

Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma: A 5-year prospective follow-up study of 42 highly trained swimmers

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Background: Mild eosinophilic airway inflammation and bronchial hyperresponsiveness—ie, mild asthma—have been shown to affect a high proportion of endurance athletes. The persistence of airway inflammation, bronchial hyperresponsiveness, and asthma in this population is not known, however, inasmuch as follow-up studies of athletes' asthma have not been performed.

Objective: The purpose of this study was to investigate effect of finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma.

Methods: Forty-two elite competitive swimmers, most of them from the Finnish national team (37/42; 88%), were followed for 5 years in a prospective manner. All of the swimmers completed questionnaires and underwent resting spirometry, histamine challenge testing, and skin prick tests at baseline and at follow-up. Twenty-nine swimmers (69%) also gave induced sputum samples on both occasions. Sixteen (38%) of the swimmers had continued their competitive careers during follow-up (active swimmers), but 26 (62%) had stopped competing more than 3 months before the follow-up examination (past swimmers).

Results: Bronchial responsiveness was increased in 7 (44%) of the 16 active swimmers at baseline and in 8 (50%) of the 16 active swimmers at follow-up; it was increased in 8 (31%) of the 26 past swimmers at baseline and in 3 (12%) of the 26 past swimmers at follow-up (McNemar test, $P = .025$). The difference in the change in bronchial hyperresponsiveness between the study groups was significant (likelihood ratio test, $P = .023$). Current asthma (defined as bronchial hyperresponsiveness and exercise-induced bronchial symptoms monthly) was observed in 5 (31%) of the active swimmers at baseline and in 7 (44%) of the active swimmers at follow-up; of the past swimmers, it occurred in 6 (23%) at baseline and in 1 (4%) at follow-up (McNemar test, $P = .025$). The difference in the change in current asthma between the study groups was significant

(likelihood ratio test, $P = .0040$). The sputum differential cell counts of eosinophils and lymphocytes increased significantly during the follow-up period in the active swimmers (Wilcoxon signed rank sum test; $P = .033$ and $P = .0029$, respectively); in the past swimmers, the sputum differential cell counts of eosinophils tended to decrease during the follow-up period ($P = .17$), whereas the differential cell counts of lymphocytes did not change significantly. The changes in the sputum differential cell counts of eosinophils between the study groups differed significantly (Mann-Whitney U test, $P = .019$).

Conclusion: In swimmers who had stopped high-level training, bronchial hyperresponsiveness and asthma attenuated or even disappeared. Mild eosinophilic airway inflammation was aggravated among highly trained swimmers who remained active during the 5-year follow-up. Our results suggest that athletes' asthma is partly reversible and that it may develop during and subside after an active sports career. (*J Allergy Clin Immunol* 2002;109:962-8.)

Key words: Asthma, athletes, airway inflammation, bronchial hyperresponsiveness, swimming, sports medicine

In the summer Olympic games, 4% to 15% of participating athletes have shown evidence of asthma or use of antiasthmatic medication.¹⁻³ Asthma is most common among those competing in endurance events, such as cycling, swimming, cross-country skiing, and long-distance running.⁴⁻⁸ Of competitive swimmers, 36% to 79% have shown bronchial hyperresponsiveness and 33% have shown asthma.^{3,6,7,9} Mild eosinophilic airway inflammation has been found to affect both highly trained swimmers¹⁰ and cross-country skiers.¹¹

Exercise might increase ventilation by up to 200 L/min for short periods in speed and power athletes and for longer periods in endurance athletes such as long-distance runners and swimmers.¹² When swimming for up to 30 h/w, competitive swimmers inhale large amounts of air immediately above the water surface and are exposed to large quantities of chlorine derivatives from swimming pool disinfectants.¹³⁻¹⁵

Follow-up studies on athletes' asthma have not been performed.¹² The persistence of bronchial hyperresponsiveness and airway inflammation after athletes discontinue their competitive careers has therefore remained unclear.

