

AQUA[®]: Allergy Questionnaire for Athletes: Development and Validation

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ABSTRACT

BONINI, M., F. BRAIDO, I. BAIARDINI, S. DEL GIACCO, C. GRAMICCIONI, M. MANARA, G. TAGLIAPIETRA, A. SCARDIGNO, V. SARGENTINI, M. BROZZI, G. RASI, and S. BONINI. AQUA[®]: Allergy Questionnaire for Athletes: Development and Validation. *Med. Sci. Sports Exerc.*, Vol. 41, No. 5, pp. 000–000, 2009. **Purpose:** Despite the high and increasing prevalence of allergic diseases in athletes, allergy diagnostics is not part of the routine medical examination in sports medicine. This study reports the development and validation of an easy and reliable questionnaire for screening allergy in athletes. **Methods:** AQUA[®] was derived from the European Community Respiratory Health Survey Questionnaire. On the basis of open interviews with team doctors, coaches, and athletes, questions were added about: the type, duration, and intensity of training; exercise-related allergic and infectious symptoms; social habits (smoking); drug and food supplements intake; antidoping regulations. The final version of the questionnaire, made of 25 selected questions, was validated in 128 professional soccer players who underwent accurate history taking, medical examination, skin prick testing, and/or specific IgE determination. On the basis of the correlation with objective allergy (positive skin tests to at least one allergen), questions were scored from 1 to 5 according to their positive likelihood ratio. **Results:** Skin tests (gold standard for validation) were positive in 46.8% of soccer players. Mean total AQUA[®] score was 9.4 ± 7.8 in allergic athletes versus 1.3 ± 2.3 in nonallergic athletes. A total AQUA[®] score of >5 was shown to have the best positive predictive value for allergy (0.94) with a specificity of 97.1% and a sensitivity of 58.3%. **Conclusions:** AQUA[®], produced in 10 European languages, is a validated, easy, and reliable tool for calling attention on the high prevalence of allergy in athletes. **Key Words:** SOCCER PLAYERS, SPORTS ALLERGY, EXERCISE-INDUCED ASTHMA, EXERCISE-INDUCED BRONCHOCONSTRICTION, UPPER RESPIRATORY TRACT INFECTIONS

Allergic diseases and sensitization are reported to occur in athletes more frequently than in the general population. The prevalence of asthma in athletes is particularly high, reaching values up to 54.8% in winter sports, swimming, and endurance disciplines (7,13,18,27). It is estimated that between 13.3% and 41.0% of athletes suffer from allergic rhinitis (3,26). The numbers may be higher because sensitization to inhalant allergens can be detected by skin prick tests in subjects with no clinical symptoms. These subjects may be considered at increased risk for allergic diseases and bronchial hyperactivity. In fact, when atopy and physical activity were

combined in a logistic regression model, the risk of asthma was 25-fold higher in atopic speed and power athletes, 42-fold greater in atopic long-distance runners, and 97-fold higher in atopic swimmers compared with healthy, nonatopic control subjects (14).

Estimates of the prevalence of allergic diseases in athletes may depend on the diagnostic methods used. However, even in studies using different methodologies, the prevalence of allergic diseases seems to be on the rise. Overall, the prevalence of asthma increased from 9.7% in 1976 to 21.9% in 1996 in the Australian Olympic delegation (from 21.0% to 25.9% in swimmers) (10,15) and from 4.3% in 1984 to 15.3% in 1996 in the US Olympic delegation (22,25).

Despite the high and growing prevalence of allergic diseases in athletes, allergy diagnosis—including specific history taking and clinical or laboratory testing—is often overlooked in sports medicine. At present, in Italy, only pulmonary function tests (PFT) are required as part of the routine examination for determining eligibility to compete. Because athletes often record higher-than-normal PFT values, the results for asthmatic athletes may be confusing—appearing to be within the “normal” range, although, in reality,

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showing a pulmonary deficit on the basis of what is “normal” for an athlete (5). Standard tests for other target organs of allergic disease are rarely done and not required as part of the routine physical.

The diagnosis of allergy should have an important role in the clinical assessment of athletes because allergic disease can have serious consequences on overall health status and quality-of-life as well as on physical performance. Moreover, an accurate diagnosis of allergy and asthma is necessary to develop an optimal management plan for the athlete—one that takes into consideration safety concerns (20,21) and potential effects on performance (16) of antiallergic and antiasthma medications and follows the recommendations for prohibited substances listed by the World Anti-Doping Agency (23).

