



Are asthma-like symptoms in elite athletes associated with classical features of asthma?

T K Lund, L Pedersen, S D Anderson, et al.

Br J Sports Med 2009 43: 1131-1135 originally published online February 6, 2009

doi: 10.1136/bjsem.2008.054924

Updated information and services can be found at:

<http://bjsm.bmj.com/content/43/14/1131.full.html>

These include:

References

This article cites 34 articles, 13 of which can be accessed free at:

<http://bjsm.bmj.com/content/43/14/1131.full.html#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To order reprints of this article go to:

<http://bjsm.bmj.com/cgi/reprintform>

To subscribe to *British Journal of Sports Medicine* go to:

<http://bjsm.bmj.com/subscriptions>

Are asthma-like symptoms in elite athletes associated with classical features of asthma?

T K Lund,¹ L Pedersen,¹ S D Anderson,² A Sverrild,¹ V Backer¹

¹ Respiratory and Allergy Research Unit, Department of Respiratory Medicine, Bispebjerg Hospital, Copenhagen University Hospital, Denmark; ² Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia

Correspondence to:
Dr T K Lund, Respiratory and Allergy Research Unit, Department of Respiratory Medicine, Bispebjerg Hospital, Copenhagen University Hospital, 2400 Copenhagen NV, Denmark; tclund@dadlnet.dk

Accepted 22 January 2009
Published Online First
6 February 2009

ABSTRACT

Background: Asthma is frequent in elite athletes and clinical studies in athletes have found increased airway inflammation.

Objective: To investigate asthma-like symptoms, airway inflammation, airway reactivity (AR) to mannitol and use of asthma medication in Danish elite athletes.

Methods: The study group consisted of 54 elite athletes (19 with doctor-diagnosed asthma), 22 non-athletes with doctor-diagnosed asthma (steroid naive for 4 weeks before the examination) and 35 non-athletes without asthma; all aged 18–35 years. Examinations (1 day): questionnaires, exhaled nitric oxide (eNO) in parts per billion, spirometry, skin prick test, AR to mannitol and blood samples. Induced sputum was done in subjects with asthma.

Results: No significant difference was found in values for eNO, AR and atopy between 42 elite athletes with and 12 without asthma-like symptoms. Elite athletes with doctor-diagnosed asthma had less AR (response dose ratio 0.02 (0.004) vs 0.08 (0.018) $p < 0.01$) and fewer sputum eosinophils (0.8% (0–4.8) vs 6.0% (0–18.5), $p < 0.01$) than non-athletes with doctor-diagnosed asthma. Use of inhaled corticosteroids was similar in the two groups (not significant). In all, 42 elite athletes had asthma-like symptoms but only 12 had evidence of current asthma. Elite athletes without asthma had asthma-like symptoms more frequently than non-athletes without asthma (68.6% vs 25.7%, $p < 0.001$).

Conclusion: Asthma-like symptoms in elite athletes are not necessarily associated with classic features of asthma and alone should not give a diagnosis of asthma. More studies are needed to further investigate if and how the asthma phenotype of elite athletes differs from that of classical asthma.

Elite athletes have a high prevalence of doctor-diagnosed asthma compared with non-athletes.^{1,2} Exercise-related asthma-like symptoms are poor predictors of exercise-induced bronchoconstriction (EIB) and asthma in elite athletes;^{3,4} furthermore, respiratory problems during exercise can occur independently of asthma.⁵ Elite athletes have a higher prevalence of airway hyper-responsiveness (AHR) to methacholine than non-athletes⁶ and an increase in airway inflammatory cell numbers, with neutrophils being the dominant cell type.^{7–9} It has been suggested that chronic endurance training might increase the number of neutrophils in the airways.^{7,10} This may reflect airway injury, and more studies are needed to investigate whether airway inflammation of elite athletes with “asthma” differs from that seen in patients with classical asthma. The use of asthma treatment in elite athletes is also currently under scrutiny in

order to reduce the risk of undertreatment,^{11–13} or overtreatment.^{14–16}

The objective of the present study was to identify the prevalence of asthma-like symptoms and examine them in relation to airway inflammation, airway reactivity to mannitol and use of asthma medication in Danish elite athletes and non-athletes.

