Relation between response to exercise and diurnal variability of peak expiratory flow in primary school children

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Abstract

Background **Variability in peak expiratory flow (PEF) has been proposed as a simple method of screening for asthma in epidemiological studies. This study was designed to assess whether the bronchial response to exercise and the diurnal variation in PEF identified the same subjects.**

Methods **Bronchial response to a free running exercise test was assessed in a cohort of 918 seven year old children and was compared with variability of PEF as assessed by twice daily recordings for a one week period. Mini Wright peak flow meters were used throughout the study.**

Results **Baseline PEFs of both tests were highly correlated but there was no significant correlation between a response to exercise and variability of PEF. Of 33 children with a physician's diagnosis of asthma, 18 had at least one abnormal test, but only five children were abnormal in both tests, showing that the tests did not identify the same subjects.**

Conclusion **Increased variability of PEF, as well as a response to exercise, was associated with respiratory symptoms, but only a response to exercise was closely associated with atopy (defined as a positive skin test to any of seven aeroallergens).**

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Non-specific bronchial hyperresponsiveness is regarded as a central feature of asthma.[1] Hence, in most population based studies on asthma, bronchial hyperresponsiveness is determined by bronchial challenge tests. A high incidence of symptom free subjects can respond to such tests, particularly children.[2] Bronchial challenge by inhalation of cold air[3] or hypotonic solutions,[4] or by exercise,[5] none of which directly act on smooth muscle, have been suggested as being more specific for asthma than pharmacological challenge tests.[6] In studies that have compared the results of such measures of bronchial hyperresponsiveness to challenge with pharmacological substances some good,[7 8] and some poor[9 10] associations have been found. Variability of peak expiratory flow (PEF) corresponds to bronchial hyperresponsiveness measured by pharmacological challenge tests.[11] Recently assessment of variability of PEF has been proposed as a simple method to screen for asthma in epidemiological studies.[12] The aim of this report was to investigate whether response to exercise and increased variability of PEF identify the same subjects. For this purpose the relations of both tests to a physician's diagnosis of asthma, atopy, and respiratory symptoms were examined in a cohort of 918 school children.

Patients and methods

POPULATION SAMPLING

This report is based on cross sectional data from an ongoing cohort study on the development of asthma and allergy in childhood currently being conducted in south western Germany. Analyses were performed with data from the first survey in 1990/1991. The study was approved by the local ethics committee and also by local school authorities. To get a representative population sample, all parents from three cities in the vicinity of Freiburg whose children were entering elementary school were invited to participate. Children took home an explanatory letter and written consent was obtained from all parents before measurements were taken.

QUESTIONNAIRES

Questionnaires were distributed in the schools and filled out by the parents. We used a translated and modified version of an American Thoracic Society questionnaire.[13] Validation of the questionnaire in a separate study on 71 children seen at the outpatient clinic of the Children's Hospital, Freiburg showed that a physician's diagnosis of asthma was reported correctly in 14 of 16 cases. A parental history of asthma was recorded. Parents were asked whether a physician had ever diagnosed asthma in their child. Different questions were posed concerning respiratory symptoms of the child preceding the study year. Wheeze was defined as a positive answer to "Did you ever hear a wheezing or whistling noise during your child's breathing?" Respiratory symptoms at night were thought to be present when the child had cough or shortness of breath during the night or in the early morning. Cough after exercise was defined as cough after exercise or when exposed to cold air or fog. Children with a history of attacks of dyspnoea were referred to as children with shortness of breath. Those with a history of cough longer than 14 days after having a cold were designated as having a prolonged cough.

ALLERGY SKIN TEST

A standardised skin prick test with seven common allergens (ALK Laboratories Denmark; weeds, birch and hazel pollen, cat and dog dander, *Dermatophagoides pteronyssinus* and *D farinae*) and a positive (10 mg/ml histamine) and a negative (NaCl) control, was performed on the right forearm of all children. The smallest and the largest diameter of any weal was measured after 15 minutes and the arithmetic mean calculated. Any weal equal to or greater than 2 mm was scored positive. (A weal produced by the negative control was subtracted from the allergen weal beforehand.) Children with at least one positive reaction to any of the allergens were considered atopic.

EXERCISE TEST

A free running test was used to measure the response to exercise; the protocol was similar to that of Tsanakas *et al.*[14] Tests were performed in the school gymnasiums between October and November 1990, usually between 8.00 am and 1.00 pm. Two teams of observers, each comprising a doctor trained in pulmonary medicine, a nurse, and two students, supervised the tests. To avoid team effects observers switched between teams each day. Children who were currently taking treatment for asthma exercised with the others. Antiasthmatic treatment was not interrupted. The children underwent physical examination including measurement of height. Those with a cough or crackles on auscultation were thought to have a current respiratory illness. Children were then instructed in the use of the mini Wright peak flow meter (Clement Clarke Ltd, London). Five values were recorded before exercise and the highest used for analysis. Heart rate was measured with a telemetric device (sport tester) before and immediately after exercise.[15] Children were instructed to run as quickly as possible. After six minutes of continuous exercise they were called back to sit down. The PEF was recorded three, six, and nine minutes after the exercise period. The highest of three readings was accepted each time.