This study reports on the development and validation of an easy and reliable questionnaire for screening allergy in athletes.

METHODS

AQUA production. The questionnaire was derived from the European Community Respiratory Health Survey Questionnaire (6,9). On the basis of open interviews with team doctors, coaches, and athletes, the questionnaire was adapted to the target population and some questions were added. These were aimed at defining the type, duration, and intensity of training, identifying the exercise-related allergic and infectious symptoms, and describing the athlete’s social habits (smoking in particular) and drug intake (aspects related to antidoping regulations).

Preliminary testing. The questionnaire prototype was circulated for comments to some experts (mentioned in the Acknowledgment) and to a representative sport population sample to assess comprehension, consistency, and reproducibility.

Validation. The final version of the questionnaire, consisting of 25 selected questions (see Appendix), was administered for validation to 128 professional soccer players from six first-division European teams. The protocol was approved by the Italian National Research Council. Written informed consent was given by all participants, and data collection and handling were conducted in respect of privacy requirements, in accordance with the ethical standards for noninterventional studies and with the Helsinki Declaration.

Soccer players (all males, aged 16–39 yr) were divided in two groups after careful history taking and physical examination on the basis of the positive or negative results of skin prick testing and/or specific IgE determination (Phadiatop; Phadia, Uppsala, Sweden). The two groups were age-matched (mean age was 23.4 ± 5.9 vs 24.6 ± 5.5 yr, respectively). For this article, allergy was defined as a sensitization documented by a positive skin test to at least one allergen and/or positive Phadiatop values. Asthma, exercise-induced bronchoconstriction, rhinitis, conjunctivi-

tis, urticaria, angioedema, atopic eczema, and contact dermatitis, in this article, are called “allergic diseases” independently of the presence of detectable IgE antibodies. Diagnosis of asthma (11), exercise-induced bronchial hyperreactivity (24), rhinitis (2), and anaphylaxis (19) was made according to criteria set by international guidelines.

Skin tests were performed using a European standard panel of allergens and methodology (12). Skin tests were considered positive in the presence of a wheal reaction to allergen ≥ 3 mm after subtraction of the wheal induced by the negative control (extract diluent).

AQUA score: specificity and sensitivity. For all questions with a potential value in predicting allergic diseases (from Q. 4 to Q. 16), responses were related to an objective documentation of allergy (positive skin tests and/or specific IgE antibody to at least one allergen). For each of these questions except for Q. 14, which is related to Q. 13 and only included to acquire information on the type of allergen responsible for sensitization, the positive likelihood ratio (LR+) was calculated on the basis of the formula: $LR+ = \text{sensitivity} / (1 - \text{specificity})$. The likelihood ratio for a positive result tells us how much the odds of the disease increase when a test is positive (8).

Each question then received a score on the basis of the value of its LR+ and according to a scale derived from the guidelines for interpreting the LR (Table 1). A total score (AQUA[®] score) was calculated for all soccer players by summing the scores of the individual questions. The total score was used to calculate sensitivity and specificity and to determine the predictive value of the questionnaire.

Translation and copyright. AQUA[®] was first produced in English and then translated to nine European languages and back by two independent translators for each language. AQUA[®] is protected by an international copyright (Barzanò and Zanardo, October 12, 2007; No. A04405).

RESULTS

IgE antibodies to at least one or more common inhalant allergens were found in 46.8% of soccer players (60 of 128). A history of asthma was present in 9.3% of allergic subjects, exercise-induced bronchospasm in 11.7%, rhinitis in 19.5%, conjunctivitis in 19.5%, and allergic dermatitis in 17.9%. Nine athletes (7.0%) had food intolerance, and four (3.1%) reported adverse reactions to drugs. Five subjects (3.9%) had documented anaphylaxis. Several subjects had more than one allergic disease. The presence of IgE antibodies was not

TABLE 1. Score assigned to individual questions on the basis of their LR+.

LR+	Interpretation	Score
≥ 20	Very large increase in the likelihood of disease	5
≥ 10	Large increase in the likelihood of disease	4
5–9.9	Moderate increase in the likelihood of disease	3
2–4.9	Small increase in the likelihood of disease	2
1–1.9	Minimal increase in the likelihood of disease	1
<1	No change in the likelihood of disease	0

associated with clinical symptoms in 12.5% of subjects with positive skin tests and/or Phadiatop/RAST results. “Allergic diseases” were also present in subjects with no detectable IgE antibodies: asthma in 2.9%, exercise-induced bronchial hyperreactivity in 7.3%, rhinitis in 1.4%, conjunctivitis in 7.3%, dermatitis in 7.3%, and anaphylaxis in 1.4%.