METHODS

Subjects

The study group consisted of 3 groups: (1) 54 elite athletes, (2) 22 non-athletes with asthma and (3) 35 non-athletes without asthma. All participants volunteered and all met the inclusion criterion of being between 18–35 years and the exclusion criterion of not having had a recent chest infection (past month). All participants lived in Copenhagen or in a radius of 80 km of Copenhagen (Zealand). All gave their written informed consent and the local ethics committee approved the study (no.s KF262958 and KF262754). None of the non-athletes were involved in active competitive sports.

Group 1: elite athletes who were financially supported by Team Denmark ($n = 145$) were invited and 54 (37%) volunteered to participate in the study. They were identified from a previous study¹³ in which willingness to participate in further investigations was assessed. Group 1 was divided in two subgroups: elite athletes with asthma ($n = 19$) and elite athletes without asthma ($n = 35$).

Group 2: non-athletes with asthma ($n = 22$). Members of group 2 were recruited through advertisements in the local newspaper and they met the additional inclusion criterion of already having doctor-diagnosed asthma.

Group 3: non-athletes without asthma. A random population sample of 585 subjects aged 18–24 years was drawn from the civil register. This group was part of a population study by AS. In the present study, the first 35 examined subjects with no history of doctor-diagnosed asthma and no current or previous use of asthma medication were included.

Study design

A cross-sectional study was performed. All participants were asked to refrain from taking short-acting β_2 agonists (SABA) for 6 h, long-acting β_2 agonists (LABA) for 12 h and antihistamines for 3 days before the visit. No inhaled corticosteroids (ICS) were taken on the day of the study. Further, all non-athletes with asthma were asked to refrain from taking ICS for 4 weeks before their visit; this was, however, not practical for the elite athletes.

Original article

Nine elite athletes used ICS on a daily basis. All participants visited the research unit once and all elite athletes were asked not to train on the day of examination. The study was carried out from autumn 2006 to spring 2007. The non-athletes with asthma were examined from autumn 2005 to spring 2006.

All subjects answered a questionnaire; all were interviewed by one of the authors and all had a measurement made of exhaled nitric oxide (eNO) in parts per billion. Then, spirometry was measured at rest and in response to a mannitol challenge test. Skin prick tests were performed and blood samples were taken. Sputum induction was carried out only in athletes and non-athletes with doctor-diagnosed asthma or current asthma.

Questionnaire and interview

All participants received two questionnaires; one had four question groups: (a) sport and training hours (only for athletes), (b) asthma-like symptoms, (c) doctor-diagnosed asthma, family history of asthma and childhood asthma, and (d) smoking habits. This questionnaire was a non-validated standard questionnaire for athletes used in Bispebjerg Hospital, Copenhagen, Denmark.

To determine doctor-diagnosed asthma, the following question was used: "Has a doctor diagnosed you with asthma?" Questions on asthma-like symptoms in groups 1 and 2 were in accordance with the Global Initiative for Asthma (GINA) guidelines:¹⁷ "Do you experience wheezing, breathlessness, chest tightness or cough" (a separate question for each symptom): (1) never, (2) less than once a week, (3) more than once a week but less than once a day, (4) daily, (5) daily with limitation of physical activities? Asthma-like symptoms in group 3 were documented by two questions: (1) "Have you ever experienced wheezing, breathlessness, chest tightness or cough at rest?" and (2) "Have you ever experienced wheezing, breathlessness, chest tightness or cough related to exercise?" The other questionnaire was a validated asthma control questionnaire.¹⁸ All participants were interviewed about their use of asthma medication.

Spirometry, blood samples, skin prick testing and exhaled nitric oxide

Spirometry was performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations.¹⁹ The forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured using a 7-litre dry wedge spirometer (Vitalograph, Buckingham, UK). Predicted values of FEV₁ and FVC were based on reference values according to Nysom *et al.*²⁰ Blood samples were taken and a differential cell count was performed. A skin prick test to 10 aeroallergens (birch, grass, mugwort, horse, dog, cat, house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and moulds (alternaria and cladosporium) (ALK-Abello, Hoersholm, Denmark)) was performed in duplicate according to the European Academy of Allergy and Clinical Immunology (EAACI) recommendations. A positive result was defined as a wheal of at least 3 mm in diameter to one or more allergens.²¹ eNO was measured according to ATS guidelines²² using the Nitric Oxide Analyzer (NIOX, Aerocrine AB, Solna, Sweden).