Our aim here was to prospectively follow 42 highly trained swimmers to investigate the effects of continuing

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Abbreviation used

PD₁₅FEV₁: Dose of histamine causing a 15% fall in FEV₁

or finishing an elite sports career on bronchial hyperresponsiveness, airway inflammation, and asthma. By comparing swimmers who continued intense training with swimmers who stopped, we tested the hypothesis that symptoms indicating mild asthma might result from high swimming activity and might thus be partly reversible.

METHODS

Study design

This prospective, 5-year follow-up study consisted of a baseline examination administered between February and April 1996 and a follow-up examination administered between February and April 2001. Forty-two swimmers were recruited from the Finnish national team and from a swimming club in the city of Helsinki during the World Cup Race, held in Espoo, Finland, on January 27 and 28, 1996.⁷ The swimmers were given a brief description of the purpose of the study. Forty-two (79%) of the 53 swimmers who attended the information session took part in the baseline study; these represented 49% of the swimmers in the national team or in the swimming club. Eleven (21%) of the 53 eligible swimmers were unable to participate in further studies. Three of them reported having physician-diagnosed asthma, which they considered to be well controlled. The remaining 42 swimmers all participated in the study both at baseline and at follow-up. Twenty-nine (69%) of them gave induced sputum samples at baseline and at follow-up. The mean (SD) follow-up period was 5.0 (0.2) years.

The baseline and follow-up examinations consisted of similar 2-day protocols. On their first visit, the swimmers completed 2 questionnaires, one pertaining to respiratory symptoms¹⁶ and the other pertaining to allergies⁷; they were then interviewed and clinically examined by one of the authors (I.H.) and underwent skin prick testing, resting spirometric examination, and histamine challenge testing. On the second visit (within 1 week of the first visit but not within the first 24 hours), induced sputum samples were obtained from the subgroup of 29 swimmers. Pulmonary function tests or sputum induction were not performed if a swimmer reported a history of upper or lower respiratory tract infection within 4 weeks before the study.

Subjects

Forty-two elite swimmers (37 from the Finnish national teams) who participated in the study gave their written informed consent, and the study protocol was approved by the local ethics committee. At baseline, all swimmers were active competitors. At follow-up, the swimmers were divided into 2 groups: (1) active swimmers (N = 16), who had trained throughout the follow-up period or had stopped training less than 3 months before the examination; (2) past swimmers (N = 26), who had stopped training more than 3 months before the follow-up examination. The clinical characteristics of the study groups are given in Table I.

A history of physician-diagnosed asthma was reported by 3 (19%) of the active swimmers (2 cases had been diagnosed during the athletes' active competitive careers) and 5 (19%) of the past swimmers (4 cases had been diagnosed during the athletes' active competitive careers) at baseline. Five active swimmers and 1 past swimmer currently used inhaled corticosteroids and inhaled short-acting β_2 -agonists when needed; in addition, 1 past swimmer cur-

rently used inhaled β_2 -agonists when needed. Two past swimmers had stopped using inhaled corticosteroids and inhaled β_2 -agonists, and 2 past swimmers had stopped inhaling β_2 -agonists during the follow-up period.

Questionnaires

The athletes completed 2 questionnaires. One of them, a respiratory symptom questionnaire, contained questions about the diagnosis of asthma and allergy made previously by a physician, use of antiasthmatic medication, family history of asthma and allergic rhinitis, exercise-induced bronchial symptoms, competitive status, and smoking habits.¹⁶ The other questionnaire, which pertained to allergies, inquired about symptoms of rhinitis (running or stuffy nose), conjunctivitis (itching or red eyes), and eczema; allergens (pollens, animal dander, house dust, food, drugs) causing symptoms; and antiallergic medication.⁷ Answers to the questionnaires were confirmed in personal interviews.

Resting spirometry, histamine challenge testing, and skin prick testing

Resting spirometry was carried out according to the recommendations of the American Thoracic Society¹⁷ with a flow-volume spirometer (Medikro, Medikro Oy, Kuopio, Finland). Values are expressed as percents of reference (predicted) values for adult Finns.¹⁸

Histamine challenges were performed through use of the dosimetric method with controlled tidal breathing.¹⁹ Noncumulative histamine doses of 0.025, 0.1, 0.4, and 1.6 mg were inhaled and FEV₁ values measured 90 seconds after each inhalation. The dose of histamine that caused a 15% fall in FEV₁ (PD₁₅FEV₁) was determined by logistic interpolation.