The presence of a running and itchy nose associated with frequent sneezing was determined to be the condition with the highest positive likelihood ratio, followed by a medical diagnosis of allergic disease and then by the “suspicion of allergy” even in the absence of a medical diagnosis (Fig. 1).

F1

Mean total AQUA[®] scores were 9.4 ± 7.8 (range, 0–24) in subjects with IgE antibodies versus 1.3 ± 2.3 (range, 0–11) in subjects without IgE antibodies (Fig. 2). Sensitivity and specificity were calculated at different thresholds of AQUA[®] scores. A score ≥ 5 was found to have the best positive predictive value for allergy (0.94) with a specificity of 97.1% and a sensitivity of 58.3%.

F2

Some athletes (5.4%) reported experiencing recurrent upper respiratory tract infections (URTI) that affected their regular training and performance.

Athletes, in general, were high “drug consumers”: 85.7% of subjects in our sample had undergone more than three cycles of drug treatment in the last year (mainly nonsteroid anti-inflammatory drugs (NSAID), antibiotics, and analgesics); 35.1% reported using various medicines in the week before the survey. Almost half of athletes (47.6%) used food supplements (e.g., vitamins, amino acids, creatine), and 10.1% were current smokers.

DISCUSSION

Sensitization to commonly inhaled allergens was detectable in a high percentage (almost 1 of 2) of the study population of soccer players, supporting previous findings in other elite athletes of various disciplines (3,7,13,18,26,27). The prevalence of sensitization and allergic diseases in athletes reported in epidemiological studies, although high, may be underestimated owing to the lack of routine allergy screening in current sports medicine practice. Several questionnaires are available to screen allergic diseases in the general population, and these can be used for athletes (7). However, these questionnaires are often specific for asthma or rhinitis and not for allergic disorders in general. AQUA[®] is the first validated questionnaire for screening allergy in athletes, which also gathers information on the athletic discipline, intensity of training, and relevant social habits. The questionnaire is a simple, easy-to-use, self-administered tool that permits identification, with a high positive predictive value (0.94), of subjects who require further allergy testing.

The importance of identifying sensitization to common allergens in athletes is supported by the different distributions of asthma, rhinitis, conjunctivitis, dermatitis, and anaphylaxis reported for allergic versus nonallergic athletes. In a young population sample such as athletes, these diseases are often allergic in origin. Therefore, diagnosing allergy may also help with the early identification of mild forms of bronchial obstruction or rhinoconjunctivitis that, although often not reported by athletes, may still influence optimal physical performance.