Mannitol challenge test

Bronchial provocation with mannitol powder (Aridol, Pharmaxis, Frenchs Forest, Australia) contained in capsules and inhaled from a dry powder inhaler (RS 01, Plastiap, Osnago, Italy) up to a cumulative dose of 635 mg was

performed.^{23–25} Airway reactivity to mannitol is expressed as the response dose ratio (RDR). This value allows evaluation of all subjects, not only those with a 15% fall in FEV₁. The RDR is the percentage fall in FEV₁ measured after the final dose of mannitol, divided by the cumulative dose in mg administered to induce that percentage fall in FEV₁. For those having a negative or 0% fall in FEV₁ a value for FEV₁ of 0.1% was assumed in the equation.

Induced sputum

Sputum induction was conducted after the mannitol challenge and according to ERS recommendations using a nebuliser (Easynb II, Flaemnuova, Brescia, Italy). After inhalation of 1 mg terbutaline, sputum was induced by inhalation of hypertonic saline in increasing concentrations (3%, 4% and 5%) for three periods each of 7 min. Sputum plugs were selected and processed within 2 h of collection, cytospins were prepared using standard methods, and a differential cell count was performed.^{26 27} The cells were expressed as a percentage of the total non-squamous cells (100–400 cells).

Definitions

Elite athletes were defined as athletes financially supported by Team Denmark. Team Denmark is an institution charged with the overall planning of elite sports in Denmark, including individual financial support for top-level athletes. Asthma was defined as doctor-diagnosed asthma diagnosed before entering the study (ever diagnosed asthma). A diagnosis of current asthma was made on the basis of asthma-like symptoms in combination with a current positive mannitol challenge (15% decrease in FEV₁) and/or current daily use of ICS. Never ICS was defined as no current or previous use of ICS. The athletes' sports classifications were made according to our previous classification:¹³ endurance sports (rowing, cycling, swimming etc), power sports (gymnastics, athletics, wrestling etc), intermediate sports (handball, soccer, ice hockey etc) and other sports (golf, curling, bowling etc).

Statistics

The data were analysed using SPSS V.14.0 (SPSS, Chicago Illinois, USA). Frequencies were calculated for the entire group. Continuous variables were analysed using analysis of variance (ANOVA), followed by Student t test for normally distributed data. Results for continuous data are presented as mean (standard error of the mean (SEM)). Skewed data (induced sputum) are presented in median (range). Differences for skewed data were assessed by the Mann-Whitney U test. Differences for categorical data were assessed by χ^2 tests and Fisher exact test when appropriate. A p value <0.05 was considered to be statistically significant.

RESULTS

Table 1 shows the basic characteristics of the study group. Of the elite athletes, 27 (50%) performed endurance sports, 5 (9%) performed power sports, 18 (33%) performed intermediate sports and the remaining 4 (7%) were from other sports. The athletes' weekly training was 23.8 (1.3) h and the duration of their active sport career at this level was 5.9 (0.4) years, with no difference between elite athletes with and without asthma.

The prevalence of any asthma-like symptoms was higher in the participating athletes (n = 54) than in those athletes invited but who declined to participate (n = 91) (p < 0.05) (data not shown). Table 2 shows the characteristics for elite athletes with

Table 1 Basic characteristics for elite athletes and non-athletes

	Elite athletes		Non-athletes		p Value*	p Value†
	Asthma	Non-asthma	Asthma	Non-asthma		
Subjects, n	19	35	22	35	—	—
Sex (M:F)	11:8	25:10	17:5	11:24	NS	<0.01
Age, years	24.0 (0.75)	25.1 (0.70)	27.8 (0.83)	20.4 (0.33)	<0.01	<0.001
Current smoker, n (%)	0 (0)	0 (0)	0 (0)	7 (20.0)	NS	<0.05‡
FEV ₁ , litres	4.37 (0.19)	4.91 (0.15)	3.73 (0.14)	3.87 (0.13)	<0.01	<0.001
FEV ₁ , % predicted	98.2 (1.94)	105.4 (2.10)	82.6 (2.63)	96.9 (1.82)	<0.001	<0.01
FVC, litres	5.51 (0.30)	5.85 (0.19)	5.06 (0.25)	4.50 (0.17)	NS	<0.001
FVC, % predicted	106.2 (2.17)	107.8 (2.45)	95.2 (3.06)	97.9 (2.01)	<0.01	<0.01
FEV ₁ /FVC ratio, %	80.4 (1.71)	84.5 (1.30)	75.1 (1.95)	86.5 (0.97)	0.052	NS