COLLECTION OF PEF DATA

After the exercise test the children's homes were visited between December 1990 and March 1991. Children and their parents were instructed in the correct use of the mini Wright peak flow meter. Parents were asked to record the highest of the three readings that their child achieved twice daily (7.00–9.00 am and 4.00–7.00 pm). Tests were performed in a standing position. Measurements were recorded on a specially designed sheet with the verbal instructions reinforced. The importance of adhering to the same time for the measurements was emphasised and parents were encouraged to insert blanks rather than inaccurate data. Peak flow meters were collected after one week and sheets checked to see whether parents had filled in the data according to instructions. The parents were asked to report on their child's respiratory symptoms during the study week. Current respiratory illness was defined as cough on more than two days during the study week.

DATA ANALYSIS

The mean (SD) response to exercise expressed as the percentage change from resting PEF was −3·82% (8·12%) at three minutes, −1·45% (8·19%) at six minutes, and +0·08% (8·41%) at nine minutes after exercise. Hence, the change in PEF from baseline to the value three minutes after exercise was used to describe the bronchial response after exercise.

As an index of variability of PEF we calculated for each day the amplitude (higher value − lower value) as a percentage of the mean PEF.[16] Diurnal variability in PEF was calculated as the average amplitude as a percentage of the mean for the observation time for those children who had measured their PEF twice daily for at least five days. Because of the skewed distribution of average amplitude as a percentage of mean, Spearman's rank correlation coefficient was used to assess the association between a response to exercise and variability of PEF.

To define cut off points that identify equal proportions of children (the 10% most reactive) for both tests, percentiles were calculated for the distribution of change in PEF after exercise and average amplitude as a percentage of the mean. For change in PEF after exercise the value of the 10% percentile could not be precisely determined because of a small digit preference. Therefore, cut off points were chosen at 9·7% of each distribution. These points correspond to a $\leqslant -12{\cdot}6\%$ change in PEF after exercise and a $\geqslant 12{\cdot}4\%$ average amplitude as a percentage of mean.

For each of the two tests sensitivity, specificity, and positive and negative predictive values, as well as accuracy (ratio of true positive + true negative tests by all tests) were calculated for a physician's diagnosis of asthma. Analyses were performed with the statistical analysis system (SAS).

Results

Of 2604 families contacted 1812 (69·6%) participated. The children's mean age was 7·3 (SD 0·4) years. Permission to perform the exercise test was refused by 226 parents, 104 children were absent, 15 children refused to participate, and six children were unwilling to complete the exercise. Hence data for 1461 (81%) children were available. In 98·8% of these the mean heart rate increased to 170 beats/min or more, a work load sufficient to elicit bronchoconstriction in sensitive subjects.[17]

Measurements of PEF were performed by 1237 children. Revision of PEF data sheets showed that for eight children PEF values were the same on most occasions. As these values were possibly filled in without measurement, they were excluded from further

Table 1 Characteristics of subjects with complete data for the exercise test and for PEF measurements

	Exercise test (n = 1461) No (%)	*PEF records (n = 991) No (%)*	*Total sample (n = 1812) No (%)*
Boys	696 (47·6)	474 (47·8)	882 (48·7)
Girls	765 (52·4)	517 (52·2)	930 (51·3)
Asthma (diagnosed by physician)	48 (3·3)	35 (3·5)	63 (3·5)
Atopy (skin test positive)	297* (21·8)	214† (23·6)	320 (21·8)
Current respiratory illness (for definition see methods)	304 (20·8)	143 (14·6)	—
Family history of asthma (father or mother)	117 (8·0)	81 (8·2)	134 (7·4)

*Number of children tested—1363.
†Number of children tested—908.

analyses. Hence, data for 1229 children remained. Diurnal variability of PEF could be calculated for 991 (80·6%) children, 140 (11·4%) had performed only four days of PEF measurement twice daily and 98 (8·0%) children only one to three days. Mean average amplitude as a percentage of mean was 7·3% (fifth percentile 2·3%; median 6·3%; 95th percentile 15·8%).

Complete information on results of the exercise test as well as complete PEF data was available for 918 children. There were only small differences between participants in the two tests and the total sample with respect to important respiratory health variables (table 1). All further analyses were performed for the 918 children with complete data for both tests.

