantly in all subjects in the training group. In the training group the mean (SD) work load at LT assessed by the swimming ergometer increased by 0.26 (0.11) kp after training (p<0.001). In the control group the change in work load was 0.04 (0.14) kp, so the change was significantly higher in the training group than in the control group (mean difference 0.22 kp, 95% CI 0.085 to 0.355, p<0.005; fig 3). Similarly, the mean aerobic capacity by cycle ergometer increased significantly by 10.6 (4.5) W in the training group (p<0.001) and by 3.8 (5.2) W in the control group. The change was significantly

higher in the training group than in the control group (mean difference 6.8 W, 95% CI 1.59 to 12.02, p<0.01; fig 4).

EFFECT OF SWIMMING TRAINING ON EIB

The degree of EIB was reduced in the training group after the training period when challenge tests were performed using the same relative load after training as before training (fig 5). The mean maximal percentage fall in FEV$_1$ induced with the swimming ergometer work load set to 175% LT on the relative load decreased significantly in the training group from 15.4 (12.1)% before training to 4.1 (4.8)% after training (p<0.01). A similar pattern was observed at a work load of 100% LT but these changes did not reach significance. However, there were no significant differences between the change in the mean maximal percentage fall in FEV$_1$ in the training and control groups by absolute load at 100% LT (p = 0.07) or at 175% LT (p = 0.20).

The falls in FEV$_1$ induced by the cycle ergometer were greater than those induced by the swimming ergometer at both work loads. A greater fall in lung function was also induced by the higher work load (fig 6). The protective effects of training on EIB were evident when assessed with a relative load of 175% LT (38.7 (13.4)% fall in FEV$_1$ before training vs 22.5 (14.7)% after training; p<0.05). When using the pre-training absolute load protective effects were seen at both 100% LT (p<0.05) and 175% LT (p<0.01). However, there were no significant differences between the change in the mean maximal percentage fall in FEV$_1$ in either group when assessed by absolute load at 100% LT (p = 0.14) or 175% LT (p = 0.22).

EFFECT OF SWIMMING TRAINING ON HISTAMINE
RESPONSIVENESS

No changes were seen in histamine PC_{20} during
the training period in either the training group
or the control group (fig 7). The difference
between the mean change in PC_{20} in the train-
ing and control groups was not statistically sig-
nificant (p = 0.16).

Discussion

The results of this study show the benefits that
can be achieved by an individualised training
programme in asthmatic children. By setting
training intensity to 125% of each child's aero-
bic capacity and increasing the intensity weekly
to ensure that it remained at this level, we have
been able to increase each subject's aerobic
capacity. This resulted in a decrease in EIB
when assessed at the same relative load before
and after the training period. The benefits of
swimming training were not confined to swim-
ming exercise but were also seen when exercis-
ing on a cycle ergometer. However, increasing
aerobic capacity by training did not decrease
histamine responsiveness.

Several previous studies have attempted to
address the benefits of training on asthmatic
children. Some of these showed an increased
aerobic capacity, whereas the reported effects
on EIB have been more variable.[10–13] The
differences between the clear cut results of the
present study and the variable results reported
previously may be explained by methodological
differences including differences in the selec-
tion of patients, the lack of a control group, dif-
ferences in the training programme, and differ-
ences in the evaluation of EIB. No study has
previously used an individualised training pro-
gramme, nor continually reassessed the train-
ing intensity during the programme. We used
the individual's LT to determine an individual-
ised work intensity as this has previously been
reported to be a useful parameter for determin-
ing exercise intensity.[15 16] Some previous stud-
ies have used heart rate to determine the work
intensity used.[4 6 12] However, heart rate has
been reported to have a large inter-individual
variability, especially in children,[17] making it
unsuitable for individualising a training pro-
gramme. Varray *et al* reported the use of a ven-
tilatory threshold to individualise training
intensity for a swimming programme for asth-
matic children.[3] However, their protocol is time
consuming and needs special apparatus and
techniques which may limit its general
applicability.[16]

We set the intensity of our training pro-
gramme at 125% of LT, determined from an
incremental swimming ergometer test. A work
load of 125% LT was chosen for the following
reasons. The degree of EIB depends upon the
quantity of water loss from the airways as a
result of the hyperventilation induced by
exercise.[18 19] High intensity training is therefore
likely to induce EIB, especially in severe or
unstable asthmatic subjects. A training inten-
sity of 125% LT is less likely to induce signifi-
cant EIB yet, as shown by our results, it is suf-
ficient to achieve increases in aerobic capacity.