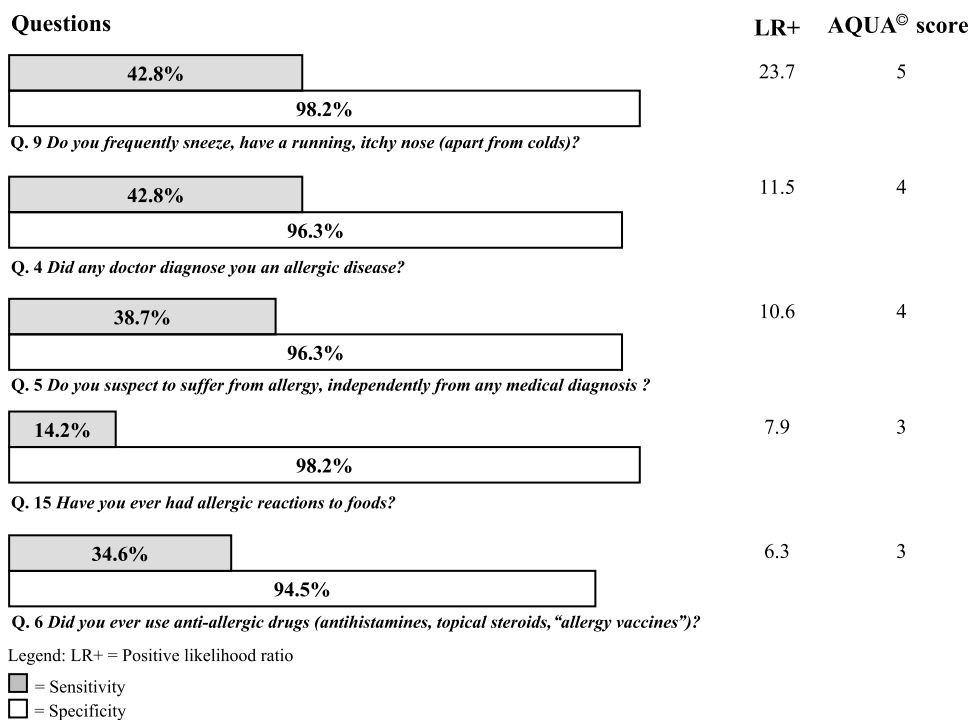


FIGURE 1—AQUA[®] questions with the highest positive likelihood ratio (LR+) and related scores.

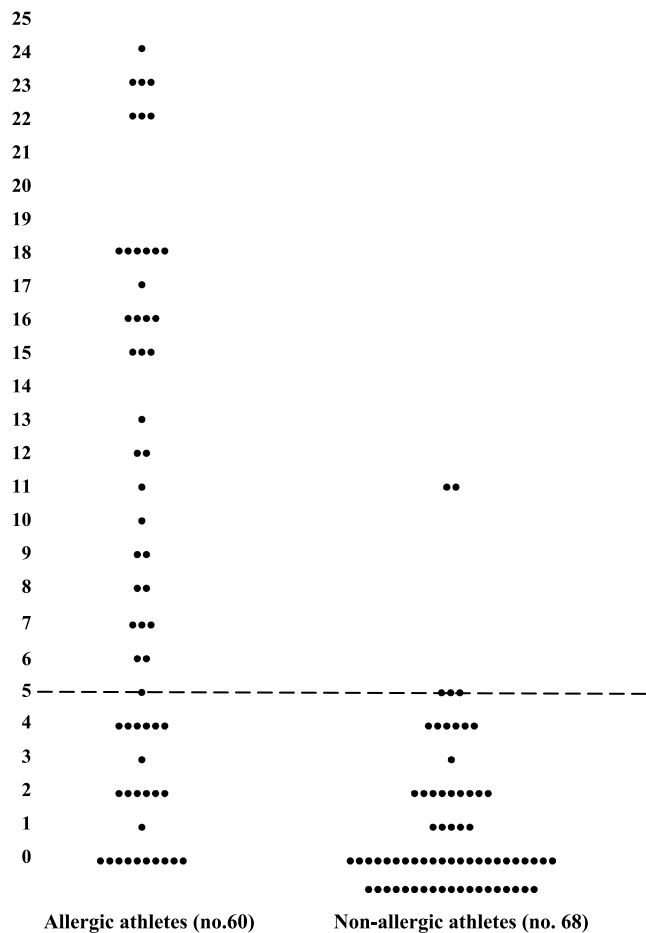


FIGURE 2—AQUA[®] scores in allergic (with IgE antibodies) and nonallergic (without demonstrable IgE antibodies) soccer players. A score ≥ 5 (dashed line) had a positive predictive value for allergic diseases of 0.94 with a specificity of 97.1% and a sensitivity of 58.3%. The AQUA[®] score represents the total score deriving from the sum of scores assigned to individual questions of potential interest for predicting allergic diseases (Q. 4 to Q. 16) on the basis of their positive likelihood ratio. See text (Methods) and Appendix for more details.

The prevalence of URTI in our sample was lower than that reported in other studies (17). However, this should not be considered an irrelevant finding in this young population that is assumed to be “more than healthy.” Further research on the relationship between allergy and respiratory infections in athletes is warranted. In addition, though this study did not focus on the medical management and social habits of athletes, the reported high consumption of drugs and food supplements, even when not justified, as well as the high number of smokers among elite soccer players suggest an opportunity for *ad hoc* studies in larger samples of both allergic and nonallergic athletes.

After preliminary testing in a large population of athletes, AQUA[®] was validated in male soccer players. The homogeneity of the selected population sample reduced the variability of responses related to age, sex, and type of sport but should not have influenced validation because an objective “gold standard,” that is, documentation of IgE antibodies to common allergens, was also used to prove allergy.

