

Respiratory pathophysiologic responses

Asthma and increased bronchial responsiveness in elite athletes: Atopy and sport event as risk factors

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Background: High prevalence of bronchial hyperresponsiveness and asthma has been found in cross-country skiers. There is limited evidence that asthma and bronchial responsiveness would be common also in athletes with summer events.

Objectives: The objective of this study was to investigate occurrence of and risk factors for increased bronchial responsiveness and asthma in elite athletes with summer events and to compare their results with those of control subjects. **Methods:** Forty-nine speed and power athletes (mean age 21.1 years, range 16 to 31), 71 long-distance runners (mean age 26.6 years, range 16 to 39), 42 swimmers (mean age 18.6 years, range 14 to 25), and 45 control subjects (mean age 26.7 years, range 21 to 37) were studied. The subjects answered questionnaires and were given a resting spirometric examination, a skin prick test, and a histamine challenge test.

Results: Current asthma (current asthmatic symptoms and increased bronchial responsiveness) was observed in 14% (22 of 162) of the athletes and in 2% (1 of 45) of the control subjects ($p = 0.041$). Total asthma (current asthmatic symptoms and increased bronchial responsiveness or physician-diagnosed asthma) occurred in 23% (37 of 162) of the athletes and in 4% (2 of 45) of the control subjects ($p = 0.0048$). Atopy according to skin prick test results was found in 48% (77 of 162) of the athletes and in 36% (16 of 45) of the control subjects (not significant). Clinical pollen allergy (positive skin test reaction to pollen and symptoms of rhinoconjunctivitis) was significantly ($p = 0.037$) more common in athletes than in control subjects. Atopic athletes showed significantly more often increased bronchial responsiveness, current asthma, and total asthma than nonatopic athletes ($p = 0.011$, $p = 0.0049$, and $p < 0.0001$, respectively), and the odds ratios of increased bronchial responsiveness and asthma increased with the number of positive skin test reactions. After adjustment for confounding factors, the odds ratio for the occurrence of current asthma was 5.49 (95% confidence interval 0.56 to 53.7) in speed and power athletes, 2.88

(0.30 to 27.7) in long-distance runners, and 10.8 (1.10 to 106.0) in swimmers compared with control subjects. The adjusted odds ratios for the occurrence of total asthma were 3.56 (0.62 to 20.5) in speed and power athletes, 6.01 (1.19 to 30.2) in long-distance runners, and 5.89 (1.00 to 34.5) in swimmers.

Conclusions: Asthma is more common in highly trained athletes than in control subjects. Asthma is especially common in elite swimmers, but the risk of asthma is increased also in long-distance runners. Increased bronchial responsiveness and asthma are strongly associated with atopic disposition and its severity in elite athletes. (*J Allergy Clin Immunol* 1998;101:646-52.)

Key words: Asthma, atopic allergy, pollen allergy, lung function, speed and power sports, long-distance running, swimming

Increased bronchial responsiveness and asthma are significantly more common in cross-country skiers compared with healthy control subjects.^{1,2} There is limited evidence that asthma would be common also in athletes with summer events. Half of American football players showed increased bronchial responsiveness in a methacholine challenge test, but so did 41% of control subjects.³ Physician-diagnosed asthma was significantly more common in track and field athletes than in control subjects.⁴ Exercise-induced bronchospasm occurred in one fourth of nonasthmatic elite runners when challenged at subzero temperature.⁵

Endurance athletes, such as cross-country skiers, long-distance runners, and swimmers, undergo lengthy training and competition with prolonged hyperventilation. Skiers are repeatedly exposed to cold air, long-distance runners to pollen allergens, and swimmers to chlorine compounds,⁶⁻⁸ which may enhance exercise-induced asthma.⁹⁻¹¹ The speed and power athletes perform high-intensity training for periods of shorter duration. However, also in these athletes the risk of physician diagnosed asthma was increased compared with that of healthy control subjects.⁴