Skin prick tests were made with 10 allergen extracts (Soluprick SQ, 10 HEP, ALK, Copenhagen, Denmark) and with positive (histamine dihydrochloride, 10 mg/mL) and negative (solvent) control solutions. The following airborne allergens were used: birch, timothy, meadow fescue, and mugwort pollen; horse, cat, dog, and cow dander; and mold spores of *Cladosporium herbarum*. The mite *Dermatophagoides pteronyssinus* was also used.

Sputum examination

Sputum was induced without pretreatment by inhalation of hypertonic saline solution generated by an ultrasound nebulizer (Spira Ultra, Hengityshoitokeskus, Hämeenlinna, Finland) for 15 minutes.²⁰

Sputum was examined as described previously.¹⁰ Differential cell counts of intact bronchial epithelial cells and leukocytes were made by counting at least 400 nonsquamous cells. The cell counts, made by 2 investigators (I.H. and P.R.) blinded to the clinical characteristics of the study subjects, were averaged to yield the final percents reported here.

Definitions

The definitions used have been described previously.⁷ Briefly, a subject was classified as atopic if any allergen caused a wheal of ≥ 3 mm in diameter while control solutions gave expected results. Hay fever was defined as at least 1 positive skin test reaction to pollen associated with symptoms of rhinoconjunctivitis during the spring or summer. Current asthma was defined as increased bronchial responsiveness (PD₁₅FEV₁ ≤ 1.6 mg) together with at least 1 exercise-induced bronchial symptom monthly during the last year (shortness of breath, wheeze, or cough). Total asthma was defined as current asthma or asthma diagnosed previously by a physician.⁷ Sputum eosinophilia was defined as a sputum differential eosinophil count of $>2\%$.²¹

TABLE I. Clinical characteristics of study subjects

Characteristic	All swimmers (N = 42)	Active swimmers (N = 16)	Past swimmers (N = 26)
Sex (M/F)	16/26	8/8	8/18
Mean (SD) age (y)	23.9 (2.6)	24.0 (2.8)	23.8 (2.6)
Mean (SD) duration of active sports career (y)	12.0 (3.8)	14.8 (3.4)	10.2 (2.9)
Mean (SD) time since finishing sports career (y)	—	—	3.3 (1.1)
Mean (SD) training amount in previous year	—	1870 (610) km	170 (140) h
History of physician diagnosed asthma (n)	8	3	5
Current use of inhaled steroids (n)	6	5	1
Family history of asthma (n)	8	3	5
Mean (SD) FEV ₁			
In liters	4.69 (0.91)	4.80 (0.88)	4.62 (0.94)
As percent of predicted*	106.6 (9.5)	107.7 (10.5)	105.9 (9.0)

*Reference values for adult Finns.¹⁸TABLE II. Occurrence of atopy, hay fever, increased bronchial responsiveness, FEV₁/FVC ratio, current asthma, and total asthma at baseline and follow-up

Characteristic	All swimmers (N = 42)		Active swimmers (N = 16)		Past swimmers (N = 26)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Exercise-induced bronchial symptoms: n (%)	24 (57)	22 (52)	10 (63)	13 (81)	14 (54)	9 (38)
Increased bronchial responsiveness: n (%)	15 (36)	11 (26)	7 (44)	8 (50)	8 (31)	3 (12)*†
Mean (SD) FEV ₁ /FVC ratio						
In percent	83.6 (6.7)	81.2 (6.8)	81.8 (5.8)	79.2 (5.6)	84.6 (7.1)	82.5 (7.3)
As percent of predicted§	93.7 (7.8)	93.1 (7.8)	91.3 (7.0)	90.8 (7.2)	95.2 (8.0)	94.5 (8.0)
Current asthma: n (%)	11 (26)	8 (19)	5 (31)	7 (44)	6 (23)	1 (4)*‡
Total asthma: n (%)	12 (29)	15 (36)	5 (31)	9 (56)*	7 (27)	6 (23)†
Atopy: n (%)	21 (50)	23 (55)	9 (56)	11 (69)	12 (46)	12 (46)
Hay fever: n (%)	12 (29)	9 (21)	6 (38)	4 (25)	6 (23)	5 (19)