Our subjects did not use premedication before
training and could do the swimming training
without the appearance of EIB.

Swimming is a recommended sport for asth-
matic children because it does not induce as
much EIB as other forms of exercise. However,
there are few reports on the effects of
endurance swimming training on EIB. In 1976
Fitch *et al*[13] reported that the subjective symp-
toms of asthma in children improved after one
year of swimming training even though lung
function and EIB did not improve. Svenonius
et al[11] reported that EIB was significantly
improved after endurance swimming training
in asthmatic patients. They used the same
absolute exercise challenge intensity before and
after training. Thus, the reports of an improve-
ment in EIB may be due to the reduction in
minute ventilation in response to a standard
work load following a training programme
which increased cardiorespiratory fitness. As
the degree of EIB depends upon the minute
ventilation achieved during exercise, less EIB
would result. In the present study it may not be
sufficient to use the LT to express the
cardiopulmonary fitness rather than the
minute ventilation to evaluate the degree of
EIB. We showed that EIB decreased not only
when assessed using the same absolute load
before and after training, but also when the
same relative loads were used. The benefits of
training are therefore not simply due to an
increase in cardiorespiratory fitness.

In an attempt to investigate the mechanism
by which swimming training protected against
EIB, we performed histamine challenge tests
before and after training. Anderton *et al*[20]
showed the close correlation between the PC_{20}
by histamine challenge test and exercise
challenge test. However, no significant changes
in histamine PC_{20} were seen in either the train-
ing or control groups in this study. The
possibility exists that the true result was missed
because of the small sample size. Martin *et al*[21]
have reported that the children who lose their
asthma symptoms and no longer exhibit EIB
often retain their bronchial hypersensitivity to
histamine. There is generally a closer relation-
ship between clinical asthma and EIB than
between clinical asthma and the results of a
histamine challenge.

The mechanism by which swimming train-
ing protects against EIB is not clear. While EIB
is thought to be triggered by a change in the
osmolarity of the airway lining fluid brought
about by loss of heat and water to the inspired
air,[18 19 22] the exact mechanism remains un-
known. The release of mediators from mucosal
mast cells is thought to be involved,[23 24] and
leukotrienes may also play a part.[25 26] Whether
long term training can influence the release of
these mediators is not known. However, short
term anaerobic exercise has been reported to
induce a rapid increase in plasma catecho-
lamine levels and an increase in the density of
lymphocytic adrenoreceptors.[27] The β adreno-
receptor system has been shown to be activated
in lymphocytes during prolonged aerobic
exercise.[28] Although these mechanisms may be

important, we did not have the opportunity to study them in our study population.

In conclusion, the individualised swimming training used in the present study resulted in improved aerobic capacity and protected against EIB. This was true whether assessed with a swimming ergometer or a cycle ergometer. This protection against EIB was not accompanied by a decrease in histamine responsiveness. The use of an individualised training programme should prove to be a useful addition to treatment in asthmatic children.