Repeated and strong exposure to pollen allergens causes not only bronchial symptoms in the athletes but also upper respiratory symptoms suggestive of hay fever.⁸ However, only a few studies have investigated occurrence of atopic disposition and clinical atopic manifestations in elite athletes. The aim of this study was to investigate occurrence of and risk factors for increased bronchial responsiveness and asthma in

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Abbreviations used

OR:	Odds ratio
PD ₁₅ FEV ₁ :	Provocative dose of histamine that causes a 15% fall in FEV ₁
95% CI:	95% confidence interval

different highly trained athlete groups with summer events and to compare their results with those of control subjects.

METHODS

Subjects

One hundred sixty-two athletes and 45 control subjects volunteered to participate. All subjects gave their written informed consent, and the study protocol was approved by the local ethics committee. The athletes were divided into three groups according to their type of training¹² and training environment: speed and power track and field athletes ($n = 49$), long-distance runners ($n = 71$), and swimmers ($n = 42$). The main events of speed and power athletes were sprinting (100 to 400 meters, hurdles; $n = 29$), jumping or decathlon (high, long, triple jump, pole vault, decathlon, heptathlon; $n = 17$), and throwing (javelin, discus, shot put; $n = 3$). The long-distance runners' main competition events were from 800 meters to marathon. The control subjects were medical students from the University of Helsinki. Of the speed and power athletes, 73% were members of the Finnish national teams, as were 73% of the long-distance runners and 88% of the swimmers. None of the control subjects were involved in active competitive sports. The clinical characteristics of the study groups are given in Table I.

Physician-diagnosed asthma was reported by 6% (three of 49) of the speed and power athletes (two of them diagnosed during competitive career), by 20% (14 of 71) of the long-distance runners (12 of them diagnosed during competitive career), by 19% (eight of 42) of the swimmers (six of them diagnosed during active competitive career), and by 2% (one of 45) of the control subjects (diagnosed early in childhood). Of the asthmatic athletes, three speed and power athletes, five long-distance runners, and four swimmers used inhaled steroids on a regular basis and inhaled β_2 -agonists as needed. Two swimmers and one control subject used only inhaled steroids on a regular basis. Nine long-distance runners and two swimmers used inhaled β_2 -agonists only before heavy training sessions to prevent respiratory symptoms. Of the nine runners, three runners with allergy to pollen used inhaled β_2 -agonist only in the pollen season. One control subject used inhaled β_2 -agonist as needed. Fifty-three percent of the speed and power athletes (26 of 49), 66% of the long-distance runners (47 of 71), 57% of the swimmers (24 of 42), and 16% of the control subjects (seven of 45) reported exercise-induced bronchial symptoms at least monthly during the last year.

Study design

The study was carried out during February and March 1994 (long-distance runners), February and March 1995 (speed and power athletes), September and October 1995 (control subjects), and from February to April 1996 (swimmers). The long-distance runners, speed and power athletes, and control subjects were identified from our previous study⁴ with a respiratory symptom questionnaire in which willingness for further

investigations was assessed. Swimmers were recruited from the Finnish national team and from one swimming club in the city of Helsinki during the World Cup Race, held in Espoo on January 27 and 28, 1996. The swimmers were given a brief description of the purpose of the study. Forty-two swimmers of the 53 (79%) who attended the information occasion took part in the study. They represented 49% of the swimmers in the national team or in the one swimming club. Eleven (21%) of those 53 eligible swimmers did not have the opportunity to participate in further studies. Three reported having physician-diagnosed asthma, which they considered to be well controlled. Two of 11 courses of medical students were randomly selected to serve as control subjects. One hundred twenty-four students answered the respiratory symptom questionnaire. Two medical students were excluded from the study because of involvement in active competition sports. Forty-six percent of the original group of speed and power athletes, 66% of the long-distance runners, and 36% of the control subjects participated in the study. All subjects answered a respiratory symptom questionnaire⁴ and a more allergy-specific questionnaire; all were interviewed by one of the authors and were given a skin prick test, resting spirometric examination, and a histamine challenge test.