*Within-group comparison; McNemar test; $P < .05$.†Between-groups comparison; likelihood ratio test; $P < .05$.‡Between-groups comparison; likelihood ratio test; $P < .01$.§Reference values for adult Finns.¹⁸

Statistical analysis

Differences in the occurrences within the study groups were examined through use of the McNemar test. Changes in categoric variables between the study groups were examined by means of the likelihood ratio test (see Appendix). The Wilcoxon signed rank sum test was used to examine differences in continuous variables within study groups, and the Mann-Whitney U test was used in the analysis between study groups (StatXact 4, Cytel Software, Cambridge, Mass). Two-tailed P values of .05 or below were considered significant.

RESULTS

None of the swimmers had a history of upper or lower respiratory tract infection within 4 weeks before the baseline or follow-up examination. Exercise-induced bronchial symptoms monthly during the last year were reported by 10 (63%) of the active swimmers at baseline and by 13 (81%) of the active swimmers at follow-up (McNemar test, $P = .18$). Similarly, symptoms were reported by 14 (54%) of the past swimmers at baseline and by 9 (38%) of the past swimmers at follow-up (McNemar test, $P = .21$).

Increased bronchial responsiveness occurred in 7 (44%) of the active swimmers at baseline and in 8 (50%) of the active swimmers at follow-up. Of the past swimmers, it occurred in 8 (31%) at baseline and in 3 (12%)

at follow-up (McNemar test, $P = .025$; Table II). The difference in the change in bronchial hyperresponsiveness between the study groups was significant (likelihood ratio test, $P = .023$). The PD₁₅FEV₁ values increased significantly among the past swimmers (Wilcoxon signed rank sum test, $P = .017$; Fig 1).

Current asthma was recorded in 5 (31%) of the active swimmers at baseline and in 7 (44%) of the active swimmers at follow-up. Of the past swimmers, it occurred in 6 (23%) at baseline and in 1 (4%) at follow-up (McNemar test, $P = .025$). The difference in the change in current asthma between the study groups was significant (likelihood ratio test, $P = .0040$). The occurrence of total asthma increased from 31% (5/16) at baseline to 56% (9/16) at follow-up in the active swimmer group (McNemar test, $P = .046$), but there was no significant change in the past swimmer group during follow-up. The difference in the change in total asthma between the study groups was significant (likelihood ratio test, $P = .028$).

Atopy occurred in 9 (56%) of the active swimmers at baseline and in 11 (69%) at follow-up; it was found in 12 (46%) of the past swimmers on both occasions. The occurrence of hay fever tended to decrease in both groups during the follow-up period.

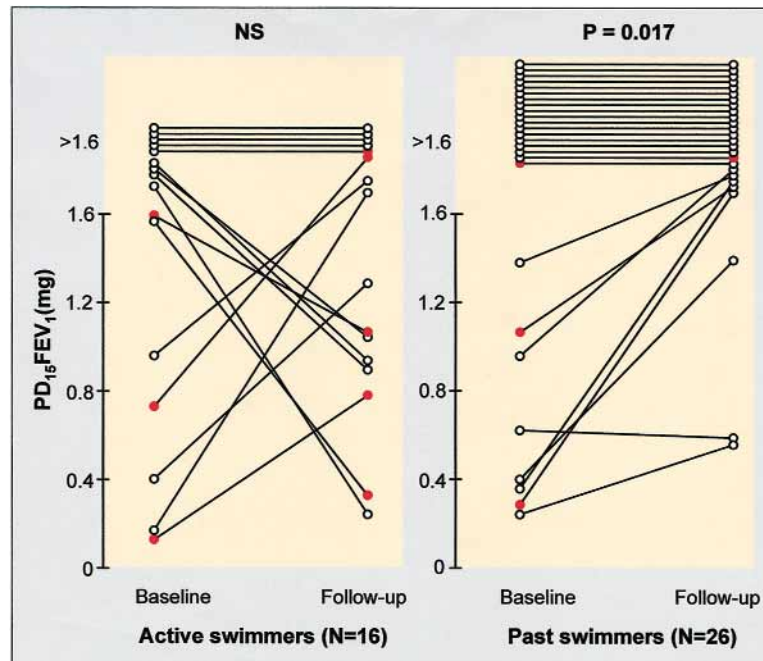


FIG 1. Results of histamine challenge tests in active and past swimmers at baseline and at follow-up examinations. *Closed circles* indicate current use of inhaled steroids.