Asthma = subjects with doctor-diagnosed asthma. Data are given as mean (standard error of the mean (SEM)) unless otherwise stated.

*Between elite and non-elite patients with asthma; †between elite and non-elite patients without asthma; ‡Fisher exact test.

FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity.

(n = 42) and without asthma-like symptoms (n = 12) and we found no differences between the groups in all variables listed.

A total of 19 elite athletes had doctor-diagnosed asthma but only 12 had evidence of current asthma. Of these 12, 1 was not aware of asthma before entering the study. No differences in current asthma or use of any asthma medication were found between the elite athletes and non-athletes with asthma (table 3).

Elite athletes without asthma had a higher prevalence of asthma-like symptoms (p<0.001) and higher values for eNO (p<0.05) than non-athletes without asthma (table 3). The values for eNO were similar in the non-atopic subjects for both groups (12.7 (1.22) vs 16.9 (1.73) ppb, p<0.05).

Table 3 also shows that elite athletes with asthma had less reactivity (lower values for RDR) than non-athletes with asthma (p<0.01). In subjects with asthma who had never used ICS the airways were still less reactive in elite athletes than in non-athletes (0.018 (0.004) vs 0.095 (0.024), p<0.01).

Of the 42 subjects with doctor-diagnosed asthma and/or current asthma, 26 were able to produce usable sputum samples giving a success rate of 62%. The examination of the sputum differential cell count in subjects with asthma revealed fewer eosinophils in elite athletes than in non-athletes (p<0.01) and more neutrophils in the elite athletes, although this difference was not significant (table 4). For subjects with current asthma there was no significant difference in sputum eosinophils between elite athletes and non-athletes (data not shown).

Sputum eosinophilia (>4%) was found in one elite athlete and in seven non-athletes with asthma (p<0.05).

No difference in ICS dose (budesonide equivalent) was found between athletes and non-athletes (622 (91) µg vs 475 (74) µg). The ICS dose for non-athletes was calculated on their regular use of ICS prior to the last 4 weeks in which they had no ICS. Of the athletes getting ICS and/or FC-ICS (fixed combination of ICS and LABA), two were positive to the mannitol test.

DISCUSSION

This study included Danish top-level athletes competing at an international level. The results of this study showed no difference in lung function, eNO, airway reactivity to mannitol and atopy between elite athletes with and without asthma-like symptoms. Moreover we found that elite athletes frequently had asthma-like symptoms but further investigation did not confirm a diagnosis of current asthma. In total, 42 elite athletes had asthma-like symptoms but only 12 had evidence of current asthma. These findings confirm the recent suggestion by the International Olympic Committee Medical Commission (IOC-MC) consensus statement on asthma (<http://www.olympic.org>) that asthma-like symptoms alone should not be relied upon to diagnose asthma. Our findings suggest that symptoms are independent of the levels of eNO, airway reactivity to mannitol and atopy in elite athletes. Earlier studies have demonstrated that exercise-related asthma-like symptoms in elite athletes are