Questionnaires

The study subjects answered two questionnaires. A respiratory symptom questionnaire contained questions on diagnosis of asthma and allergy made previously by a physician, use of anti-asthmatic medication, family history of asthma and allergic rhinitis, exercise-induced bronchial symptoms, competitive status, and smoking habits.⁴ Respiratory symptoms were determined with following question: "How often do you have cough, shortness of breath, or wheeze associated with exercise (each symptom asked separately): (a) daily, (b) weekly, (c) monthly, (d) never, or only associated with respiratory infections?" The allergy symptom questionnaire inquired about symptoms of rhinitis (running or stuffy nose), conjunctivitis (itching or red eyes), eczema, allergens (pollens, animal dander, house dust, food, and drug) causing symptoms, and antiallergic medication. Answers to the questionnaires were confirmed in personal interviews.

Resting spirometry, histamine challenge test, and skin prick test

Resting spirometry was carried out according to the recommendations of the American Thoracic Society¹³ by using a flow-volume spirometer (heated pneumotachograph, Medikro 909; Medikro Oy, Kuopio, Finland). Values are expressed as percentages of reference (predicted) values for adult Finns.¹⁴

Histamine challenges were performed with the dosimetric method with controlled tidal breathing.¹⁵ Noncumulative histamine doses of 0.025, 0.1, 0.4, and 1.6 mg were inhaled, and FEV₁ values were 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) and positive (histamine dihydrochloride, 10 mg/ml) and negative (solvent) control solutions. The airborne allergens used were birch, timothy grass, meadow fescue and mugwort pollens; horse, cat, dog, and cow dander; the mite *Dermatophagoides pteronyssinus*; and mold spores of *Cladosporium herbarum*.

Definitions

A subject was classified as atopic if any allergen caused a wheal of 3 mm or more in diameter and control solutions caused

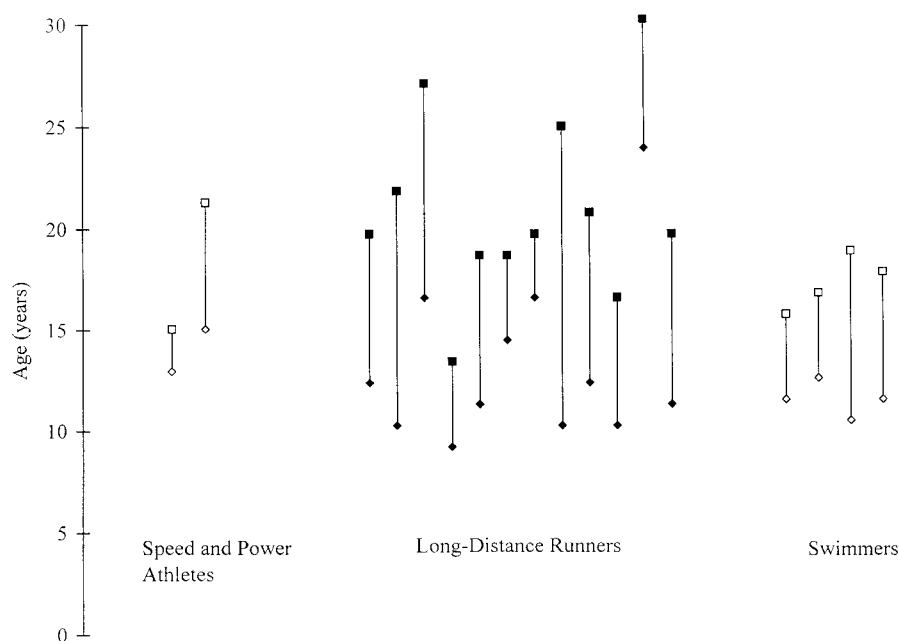


FIG. 1. Individual time intervals from start of active competitive sports to physician-diagnosed asthma in athletes who had asthma diagnosed during their sports career. *Diamonds*, Start of active competitive sports; *squares*, time of physician-diagnosed asthma.