One swimmer (from the past swimmer group) at baseline and 2 swimmers (1 from each group) at follow-up failed to give adequate sputum samples. None of the subjects experienced any adverse effects during sputum induction.

Sputum eosinophilia ($\geq 2\%$) was found in 1 (6%) of the active swimmers at baseline and in 6 (38%) of the active swimmers at follow-up (McNemar test, $P = .059$). Of the past swimmers, it was found in 5 (19%) at baseline and in 2 (8%) at follow-up.

The sputum differential cell counts of eosinophils and lymphocytes increased significantly during the follow-up period in the active swimmer group (Wilcoxon signed rank sum test, $P = .033$ and $P = .0029$; Fig 2, Table III). In the past swimmer group, the sputum differential cell counts of eosinophils tended to decrease during the follow-up period (Wilcoxon signed rank sum test, $P = .17$), but there was no change in the differential cell count of lymphocytes. The changes in the sputum differential cell counts of eosinophils between the study groups differed significantly (Mann-Whitney U test for the differences, $P = .019$). The sputum differential cell counts of neutrophils, macrophages, and bronchial epithelial cells did not change during follow-up.

No correlation was found between exercise-induced bronchial symptoms and the percentage of sputum eosinophils. Of the 6 swimmers currently using inhaled steroids, 1 showed sputum eosinophilia ($>2\%$) at baseline and 2 showed it at follow-up. In addition, 4 of these swimmers showed increased bronchial responsiveness at baseline and 3 showed it at follow-up.

DISCUSSION

This study is observational, because adequate control subjects are very difficult to include in this kind of long-term follow-up. However, a natural intervention occurred in that 38% of the study subjects continued their sporting careers and 62% discontinued their careers. Recruitment of the study subjects was carefully recorded. None of the subjects was lost during follow-up. The follow-up study was performed through use of exactly the same methods and definitions that were used for the baseline measurements.⁷ Both the baseline and the follow-up measurements were made at the same time of year. The repeatability of the histamine challenge test¹⁹ and the sputum inflammatory differential cell counting have been reported earlier.²² Current asthma was defined as increased bronchial responsiveness and exercise-induced bronchial symptoms. Symptoms induced by exercise were selected for the definition because they are the first signs of asthma.²³ Even athletes who had finished their sports careers continued to be physically active (mean, 3 h/wk) and would thus easily have noticed symptoms caused by exercise.

In accordance with previous findings,^{6,9} the occurrence of bronchial hyperresponsiveness was high in active swimmers at baseline. Its occurrence and severity remained the same during follow-up. However, 5 of the active swimmers were currently using inhaled steroids, which certainly affected the results, whereas only 1 past swimmer was currently inhaling steroids. In contrast, 8 (31%) of the past swimmers showed increased bronchial