Table 2 Characteristics for elite athletes with and without asthma-like symptoms

	No symptoms n = 12	Asthma-like symptoms				p Value§
		All* n = 42	More than 1† n = 23	Daily n = 7	Exercise‡ n = 12	
FEV ₁ , % predicted	105.2 (3.44)	102.2 (1.79)	101.2 (2.53)	107.8 (4.83)	103.1 (3.76)	NS
FVC, % predicted	110.2 (5.14)	106.3 (1.73)	106.6 (2.15)	111.4 (3.54)	107.3 (3.28)	NS
eNO, ppb	19.2 (2.67)	23.7 (2.57)	30.1 (4.13)	26.7 (4.04)	19.7 (2.55)	NS
B eosinophils, 10 ⁹ /litre	0.12 (0.02)	0.15 (0.01)	0.15 (0.02)	0.17 (0.04)	0.13 (0.02)	NS
Atopy, n (%)	7 (58.3)	22 (52.4)	14 (60.9)	4 (57.1)	6 (50.0)	NS
Mannitol test, n (%)¶	0 (0)	5 (11.9)	5 (21.7)	0 (0)	2 (16.7)	NS
RDR	0.008 (0.002)	0.012 (0.002)	0.017 (0.003)	0.011 (0.003)	0.011 (0.003)	NS
Current asthma, n (%)**	1 (8.3)††	11 (26.2)	9 (39.1)	2 (28.6)	5 (41.7)	NS

*All symptoms (exercise+rest); †symptoms more than once a week; ‡only symptoms after exercise: include athletes from the different symptom groups "less than once a week", "more than once a week" and "daily" (the group of athletes with asthma-like symptoms "less than once a week" (n = 12) is not shown); §p value between groups; ¶a positive mannitol challenge test;

**asthma-like symptoms+positive mannitol test and/or current use of daily ICS; ††well controlled asthmatic using ICS.

eNO, exhaled nitric oxide (parts per billion); FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; ICS, inhaled corticosteroids; NS, not significant; RDR, response dose ratio.

Original article

Table 3 Clinical characteristics for elite athletes and non-athletes

	Elite athletes		Non-athletes		p Value*	p Value†
	Asthma (n = 19)	Non-asthma (n = 35)	Asthma (n = 22)	Non-asthma (n = 35)		
eNO, ppb	25.2 (3.84)	21.3 (2.47)	43.4 (7.85)	14.7 (1.34)	NS (0.056)	<0.05
Atopy, n (%)	11 (57.9)	18 (51.4)	22 (100)	10 (28.6)	<0.01	0.051
Mannitol test, n (%)‡	4 (21.1)	1 (2.9)	18 (81.8)	2 (5.7)	<0.001	NS
RDR	0.018 (0.004)	0.007 (0.001)	0.083 (0.018)	0.011 (0.004)	<0.01	NS
B eosinophils, 10 ⁹ /litre	0.17 (0.02)	0.12 (0.01)	0.29 (0.04)	0.12 (0.02)	<0.02	NS
ACQ	3.7 (1.0)	0.5 (0.2)	7.4 (1.3)	0.2 (0.2)	<0.05	NS
Symptoms, n (%)§	18 (94.7)	24 (68.6)	21 (95.5)	9 (25.7)	NS	<0.001
Current asthma, n (%)	11 (57.9)	1 (2.9)	18 (81.8)	0 (0)	NS	NS
Treatment, n (%)¶	15 (78.9)	0 (0)	21 (95.5)	0 (0)	NS	NS

Asthma = subjects with doctor-diagnosed asthma before entering the study. One athlete with “non-asthma” had a positive mannitol challenge test and asthma-like symptoms and was classified as having current asthma.

*Between elite and non-elite patients with asthma; †between elite and non-elite patients without asthma; ‡a positive mannitol challenge test; §all asthma-like symptoms (rest+exercise); ¶use of any asthma medication.

ACQ, asthma control questionnaire (mean score); eNO, exhaled nitric oxide (parts per billion); RDR, response dose ratio.

not predictive of EIB and that they are also poor indicators of asthma in this group of patients.^{3 4}

We found that elite athletes with asthma had less airway reactivity and fewer sputum eosinophils than did non-athletes with asthma. Others have also examined airway inflammation in elite athletes.^{2 8 9 28} Lumme *et al*² made the interesting observation that there was no difference in sputum differential cell counts of eosinophils and neutrophils between athletes with and without asthma-like symptoms and AHR to methacholine, suggesting that symptoms are independent of sputum eosinophils and neutrophils as well. It seems that a “healthy” group of elite athletes have some kind of airway inflammation possibly related to airway injury that is independent of asthma. We found that this group of “healthy” elite athletes without asthma had increased eNO compared with “healthy” non-athletes without asthma, even in the non-atopic subjects. The difference was small and the healthy athletes had more atopy than the healthy non-athletes ($p = 0.051$). A recent study has confirmed earlier suggestions from studies in children that eNO is an index of atopy.²⁹

Studies on the effects of asthma medication, such as montelukast³⁰ and budesonide,³¹ on asthma-like symptoms in elite ice hockey players and cross-country skiers have reported no beneficial effect on asthma-like symptoms, AHR or airway cellular inflammation. All these findings support the concept that many athletes with symptoms simply do not have classical asthma or respond to classical asthma treatments. We think there might be a difference in the asthma phenotype of some

elite athletes compared to non-athletes, but this area needs further investigation.