TABLE I. Clinical characteristics of the study groups

	Speed and power athletes (n = 49)	Long-distance runners (n = 71)	Swimmers (n = 42)	Control subjects (n = 45)
Sex (M/F)	32/17	55/16	16/26	34/11
Mean (SD) age (years)	21.1 (3.8)	26.6 (5.5)	18.6 (2.7)	26.7 (6.2)
Mean (SD) duration of active sports career (yrs)	8.3 (4.6)	9.4 (4.0)	8.5 (3.5)	—
Mean (SD) training amount in the previous year (km, hr)	520 (140)†	4470 (1630)*	1780 (710)*	170 (130)†
History of physician-diagnosed asthma	3 (6.1%)	14 (19.7%)	8 (19.0%)	1 (2.2%)
Use of inhaled steroids	3 (6.1%)	5 (7.0%)	6 (14.3%)	1 (2.2%)
Family history of asthma	7 (14.3%)	8 (11.3%)	8 (19.0%)	2 (4.4%)
FEV ₁				
In liters	4.37 (0.71)	4.50 (0.82)	4.54 (0.90)	4.42 (0.80)
As percentage of predicted ¹⁴	95.9 (9.8)	98.8 (10.2)	101.6 (9.8)	94.8 (11.8)
Current smoking	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (6.7%)

* Amount in kilometers.

† Amount in hours.

expected results. Clinical pollen allergy (hay fever) was defined as at least one positive skin test reaction to pollen associated with symptoms of rhinoconjunctivitis during the spring or summer. Current asthma was defined as increased bronchial responsiveness ($PD_{15}FEV_1 \leq 1.6 \text{ mg}^{15}$) together with at least one exercise-induced bronchial symptom (shortness of breath, wheeze, or cough) monthly during the last year. Total asthma was defined as current asthma or asthma diagnosed previously by a physician.

Statistical methods

Odds ratios (OR) for the presence of disease and their 95% confidence intervals (95% CI) for different athlete

groups compared with control subjects were analyzed with logistic regression models (BMDP Statistical Software). Age, sex, and family history of allergic rhinitis or asthma were considered as potential confounding factors in the analyses. Differences in the prevalence rates and trends in prevalence rates were examined by use of Fisher's exact test, and χ^2 test for trend (StatXact 3, Cytel Software). Two-tailed *p* values of 0.05 or below were considered significant. The significance of the differences in $PD_{15}FEV_1$ values between the athlete groups and the control group was estimated with the Kruskal-Wallis one-way analysis of variance by ranks and Dunn's multiple comparison test.

TABLE II. Occurrence of atopy, clinical pollen allergy, increased bronchial responsiveness, current asthma, and total asthma

	Atopy	Pollen allergy	Increased bronchial responsiveness	Current asthma	Total asthma
Athletes (<i>n</i> = 162)	77 (47.5%)	48 (29.6%)*	30 (18.5%)	22 (13.6%)*	37 (22.8%)†
Speed and power athletes (<i>n</i> = 49)	21 (42.9%)	12 (24.5%)	9 (18.4%)	6 (12.2%)	8 (16.3%)
Long-distance runners (<i>n</i> = 71)	35 (49.3%)	24 (33.8%)*	6 (8.5%)	5 (7.0%)	17 (23.9%)†
Swimmers (<i>n</i> = 42)	21 (50.0%)	12 (28.6%)	15 (35.7%)†	11 (26.2%)†	12 (28.6%)†
Control subjects (<i>n</i> = 45)	16 (35.6%)	6 (13.3%)	5 (11.1%)	1 (2.2%)	2 (4.4%)