Of these children, 89 (9·7%) were classified as abnormal in each test and 164 (17·9%) in one of the two tests. Only 14 children (1·5%) were abnormal in both tests. The mean difference between PEF averaged for the week of PEF measurements and the corresponding resting PEF before exercise was 22·24 (SD 29·96) l/min, most likely due to growth. Spearman's correlation coefficient between both baseline measurements was 0·69 (p = 0·0001), but there was no significant correlation between fall of PEF after exercise and variability of PEF as assessed by average amplitude as a percentage of the mean ($r = -0·05$; p = 0·1) (fig 1).

Of 33 children with a physician's diagnosis of asthma 12 had a positive response to the exercise test and 11 showed increased variability of PEF. If the tests were regarded as screening tests for asthma, these results would represent a sensitivity of 36·4% for the exercise test and of 33·3% for increased variability of PEF (table 2). Specificity would be 91·3% for the exercise test and 91·2% for increased variability of PEF. Eighteen children with a physician's diagnosis of asthma had at least one abnormal test and five were abnormal in both tests. In 739 of 885 children (83·5%) without asthma both tests were normal.

Figure 2 shows the association between a response to the exercise test or an increased variability of PEF and respiratory symptoms or atopy. A higher frequency of increased

Table 2 Test criteria for exercise challenge and PEF variability as screening tests for asthma diagnosed by a physician (lifetime prevalence)

	Exercise test	*PEF variability*
Sensitivity	36·4	33·3
Specificity	91·3	91·2
Positive predictive value	13·5	12·4
Negative predictive value	97·5	97·4
Accuracy	89·3	89·1

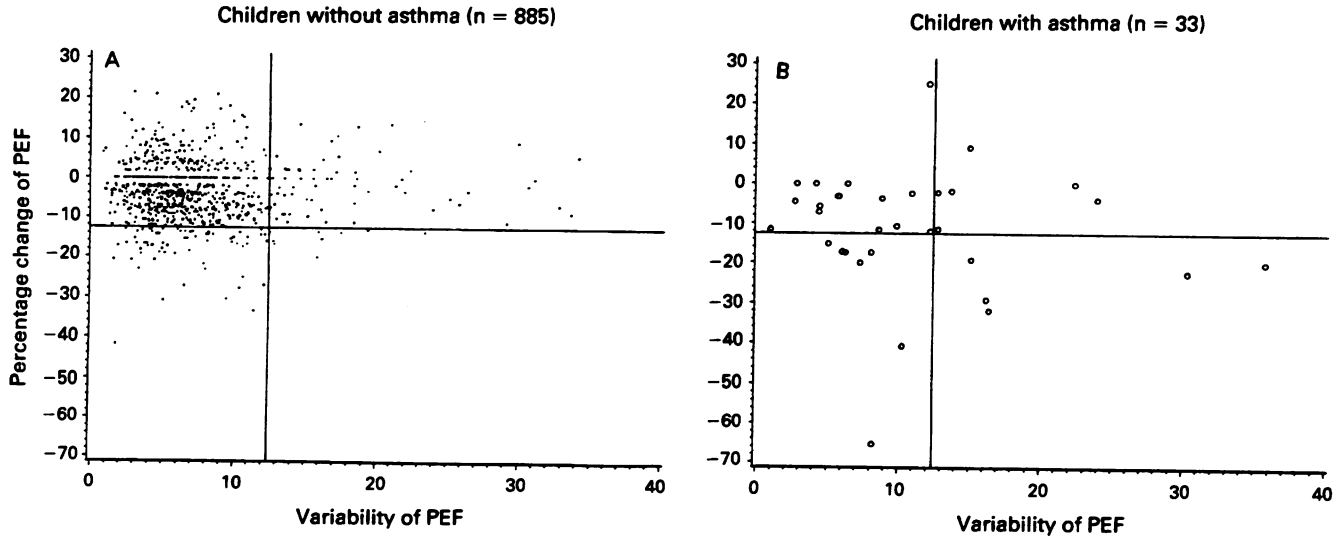

Figure. 1 Response to exercise and variability of PEF in 918 seven year old children (A) with or (B) without a physician's diagnosis of asthma. Variability of PEF = amplitude (higher value − lower value) as a percentage of the mean averaged over one week. Percentage change of PEF = percentage change from resting PEF to PEF three minutes after exercise. Vertical reference line represents normal limits for PEF variability and horizontal reference line normal limits for response to exercise.