Karjalainen *et al*⁸ examined bronchial biopsies from 40 elite skiers without a diagnosis of asthma, 12 subjects with mild asthma and 12 healthy controls; they found lower cell counts of eosinophils, mast cells and macrophages in skiers with and without AHR than in subjects with asthma. Furthermore, the skiers were found to have higher neutrophil counts than subjects with asthma. Undiagnosed asthma in the skiers could, however, not be excluded and Karjalainen *et al*⁸ suggested that the inflammatory process in these athletes was different from that in subjects with asthma. This may relate to airway injury.³²

Helenius *et al*²⁸ and Lumme *et al*² examined induced sputum of elite swimmers and ice hockey players. These studies concluded that the athletes had higher sputum eosinophil and neutrophil cell counts than did controls. In both studies, however, athletes had increased atopy, AHR and asthma compared to controls.

Some studies have indicated a high use of asthma medication among elite athletes^{14 16 33} but they did not indicate whether they thought that the athletes were overtreated. We found minor signs of undertreatment in elite athletes with asthma. Of the 12 athletes with current asthma, 4 had a positive mannitol test despite treatment with asthma medication (2 on ICS and 2 on SABA only), and 1 had sputum eosinophilia. Further, four athletes without current asthma were taking asthma medication (SABA only). Undertreatment and inappropriate treatment of elite athletes with asthma has been discussed in earlier studies.^{12 34 35}

The limitations of this study were as follows: we found less airway reactivity and fewer sputum eosinophils in elite athletes with asthma compared with non-athletes with asthma. This may to some extent be accounted for by the greater level of atopy in the non-athletes with asthma, a finding that might have increased the general level of airway inflammation in this group. Further, the non-athletes had their treatment with ICS discontinued for 4 weeks before the examination. It was not practical to discontinue ICS in elite athletes as they had a busy schedule with competitions and training. This may have accounted for the findings of a reduced general level of airway inflammation in the athletes.

In conclusion, asthma-like symptoms in elite athletes are not necessarily associated with classic features of asthma and alone should not be relied upon to make a diagnosis of asthma. This indicates that the athletes' care needs further attention and more studies are needed to further investigate if and how the

Table 4 Sputum differential cell count

	Asthma subjects*		p Value†
	Elite athletes (n = 20)	Non-athletes (n = 22)	
Usable samples, n (%)	13 (65)	13 (59)	NS
Total cell count	430 (248–1307)	518 (212–1252)	0.28
Eosinophils, %	0.8 (0–4.8)	6.0 (0–18.5)	<0.01
Neutrophils, %	39.3 (2.8–89.0)	23.5 (0–98.0)	0.32
Lymphocytes, %	1.5 (0–6.0)	1.8 (0–14.1)	0.84
Macrophages, %	39.8 (2.5–87.3)	43.0 (0.5–87.5)	0.72
Bronchial epithelial cells, %	7.8 (0.3–38.8)	8.5 (0.5–45.5)	0.79

Data is shown as median (range).

*Subjects with doctor-diagnosed asthma and/or current asthma; †Mann–Whitney test (athletes vs non-athletes).

NS, not significant.

What is already known on this topic

- When diagnosing asthma most guidelines still recommend symptom scoring.
- Exercise-related asthma-like symptoms are poor predictors of asthma in elite athletes and it seems that elite athletes have an increased number of airway inflammatory cells but our knowledge about this is still limited.
- The role of asthma-like symptoms in elite athletes remains somewhat unclear.

What this study adds

- This study brings knowledge about management of asthma-like symptoms and asthma in elite athletes.
- Asthma-like symptoms in elite athletes alone should not be relied upon to make a diagnosis of asthma and use of objective measurements for diagnosing asthma is recommendable.

asthma phenotype of elite athletes differs from that of classical asthma.