* $p < 0.05$.† $p \leq 0.01$ versus control subjects.**TABLE III.** Logistic regression analysis: Odds ratios and confidence intervals for bronchial hyperresponsiveness, current asthma, and total asthma

Characteristic	Increased bronchial hyperresponsiveness			Current asthma			Total asthma		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Age (yrs)									
Below 20	1			1			1		
20-25	1.92	0.74-4.99	0.18	1.15	0.38-3.49	0.81	0.70	0.27-1.80	0.46
Over 25	1.33	0.35-5.01	0.68	1.5	0.22-5.15	0.95	1.09	0.36-3.34	0.88
Sex									
F	1			1			1		
M	0.50	0.21-1.21	0.12	0.33	0.11-0.94	0.04	0.44	0.18-1.06	0.07
Family history of allergic rhinitis or asthma									
No family history	1			1			1		
Family history	0.93	0.40-2.15	0.86	0.57	0.20-1.65	0.29	1.12	0.49-2.55	0.79
Atopy									
Nonatopic	1			1			1		
Atopic	3.90	1.66-9.15	0.002	7.14	2.29-22.2	0.001	7.54	3.03-18.7	0.00001
Sport event									
Control subjects	1			1			1		
Speed and power sports	1.97	0.54-7.19	0.30	5.49	0.56-53.7	0.14	3.56	0.62-20.5	0.15
Long-distance running	0.75	0.20-2.79	0.66	2.88	0.30-27.7	0.36	6.01	1.19-30.2	0.03
Swimming	4.24	1.11-16.2	0.03	10.8	1.10-106.0	0.04	5.89	1.00-34.5	0.05

RESULTS

The mean time from the beginning of active competition sports to the physician diagnosed asthma was 4 years (range, 2 to 6 years) in the two-speed and power athletes, 7.3 years (range, 3 to 14 years) in the 12 long-distance runners, and 5.7 years (range, 2 to 10 years) in the six swimmers who had asthma diagnosed during their sports career (Fig. 1).

Increased bronchial responsiveness occurred in a similar rate among athletes and control subjects, but as a subgroup, swimmers showed significantly more often increased bronchial responsiveness than did control subjects ($p = 0.013$), with their $PD_{15}FEV_1$ values being also significantly lower than those of the control subjects ($p = 0.011$, multiple comparison corrected) (Table II). Current asthma was observed in 14% (22 of 162) of the athletes and in 2% (1 of 45) of the control subjects ($p = 0.041$). Total asthma occurred in 23% (37 of 162) of the athletes compared with 4% (two of 45) of the control subjects ($p = 0.0048$).

Atopy was found in 48% (77 of 162) of the athletes and in 36% (16 of 45) of the control subjects, with the difference not reaching significance (Table II). Atopic athletes had significantly more often increased bronchial responsiveness, current asthma, and total asthma compared with nonatopic athletes ($p = 0.011$, $p = 0.0049$, $p < 0.0001$, respectively).

Age, sex, family history of allergic rhinitis or asthma, and atopy were included in fixed logistic regression models with the three different athlete groups to find out their associations with increased bronchial responsiveness, as well as presence of current and total asthma (Table III). Swimmers had significantly higher odds ratios (4.24; 95% CI, 1.11 to 16.2) for the occurrence of increased bronchial responsiveness compared with control subjects. For the presence of current asthma, swimmers (OR, 10.8; 95% CI, 1.10 to 106.0), but not speed and power athletes or long-distance runners, had higher ORs compared with control subjects. The adjusted ORs for the occurrence of total asthma were 3.56 (95% CI, 0.62 to 20.5) for speed and

TABLE IV. Crude odds ratios and their 95% confidence intervals for the occurrence of increased bronchial responsiveness, current asthma, and total asthma according to the number of positive skin prick test reactions in elite athletes

Number of positive skin test reactions	Increased bronchial responsiveness		Current asthma		Total asthma	
	OR	95% CI	OR	95% CI	OR	95% CI
0 reactions	1		1		1	
1-2 reactions	2.13	0.87-5.24	3.25	1.08-10.02	1.59	1.59-10.61
3-4 reactions	2.70	1.15-6.32	3.04	0.95-9.72	3.54	1.30-9.66
≥5 reactions	3.15	1.28-7.74*	4.72	1.72-12.98†	5.51	2.10-14.45†

χ^2 test for trend.