A total AQUA[®] score ≥ 5 was chosen on the basis of the best predictive value for allergy. Despite a high specificity (97.1%) for the presence of allergy, the sensitivity of the questionnaire at this threshold level was not satisfactory (58.3%). This probably reflects the “gold standard” used to prove allergy (i.e., positive skin tests or positive serum IgE antibodies) as opposed to the power of the questionnaire. Not all “allergic diseases” are IgE-mediated, particularly in athletes in whom allergy symptoms of exercise-induced bronchial hyperreactivity, rhinitis, or a red eye may occur in the absence of any detectable sensitization, for example, in relation to various intrinsic or environmental conditions such as chlorine exposure or hyperventilation in cold air (1,4,11). Indeed, the presence of exercise-induced bronchial hyperreactivity, rhinitis, or urticaria in a significant number of athletes with negative skin tests or no IgE antibodies produced a high AQUA[®] score even in some nonallergic subjects (Fig. 2). Depending on the specific targets for which the questionnaire is used, a lower threshold of AQUA[®] may be adopted. This will increase its sensitivity but reduce its specificity about IgE-mediated allergy. For instance, a threshold AQUA[®] score ≥ 3 would increase the sensitivity of the questionnaire to 70.0% while reducing its specificity to 83.8%.

Interestingly, a positive answer to Q. 9, “Do you frequently sneeze, have a running, itchy nose?” alone was found to reach the threshold chosen for a legitimate suspicion of allergy. Should this be confirmed by data on a larger population sample, it would be possible to reduce the number of questions to a few key items that would permit prediction of allergy in athletes with satisfactory specificity and sensitivity.

Data about the prevalence of allergy, obtained with different questionnaires, are often discordant, possibly because of the heterogeneity of instruments used (7). AQUA[®] is available in several languages and may provide a standardized tool allowing aggregation and comparison of data from different population studies. In fact, the questionnaire has been selected to be used in a polycentric study of approximately 2000 athletes from 10 national delegations participating in the Beijing Olympic Games. It is hoped that the results of this study will provide independent evidence of the reproducibility of AQUA[®] in a larger and less homogeneous population sample of athletes.

AQUA[®] was recently adapted to nonprofessional exercisers (AQUE[®], Allergy Questionnaire for Exercisers). AQUA[®] and AQUE[®] may be useful tools for calling attention to the high prevalence of allergy in exercisers and might provide the initial step toward developing flowcharts for allergy diagnosis and management in sports medicine.

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AQ2

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APPENDIX

AQUA[®] 2007

Allergy Questionnaire for Athletes

Allergic diseases (bronchial asthma; rhinitis; conjunctivitis; eczema, urticaria and dermatitis; allergic and anaphylactic reactions to drugs, foods, and insect venoms; etc.) represent a third millennium epidemic based on their increasing prevalence, particularly in industrialized countries. The high prevalence of these diseases (25–40% of the population) has led the World Allergy Organization to call for specific actions aimed at diagnosis and prevention (www.ginasthma.com; www.whiar.com; www.goldcopd.com).

Studies performed in several national Olympic delegations have shown that allergic diseases occur frequently in elite athletes, with a prevalence of asthma even higher than that recorded in the general population. Moreover, allergic diseases are often associated with infections, particularly of the upper respiratory tract.

Although allergic diseases do not prevent excellence in sports, the lack of diagnosis may influence the quality of competitive physical performance.

The treatment of allergic diseases in athletes should be based on using safe medications that will not affect performance (without side effects on the cardiovascular and nervous system, etc.) and which are permitted by the current anti-doping regulations (www.wada-ama.org).

This survey is part of an international project involving 24 European Centers of Excellence in allergic diseases (www.ga2len.net), which, with the support of the European Community, aims at prevention and treatment of allergy.

Participation in the survey is certainly helpful for the health of athletes. The survey respects privacy needs and does not influence any decision about the identity of participants to sports activity.