Acknowledgements: Mannitol test kits were kindly provided by Pharmaxis (Frenchs Forest, Australia). Flaemnuova (Brescia, Italy) provided the Easyneb II devices.

Funding: Anti-Doping Denmark, Team Denmark, Research Foundation of Bispebjerg Hospital and the Beckett Foundation financially supported the study.

Competing interests: TKL has received financial support from GlaxoSmithKline. LP has received financial support from The Academy of Muscle Biology, Exercise and Health Research, The Health Insurance Foundation, Team Denmark and Anti-Doping Denmark. SDA is the inventor of the mannitol test, although it is owned by her employer the Sydney South West Area Health Service (SSWAHS). SDA owns shares in Pharmaxis Ltd that were purchased by the author in 2001. SDA does not own any options. SDA may benefit from royalties in the future. As an employee of SSWAHS, SDA acts as a consultant and invoices are issued by SSWAHS. AS has received mannitol test kits from Pharmaxis Ltd. VB has received financial support from Pharmaxis Ltd and the Danish Lung Association.

Ethics approval: The Danish National Committee on Biomedical Research Ethics approved this study.

Provenance and peer review: Not commissioned; externally peer reviewed.

REFERENCES

- Helenius IJ, Tikkanen HO, Sarna S, *et al.* Asthma and increased bronchial responsiveness in elite athletes: atopy and sport event as risk factors. *J Allergy Clin Immunol* 1998;**101**:646–52.
- Lumme A, Haahtela T, Öunap J, *et al.* Airway inflammation, bronchial hyperresponsiveness and asthma in elite ice hockey players. *Eur Respir J* 2003;**22**:113–7.
- Holzer K, Anderson SD, Douglass J. Exercise in elite summer athletes: challenges for diagnosis. *J Allergy Clin Immunol* 2002;**110**:374–80.
- Rundell KW, Im J, Mayers LB, *et al.* Self-reported symptoms and exercise-induced asthma in the elite athlete. *Med Sci Sports Exerc* 2001;**33**:208–13.
- Ringsberg KC, Wetterqvist H, Lowhagen O, *et al.* Physical capacity and dyspnea in patients with asthma-like symptoms but negative asthma tests. *Allergy* 1997;**52**:532–40.
- Langdeau JB, Turcotte H, Bowie DM, *et al.* Airway hyperresponsiveness in elite athletes. *Am J Respir Crit Care Med* 2000;**161**:1479–84.
- Bonsignore MR, Morici G, Vignola AM, *et al.* Increased airway inflammatory cells in endurance athletes: what do they mean? *Clin Exp Allergy* 2003;**33**:14–21.
- Karjalainen EM, Laitinen A, Sue-Chu M, *et al.* Evidence of airway inflammation and remodelling in ski athletes with and without bronchial hyperresponsiveness to methacholine. *Am J Respir Crit Care Med* 2000;**161**:2086–91.
- Sue-Chu M, Larsson L, Moen T, *et al.* Bronchoscopy and bronchoalveolar lavage findings in cross-country skiers with and without “ski asthma”. *Eur Respir J* 1999;**13**:626–32.
- Boulet LP, Turcotte H, Langdeau JB, *et al.* Lower airway inflammatory responses to high-intensity training in athletes. *Clin Invest Med* 2005;**28**:15–22.
- Alaranta A, Alaranta H, Palmu P, *et al.* Asthma medication in Finnish Olympic athletes: no signs of inhaled β_2 -agonist overuse. *Med Sci Sports Exerc* 2004;**36**:919–24.
- Corrigan B, Kazlauskas R. Medication use in athletes selected for doping control at the Sydney Olympics (2000). *Clin J Sport Med* 2003;**13**:33–40.
- Lund T, Pedersen L, Larsson B, *et al.* Prevalence of asthma-like symptoms, asthma and its treatment in elite athletes. *Scand J Med Sci Sports* 2009;**19**:174–8.
- Helenius IJ, Haahtela T. Allergy and asthma in elite summer sport athletes. *J Allergy Clin Immunol* 2000;**106**:444–52.