Asthma, rhinitis,
other respiratory
diseases

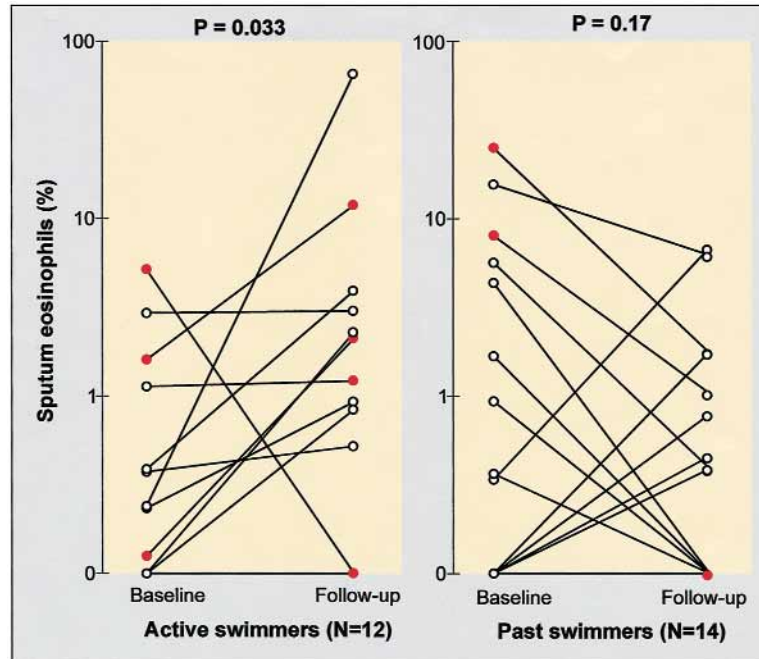


FIG 2. Differential cell counts of eosinophils (percents) in baseline and follow-up samples of active and past swimmers (logarithmic scale). Closed circles indicate current use of inhaled steroids.

TABLE III. Sputum differential cell counts in active and past swimmers

Characteristic	All swimmers (N = 29)		Active swimmers (N = 13)		Past swimmers (N = 16)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Total cell count ($10^3/\text{mg}$)	6.6 (0.1-47.5)	2.4 (0.5-6.0)	4.1 (0.1-17.6)	2.6 (0.5-6.0)	8.9 (0.3-47.5)	2.2 (0.7-4.3)
Eosinophils (%)	2.7 (0-25.4)	4.2 (0-65.7)	0.9 (0-5.2)	7.7 (0-65.7)*	4.2 (0-25.4)	1.3 (0-6.9)†
Neutrophils (%)	54.7 (1.7-92.5)	51.5 (1.9-81.2)	57.7 (7.0-92.5)	54.1 (29.4-70.1)	52.1 (1.7-87.8)	49.4 (1.9-81.2)
Lymphocytes (%)	0.7 (0-3.5)	2.1 (0-4.8)‡	0.5 (0-1.9)	2.7 (0.4-4.8)‡	0.9 (0-3.5)	1.6 (0-4.3)
Macrophages (%)	38.4 (1.7-93.0)	41.0 (0.9-94.2)	40.5 (6.4-93.0)	33.8 (0.9-59.7)	36.6 (1.7-68.5)	46.7 (16.0-94.2)
Bronchial epithelial cells (%)	0.3 (0-2.7)	1.3 (0-6.7)	0.4 (0-2.7)	1.7 (0-6.8)	0.2 (0-1.7)	0.9 (0-5.3)

*Within-group comparison; Wilcoxon signed rank sum test; $P < .05$.

†Between-groups comparison; Mann-Whitney test for differences; $P < .05$.

‡Within-group comparison; Wilcoxon signed rank sum test; $P < .005$.

responsiveness at baseline, whereas only 3 (12%) showed it at the follow-up examination.

Kujala et al²⁴ studied 1282 former Finnish elite athletes (including 205 endurance sports athletes) and 777 control subjects matched for age, sex, and area of residence. The occurrence of asthma in the former athletes did not differ from that seen in the controls. However, many things have changed during the last 30 years that could explain the discrepancy between former and current athletes: the occurrence of asthma has increased 8-fold in Finland,²⁵ training volumes have increased, records have improved, and indoor training has become more important. In addition, our results suggest that bronchial hyperresponsiveness and asthma might disappear—that is, that these conditions are reversible—after elite athletes finish high-level training.

Mild eosinophilic airway inflammation has been shown to affect swimmers¹⁰ and cross-country skiers.¹¹ Karjalainen et al¹¹ could not show any correlation

between airway inflammatory cell counts and bronchial hyperresponsiveness. Similarly, we could not find any correlation between sputum eosinophil percentage and exercise-induced bronchial symptoms or bronchial hyperresponsiveness. However, the eosinophilic airway inflammation tended to attenuate during follow-up in swimmers who finished their sports careers during the follow-up period. During the same period, the occurrence of exercise-induced bronchial symptoms tended to decrease.