* $p < 0.005$.

† $p \leq 0.001$.

TABLE V. Logistic regression: Odds ratios and confidence intervals for clinical pollen allergy

Characteristic	Clinical pollen allergy (hay fever)		
	OR	95% CI	<i>p</i>
Age (yrs)			
Below 20	1		
20-25	0.64	0.28-1.47	0.29
Over 25	0.42	0.15-1.17	0.10
Sex			
F	1		
M	2.48	1.10-5.57	0.03
Family history of allergic rhinitis or asthma			
No family history	1		
Family history	5.01	2.44-10.3	0.00001
Sport event			
Control subjects	1		
Speed and power sports	1.52	0.45-5.13	0.50
Long-distance running	3.15	1.07-9.29	0.04
Swimming	1.99	0.55-7.22	0.29

power athletes, 6.01 (95% CI, 1.19 to 30.2) for long-distance runners, and 5.89 (95% CI, 1.00 to 34.5) for swimmers compared with control subjects. Atopy was significantly ($p < 0.002$) associated with increased bronchial responsiveness, as well as with current and total asthma after adjustment for possible confounding factors in the logistic regression models. The odds for the occurrence of increased bronchial responsiveness and current asthma and total asthma increased with the number of positive skin test reactions ($p = 0.0045$, $p = 0.0013$, $p < 0.001$, respectively) (Table IV).

Clinical pollen allergy was significantly more common in athletes compared with control subjects ($p = 0.037$) (Table II). When adjusted for age, sex, and family history of allergic rhinitis or asthma, the odds ratios for the occurrence of pollen allergy was 1.52 (95% CI, 0.45 to 5.13) for speed and power athletes, 3.15 (95% CI, 1.07 to 9.29) for long-distance runners, and 1.99 (95% CI, 0.55 to 7.22) for swimmers (Table V).

DISCUSSION

The subjects of this study were selected by using our previous respiratory symptom questionnaire for elite athletes⁴ in which willingness for further investigations was questioned. Self-selection may have occurred, with healthier or symptom-free subjects less likely to take part. However, such selection should have occurred in control subjects with equal extent. The results of our previous study compared with this one does not support any significant selection bias. A similar prevalence rate for physician-diagnosed asthma and allergy or reported exercise-induced bronchial symptoms were observed in the current athlete population compared with the previous population of long-distance runners, speed and power athletes, and control subjects.⁴ Of those swimmers who did not participate in this study, 27% reported physician-diagnosed asthma. The study groups were not similar with respect to age, sex, and family history of allergic rhinitis and asthma. However, these confounding factors were adjusted by logistic regression models, the results of which are reported here. The study subjects were studied out of pollen season, the control subjects in autumn, and the athlete groups in spring. It seems unlikely that this arrangement influenced the results. Current asthma was defined as bronchial responsiveness and at least one exercise-induced bronchial symptom. Symptoms induced by exercise were selected for the definition because they commonly appear as one of the first symptoms or signs of asthma.¹⁶ Additionally, all participants were young adults, who, including control subjects not taking part in competitive sports, are daily physically active, and thus would easily notice symptoms caused by exercise.

The high prevalence of asthma, especially in swimmers, might be due to the fact that asthmatic athletes choose swimming as their primary event. It is well recognized that swimming does not cause as much exercise-induced asthma as running,¹⁷ and in indoor pools swimmers avoid exposure to outdoor allergens. In this study, two swimmers had asthma when they began swimming. In those swimmers who had asthma diagnosed during competitive career the mean time from start of swimming to the physician-diagnosed asthma was 5.7 years.