- Sue-Chu M, Karjalainen EM, Altraja A, *et al.* Lymphoid aggregates in endobronchial biopsies from young elite cross-country skiers. *Am J Respir Crit Care Med* 1998;**158**:597–601.
- Weiler JM, Layton T, Hunt M. Asthma in United States Olympic athletes who participated in the 1996 summer games. *J Allergy Clin Immunol* 1998;**102**:722–6.
- O’Byrne P, Bateman ED, Bousquet J, *et al.* Global Initiative for Asthma. Global strategy for asthma management and prevention. WHO/NHLBI workshop report. NIH Publication no. 02-3659. Updated 2006. <http://www.ginasthma.com/> (accessed 6 Sep 2008).
- Juniper EF, O’Byrne PM, Guyatt GH, *et al.* Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;**14**:902–7.
- Miller MR, Hankinson J, Brusasco V, *et al.* ATS/ERS Task Force. Standardisation of spirometry. *Eur Respir J* 2005;**26**:319–38.
- Nysom K, Ulrik CS, Hesse B, *et al.* Published models and local data can bridge the gap between reference values of lung function for children and adults. *Eur Respir J* 1997;**10**:1591–8.
- Dreborg S. Skin test used in type I allergy testing (position paper). *Allergy* 1989;**44**(Suppl 10):22–30.
- American Thoracic Society. ATS workshop proceedings: exhaled nitric oxide and nitric oxide oxidative metabolism in exhaled breath condensate: executive summary. *Am J Respir Crit Care Med* 2006;**173**:811–3.
- Anderson SD, Brannan J, Spring J, *et al.* A new method for bronchial-provocation testing in asthmatic subjects using a dry powder of mannitol. *Am J Respir Crit Care Med* 1997;**156**:758–65.
- Brannan JD, Anderson SD, Perry CP, *et al.* Aridol Study Group. The safety and efficacy of inhaled dry powder mannitol as a bronchial provocation test for airway hyperresponsiveness: a phase 3 comparison study with hypertonic (4.5%) saline. *Respir Res* 2005;**6**:144.
- Leuppi JD, Brannan JD, Anderson SD. Bronchial provocation tests: The rationale for using inhaled mannitol as a test for airway hyperresponsiveness. *Swiss Med Wkly* 2002;**132**:151–8.
- Leuppi JD, Salome CM, Jenkins CR, *et al.* Markers of airway inflammation and airway hyperresponsiveness in patients with well-controlled asthma. *Eur Respir J* 2001;**18**:444–50.
- Paggiaro PL, Chanez P, Holz O, *et al.* Sputum induction. *Eur Respir J* 2002;**37**(Suppl):3–8.
- Helenius IJ, Ryttilä P, Metso T, *et al.* Respiratory symptoms, bronchial responsiveness, and cellular characteristics of induced sputum in elite swimmers. *Allergy* 1998;**53**:346–52.
- van Asch CJJ, Balemans WAF, Rovers MM, *et al.* Atopic disease and exhaled nitric oxide in an unselected population of young adults. *Ann Allergy Asthma Immunol* 2008;**100**:59–65.
- Helenius I, Lumme A, Öunap J, *et al.* No effect of montelukast on asthma-like symptoms in elite ice hockey players. *Allergy* 2004;**59**:39–44.
- Sue-Chu M, Karjalainen EM, Laitinen A, *et al.* Placebo-controlled study of inhaled budesonide on indices of airway inflammation in bronchoalveolar lavage fluid and bronchial biopsies in cross-country skiers. *Respiration* 2000;**67**:417–25.
- Anderson SD, Kippelen P. Exercise-induced bronchoconstriction: Pathogenesis. *Curr Allergy Asthma Rep* 2005;**5**:116–22.
- Helenius IJ, Tikkanen HO, Haahtela T. Association between type of training and risk of asthma in elite athletes. *Thorax* 1997;**52**:157–60.
- Anderson SD, Sue-Chu M, Perry CP, *et al.* Bronchial challenges in athletes applying to inhale a β_2 -agonist at the 2004 Summer Olympics. *J Allergy Clin Immunol* 2006;**117**:767–73.
- Dickinson JW, Whyte GP, McConnell AK, *et al.* Impact of changes in the IOC-MC asthma criteria: a British perspective. *Thorax* 2005;**60**:629–32.