1 Itkin IH, Nacman M. The effect of exercise on the hospitalized asthmatic patient. *J Allergy* 1966;**37**:253–63.
2 Bundgaard A, Ingemann-HansenT, Halkjaer-Kristensen J, *et al*. Short-term physical training in bronchial asthma. *Br J Dis Chest* 1983;**77**:147–52.
3 Varray AL, Mercier JG, Terral CM, *et al*. Individualized aerobic and high intensity training for asthmatic children in an exercise readaptation program: is training always helpful for better adaptation to exercise? *Chest* 1991;**99**:579–86.
4 Cochrane LM, Clark CJ. Benefits and problems of a physical training programme for asthmatic patients. *Thorax* 1990;**45**:345–51.
5 Szentágothai K, Gyene I, Szócska M, *et al*. Physical exercise program for children with bronchial asthma. *Pediatr Pulmonol* 1987;**3**:166–72.
6 Ludwick SK, Jones JW, Jones TK, *et al*. Normalization of cardiopulmonary endurance in severely asthmatic children after bicycle ergometry therapy. *J Pediatr* 1986;**109**:446–51.
7 Fitch KD, Morton AR. Specificity of exercise in exercise-induced asthma. *BMJ* 1971;4:577–81.
8 Godfrey S, Silverman M, Anderson SD. Problems of interpreting exercise-induced asthma. *J Allergy Clin Immunol* 1973;**52**:199–209.
9 Reggiani E, Marugo L, Delpino A, *et al*. A comparison of various exercise challenge tests on airway reactivity in atopical swimmers. *J Sports Med Physic Fitness* 1988;**28**:394–401.
10 Nickerson BG, Boutista DB, Namey MA, *et al*. Distance running improves fitness in asthmatic children without pulmonary complications or changes in exercise-induced bronchospasm. *Pediatrics* 1983;**71**:147–52.
11 Svenonius E, Kautto R, Arborlius M. Improvement after training of children with exercise-induced asthma. *Acta Paediatr Scand* 1983;**72**:23–30.
12 Haas F, Pasierski S, Levine N, *et al*. Effect of aerobic training on forced expiratory airflow in exercising asthmatic humans. *J Appl Physiol* 1987;**63**:1230–5.
13 Fitch KD, Morton AR, Blanksby BA. Effect of swimming training on children with asthma. *Arch Dis Child* 1976;**51**:190–4.
14 American Thoracic Society. Definition and classification of chronic bronchitis, asthma and pulmonary emphysema. *Am Rev Respir Dis* 1962;**85**:762–9.
15 Katch V, Weltman A, Sady S, *et al*. Validity of the relative percent concept for equating training intensity. *Eur J Appl Physiol* 1978;**39**:219–27.
16 Tanaka H. Predicting running velocity at blood lactate threshold from running performance tests in adolescent boys. *Eur J Appl Physiol* 1986;**55**:344–8.
17 Tanaka H, Shindo M. Running velocity at blood lactate threshold of boys aged 6–15 years compared with untrained and trained young males. *Int J Sports Med* 1985;**6**:90–4.
18 Chen WY, Horton DJ. Heat and water loss from airways and exercise-induced asthma. *Respiration* 1977;**34**:305–13.
19 Hendrickson CD, Lynch JM, Gleeson K. Exercise induced asthma: a clinical perspective. *Lung* 1993;**172**:1–14.
20 Anderton RC, Cuff MT, Frith PA, *et al*. Bronchial responsiveness to inhaled histamine and exercise. *J Allergy Clin Immunol* 1979;**63**:315–20.
21 Martin AJ, Landau LI, Phelan PD. Lung function in young adults who had asthma in childhood. *Am Rev Respir Dis* 1980;**122**:609–16.
22 Anderson SD, Daviskas E, Smith CM. Exercise-induced asthma: a difference in opinion regarding the stimulus. *Allergy Proc* 1989;**10**:215–26.
23 Lee TH, Brown MJ, Nagy L, *et al*. Exercise-induced release of histamine and neutrophil chemotactic factor in atopic asthmatics. *J Allergy Clin Immunol* 1982;**70**:73–81.
24 Eggleston PA, Kagey-Sobotka A, Schleimer RP, *et al*. Interaction between hyperosmolar and IgE-mediated histamine release from basophils and mast cells. *Am Rev Respir Dis* 1984;**130**:86–91.
25 Makker HK, Lau LC, Thomson HW, *et al*. The protective effect of inhaled leukotriene D_4 receptor antagonist ICI204,219 against exercise-induced asthma. *Am Rev Respir Dis* 1993;**147**:1413–8.
26 Manning PJ, Watson RM, Margolskee DJ, *et al*. Inhibition of exercise-induced bronchoconstriction by MK-571, a potent leukotriene D4-receptor antagonist. *N Engl J Med* 1990;**323**:1736–9.
27 Butler J, Kelly JG, O'Malley K, *et al*. β-adrenorecepter adaptation to acute exercise. *J Physiol* 1983;**344**:113–7.
28 Mäki T. Density and functioning of human lymphocytic β-adrenergic receptors during prolonged physical exercise. *Acta Physiol Scand* 1989;**136**:569–74.