Zwick et al.¹¹ studied a small group of swimmers and found 9 of 14 to be hyperresponsive in a metacholine test. Larsson et al.¹ observed increased bronchial responsiveness in 38% of 42 elite cross-country skiers, and an additional 21% of the skiers had asthma diagnosed by a physician. In this study, 18% of the speed and power athletes, 8% of the long-distance runners, and 36% of the swimmers had increased bronchial responsiveness, and 12%, 7%, and 26% of them, respectively, had current asthma by our definition. In contrast with our previous findings,⁴ the occurrence of increased bronchial responsiveness in the long-distance runners did not exceed the occurrence in healthy control subjects. Running is the most effective way to provoke exercise-induced bronchospasm.¹⁷ Thus long-distance runners with clearly increased bronchial responsiveness may stop their training because of cumbersome symptoms. This self-selection might therefore represent "a healthy-worker effect."¹⁸

Only a few studies have used objective methods to detect atopic allergy in elite athletes. In the study by Zwick et al.,¹¹ 9 of 14 swimmers had at least one positive reaction to a skin prick test. Of 42 cross-country skiers studied by Larsson et al.,¹ 29% were atopic according to results of skin prick testing. In this study 48% of the athletes and 36% of the control subjects were atopic according to results of skin prick testing. Twenty-four percent of the speed and power athletes, 34% of the long-distance runners, and 29% of the swimmers had clinical pollen allergy as compared with 13% of the control subjects. These observations may be explained by the high ventilation and exposure to airborne allergens in track and field athletes.^{6,8} Swimmers in Finland train mostly indoors, where exposure to pollen allergens is minimal, but still they show common sensitization to inhalant allergens and clinical pollen allergy. It has been suggested that frequent exposure to chlorine, chlorine gas, and their components during training and competition may facilitate sensitization to airborne allergens and bronchial responsiveness in highly competitive swimmers.¹¹

In contrast with the findings of Sue-Chu et al.,² atopy was significantly associated with the occurrence of increased bronchial responsiveness and asthma according to logistic regression models. Furthermore, a significant association was found between the number of positive skin test reactions (i.e., severity of the atopic disposition) and the occurrence of increased bronchial responsiveness, current asthma, and total asthma. In an unselected adult population, a significant relation between the number of skin test reactions and increased bronchial responsiveness in a histamine challenge test has been previously reported.¹⁹ Atopy is somewhat more common in athletes compared with control subjects, which partly explains the difference in the occurrence of bronchial hyperresponsiveness and asthma between athletes and control subjects. However, the surprisingly high risk for increased bronchial responsiveness, especially in swimmers, may indicate an increased clinical expression of

the atopic disposition as a result of intensive endurance training in a special environment. When the two risk factors, atopy and sporting event, are combined in a logistic regression model, the relative risk of total asthma in an atopic swimmer is 97-fold, 42-fold in an atopic long-distance runner, and 25-fold in an atopic speed and power athlete as compared with nonatopic control subjects.

Drobnik et al.²⁰ measured chlorine gas concentrations above the surface of water from swimming pools in Spain. They found a mean concentration of 0.42 mg/m³ air, and calculated that during a 2-hour training session the swimmer may be exposed to chlorine in an extent (4 to 6 gm) that exceeds the recommendation for a worker with 8 hours of exposure (4 to 7 gm) in the United States. Repeated and strong or accidental exposure to chlorine gas may cause asthma symptoms, airflow obstruction, and increased bronchial responsiveness without a latency period.²¹ Thus exposure to chlorine gas also may have direct effects on inducing asthma in swimmers.

In conclusion, asthma is significantly more common in elite athletes compared with control subjects. The risk of asthma is increased especially in swimmers but also in track and field athletes. Atopy is a major risk factor modulating the risk; the more severe the atopic disposition, the greater the risk for increased bronchial responsiveness and asthma.

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