FIRST NAME _____
PLACE OF BIRTH _____
CITY OF RESIDENCE _____
WEIGHT _____ HEIGHT _____
SPORT _____
CODE _____

SURNAME _____
DATE OF BIRTH _____
PHONE (optional) _____
TEAM _____

Code _____

- 1) How many times a week do you train?
 Up to 3 times
 More than 3 times
- 2) Every training session usually lasts:
 1–2 hours
 2–3 hours
 More than 3 hours
- 3) Do you mainly train:
 outdoor
 indoor
- 4) Did any doctor diagnose you an allergic disease?
 No
 Yes
If yes, which ones?
 Asthma
 Rhinitis
 Conjunctivitis
 Urticaria
 Eczema
 Drugs allergy
 Food allergy
 Insect venom allergy (bees, wasps)
 Anaphylaxis
- 5) Do you suspect to suffer from allergy, independently from any medical diagnosis?
 No
 Yes
- 6) Did you ever use anti-allergic drugs (antihistamines, topical steroids, “allergy vaccines”)?
 No
 Yes
- 7) Is there any allergic subject in your family?
 No
 Yes, mother and father
 Yes, mother or father
 Yes, other relatives
- 8) Have you frequently red eyes with tearing and itching?
 No
 Yes
- 9) Do you frequently sneeze, have a running, itchy nose (apart from colds)?
 No
 Yes
- 10) Did you ever feel tightness of your chest and/or wheeze?
 No
 Yes

- 11) Have you ever had itchy skin eruptions?
 No
 Yes
- 12) Have you ever had severe allergic or anaphylactic reactions?
 No
 Yes
- 13) Have you ever had shortness of breath, cough and/or itching of the throat following exercise?
 No
 Yes
 If yes, you have more difficulties:
 At the beginning of the training session
 At the end of the training session
 During the whole training session
- 14) If you suffered from any of the above, did these symptoms occur:
 mainly outdoor
 mainly indoor
 mainly in spring
 mainly in cold or humid conditions
 independently of any environmental condition
- 15) Have you ever had allergic reactions to foods?
 No
 Yes
 If yes, do you remember to which food? _____

- 16) Have you ever had allergic reactions to drugs?
 No
 Yes
 If yes, do you remember to which drug? _____

- 17) Do you know that some drugs for allergic and respiratory diseases are prohibited or under restrictions by the World Anti-Doping Agency (WADA)?
 No
 Yes
 If yes, think which substances, you think are included in this category:
 Antihistamines
 Bronchodilators
 Vasoconstrictors
 Topical steroids (metered dose inhalers or inhaled powders)
 Dermatological steroid preparations
 Injected or oral steroids
- 18) Are you afraid that anti-allergic and/or respiratory drugs may worsen your performances or make you infringing anti-doping regulations?
 No
 Yes

- 19) Do you use any foods supplements (vitamins, amino acids, creatine)?
 No
 Occasionally
 Regularly
- 20) Do you smoke?
 No
 Yes
 If yes, how many cigarettes a day?
 Less than 5
 5–20
 More than 20
- 21) Did you use during the last year the following drugs and how often?

Drugs	Never	1–3 Times	3–5 Times	5–10 Times	More Than 10 Times
Antibiotics					
Anti-inflammatory drugs					
Drugs for pain					
Drugs for fever					
Others					

- 22) Did you use any drug during the last week?
 No
 Yes
 If yes, which one? _____
- 23) Do you frequently suffer from upper respiratory infections (pharyngitis, bronchitis, colds) or fever?
 No
 Yes
 If yes, this infections are more frequent during overtraining periods?
 No
 Yes
- 24) Do you suffer for recurrent labial herpes?
 Never
 1–3 times per year
 More than 3 times per year
- 25) How many times in the last year you could not train because of infections?
 Never
 1–3 times
 More than 3 times

AQUA[®] Score

On the basis of their LR+, calculated from experimental data, relevant questions for predicting allergy were scored from 1 to 5.

AQ4

Total AQUA[®] score may be calculated summing scores assigned to individual questions with a positive answer.

A total AQUA[®] score ≥ 5 has a positive predictive value for allergy of 0.94 with a specificity of 97.1% and a sensitivity of 58.3%.

Question	Sensitivity (%)	Specificity (%)	LR+	Score
Q. 9	42.8	98.2	23.7	5
Q. 4	42.8	96.3	11.5	4
Q. 5	38.7	96.3	10.6	4
Q. 6	34.6	94.5	6.3	3
Q. 15	14.2	98.2	7.9	3
Q. 7b	—*	—*	—*	3
Q. 7c	28.5	92.6	3.8	2
Q. 7d	12.2	92.6	1.6	1
Q. 8	28.6	92.6	3.8	2
Q. 10	10.2	96.3	2.7	2
Q. 11	26.5	92.6	3.6	2
Q. 12	6.1	98.2	3.4	2
Q. 13	20.4	94.5	3.7	2
Q. 16	5.0	94.1	0.8	0

*No experimental data is available for this question in the population sample studied (i.e., no positive answers in both athletes and controls). The question was arbitrarily assigned a score of 3 in view of the scores assigned to questions 7c and 7d.