Drobnik et al¹⁴ measured the chlorine gas concentration 10 cm above the surface of water at 4 swimming pools in Spain. They found a mean chlorine gas concentration of 0.42 mg/m^3 of air and calculated that during a 2-hour training period a swimmer might be exposed to an amount of chlorine (4-6 g) that exceeds the recommendation of the National Institute for Occupational Safety and Health (US Department of Health, Education, and Welfare) for a worker with 8-hour exposure.¹⁴

The quality of water inside training pools in Finland has been examined.²⁶ Finnish swimming pools are disinfected mainly with hypochlorite liquid, but ozonation is also used. However, published data on chlorine gas concentration measurements above the surface of water at swimming pools does not exist in Finland. Repeated and strong or accidental exposure to chlorine gas might cause asthma symptoms, airflow obstruction, and increased bronchial responsiveness to methacholine without a latency period.²⁷ In such cases, histologic analysis of the bronchial mucosa has shown a thickened basement membrane, eosinophilic inflammation, and a relative lack of T lymphocytes.²⁷ Competitive swimmers inhale and microaspirate large amounts of air immediately above the water surface and are thus exposed to chlorine derivatives from swimming pool disinfectants.¹²⁻¹⁵ Inhalation of hypotonic liquid might have additive effects. This exposure could partially explain the mild eosinophilic airway inflammation that developed or was aggravated in swimmers who continued their sports career.

Sue-Chu et al²⁸ investigated the occurrence of lymphoid aggregates (follicle-like clusters of more than 50 cells) by using endobronchial biopsies in 44 cross-country skiers and 12 controls. They found lymphoid aggregates in 28 (64%) of the skiers and in 3 (25%) of the controls. The aggregates occurred more frequently in skiers who were using β_2 -agonists and who had bronchial hyperresponsiveness, but they were not associated with a history of respiratory allergy or asthma-like symptoms. In our study, the sputum differential cell counts of lymphocytes increased significantly during follow-up in the active swimmer group. The role of lymphocytic airway inflammation remains unclear in athletes' asthma.

In conclusion, in swimmers who had stopped high-level training, bronchial hyperresponsiveness and asthma attenuated or even disappeared. In contrast, mild eosinophilic airway inflammation was aggravated among highly trained swimmers who continued intensive training during the 5-year follow-up. Therefore, this study supports the hypothesis that symptoms indicating mild asthma result from high swimming activity and are partly reversible.

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APPENDIX

The likelihood ratio test for the difference in the change between time points (t) and ($t + 1$) in a categorical variable X (r categories) between the study groups (g groups). The test statistic follows χ^2 distribution with $r \cdot (r - 1) \cdot (g - 1)$ degrees of freedom and is based on Wilks's lambda criterion:

$$-2 \cdot \log \lambda = -2 \cdot \sum_{k=1}^g \sum_{i=1}^r \sum_{j=1}^r n_{ij}^{(k)} \left[\log_e \frac{\sum_{k=1}^g n_{ij}^{(k)}}{\sum_{k=1}^g n_i^{(k)}} - \log_e \frac{n_{ij}^{(k)}}{n_i^{(k)}} \right],$$

where $n_{ij}^{(k)}$ is the number of those subjects belonging to the group k who were in the category i of the variable X at the time point (t) and in the category j of the same variable at the time point $(t + 1)$.

		Time $(t + 1)$			
X		x_1	\dots	x_r	Σ
Time (t)	x_1	$n_{11}^{(k)}$	$n_{12}^{(k)}$	$n_{1r}^{(k)}$	$n_1^{(k)}$
	x_2	$n_{21}^{(k)}$	$n_{22}^{(k)}$ \dots	\cdot	
	\cdot	\cdot	\cdot	\cdot	
	\cdot	\cdot	\cdot	\cdot	
x_r	$n_{r1}^{(k)}$	\dots	$n_{rr}^{(k)}$	$n_r^{(k)}$	

Asthma, rhinitis,
 other respiratory
 diseases