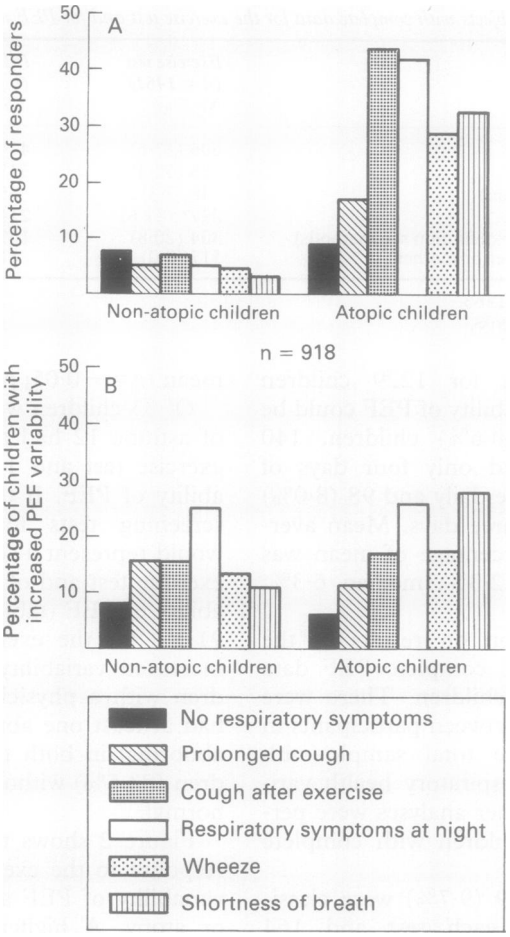

Figure 2 Association between history of respiratory symptoms and (A) response to exercise test; (B) increased variability of PEF. Atopy defined as skin test positivity to any of seven aeroallergens.

PEF variability was found in symptomatic children with or without atopy, but the proportion of responders to exercise was much higher among the 205 atopic children than among non-atopic children. Response to exercise was found in 9·0% of atopic children without respiratory symptoms compared with 28·7% of symptomatic atopic children. For non-atopic children the corresponding values were 7·7% and 4·7% respectively. The prevalences of increased variability of PEF were 6·3% in atopic children without symptoms and 14·9% in atopic children with symptoms, whereas in non-atopic children prevalences were 8·1% and 12·7% respectively.

Of children with a current respiratory illness 17·3% showed increased variability of PEF compared with 8·2% of children without a current respiratory illness ($p < 0·01$). No such association was found between a current respiratory illness and the response to exercise.

Discussion

Determination of bronchial hyperresponsiveness by an exercise test on the one hand and diurnal variability of PEF on the other produced a similar sensitivity and specificity to a physician's diagnosis of asthma in seven to eight year old children. About one third of those with asthma exceeded our chosen normal limits in each test, but only five out of 33 children were abnormal in both tests, showing that the two tests did not identify the same asthmatic children.

We do not think that a change in the respiratory health of the children between the two tests could have caused our findings. Questionnaires were distributed during the spring of 1990 and both the exercise test and measurement of PEF took place during the autumn and winter of 1990/1991. Lung function was measured with mini Wright peak flow meters throughout the study. A high correlation between baseline PEF values in both tests indicated that measurement error had not substantially contributed to our findings. The stronger association between atopy and the exercise test is unlikely to be due to change in exposure to allergens between the tests. Exposure to pollen is low in autumn and winter, whereas exposure to dust mites has been shown to be unaffected by season in Germany.[18]

A different definition for current respiratory illness was employed for both tests as the exercise test was performed on a single day, whereas the measurement of variability of PEF lasted one week. There was, however, a positive association between a current respiratory illness and variability of PEF but not with response to exercise, which might not be explained exclusively by different definitions. Season can influence the prevalence of respiratory viral infection, but the prevalence itself cannot influence the relations to both tests. Different viruses, however, might be involved at different seasons and affect the airways to a variable extent (for example respiratory syncytial virus). Such an effect cannot be ruled out completely.

Asthma can be defined as variable airflow obstruction over short periods.[19] In selected populations it has been shown that increased variability of PEF[11] corresponds to bronchial hyperresponsiveness as assessed by pharmacological challenge tests. Clifford *et al* performed methacholine challenge tests in seven and 11 year old children and found a higher prevalence of wheezy children with bronchial hyperresponsiveness unassociated with atopy in the younger age group.[20] They speculated about a subgroup of young children with non-allergic asthma, who are characterised by an increased susceptibility to viral infections and varying levels of bronchial hyperresponsiveness and lose their respiratory symptoms as they grow older. We have no information on the incidence of viral infections in our children. Our data suggest an association between an acute respiratory illness and increased variability of PEF but not with a positive response to exercise. This observation, however, should not be overemphasised because different definitions for acute respiratory illness were used.

Determination of variability of PEF[12] as well as exercise challenge tests[14] were pro-

posed as asthma screening tests. Our findings suggest that in population based studies different subjects are identified, depending on the test used.

It seems that a response to exercise corresponds to allergic airways disease, whereas increased variability of PEF might be linked to viral infection in susceptible children. This finding supports the hypothesis that asthma is a heterogenous syndrome in paediatric populations.[10 20–23] In epidemiological research on asthma the choice of the appropriate screening test should depend on the objectives of the study.

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