This study was aimed at the following: (1) the prevalence of airway hyperresponsiveness (AHR) and exercise-induced bronchoconstriction (EIB) in swimmers and winter sport athletes according to the previously recommended regulatory sport agencies criteria, (2) the relationship between respiratory symptoms and AHR/EIB, (3) the impact of the chosen cutoff value for AHR on its prevalence, and (4) the effect on the prevalence of the positive eucapnic voluntary hyperpnea (EVH) test of using the highest vs the lowest spirometric post-EVH values to calculate the magnitude of the airway response. We compared the prevalence of respiratory symptoms with responses to methacholine challenge and EVH in 45 swimmers, 45 winter sport athletes, and 30 controls. Two methacholine challenge cutoffs for AHR were analyzed: ≤4 mg/mL (the sport agencies’ criteria for AHR) and ≤16 mg/mL. Sixty percent of swimmers, 29% of winter sport athletes, and 17% of controls had evidence of EIB or AHR (with the ≤4 mg/mL criteria). Among athletes with a methacholine provocative concentration inducing a 20% decrease in the FEV₁ between 4 and 16 mg/mL, 43% of swimmers and 100% of winter sport athletes were symptomatic (P < .05). Prevalence of positive EVH tests were 39% in swimmers, 24% in winter sport athletes, and 13% in controls when the highest FEV₁ value measured at each time point post-EVH was used to identify maximal response for calculation of airway response, although these prevalences were higher if we used the lowest value. This study suggests that AHR/EIB is frequent in swimmers, whereas the frequently reported respiratory symptoms in winter sport athletes are often not related to AHR/EIB. Furthermore, the choice of methods for assessing methacholine challenge and EVH responses influences the prevalences of AHR and EIB.

**Trial registration:** clinicaltrials.gov; Identifier NCT 00686491 and NCT 00686452.

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**Abbreviations:** AHR = airway hyperresponsiveness; EIB = exercise-induced bronchoconstriction; EVH = eucapnic voluntary hyperpnea; ICS = inhaled corticosteroids; IOC-MC = International Olympic Committee-Medical Commission; PC₂₀ = provocative concentration causing a 20% fall in FEV₁; WADA = World Anti-Doping Agency.
mixture containing 5% CO₂ at room temperature for 6 min. The target ventilation was 30 × FEV₁, FEV₁ was measured before the test and at 3, 5, 10, 15, 20, 25, and 30 min after EVH. At each time interval, FEV₁ was measured twice, and if there was a >10% difference between the FEV₁ at each attempt, a third FEV₁ was performed. We used both the lowest and the highest of the two reproducible measurements after the test to calculate the lowest post-challenge value (therefore generating two sets of data), to verify the impact of these different methods to calculate the maximal decrease in FEV₁. In keeping with IOC recommendations, we used the higher of the two reproducible values to discuss the prevalence of EIB to EVH, as previously suggested.²²

### Study Subjects

Swimmers, winter sport athletes, and nonathlete controls were recruited. Athletes and controls had to be nonsmokers, nonobese, and free of any disease that may interfere with the study. Controls taking asthma medication were excluded. To be included, swimmers and winter sport athletes had to be active competitors and train at least 10 h per week in a chlorinated swimming pool and outside in winter, respectively. Winter sport athletes were not exposed to chlorinated environments and all athletes performed the respiratory tests out of pollen season and during their training period, in fall or winter. Controls had to be nonasthmatic and take part in physical activities for <6 h per week. They were matched for age (±5 years) and sex with swimmers and winter sport athletes. No control was involved in a competitive sport or an outdoor winter sport activity, or was exposed to a chlorinated environment. All subjects gave their written informed consent. The study protocol was approved by our institutional ethics committee and was registered at www.clinicaltrials.gov (NCT 00086491 and NCT 00086452).

### Study Design

Each set of the tests was performed at least 14 h after the last training session for all athletes. A physical examination and allergy skin-prick tests were done, and a questionnaire on current health status and training was administered. EVH and methacholine challenges were performed consecutively after recovery of expiratory flows within 10% of baseline.

### Baseline Spirometry

Spirometry was carried out according to the American Thoracic Society specifications.² Predicted spirometric values were defined according to Knudson et al.²³ Three reproducible measurements of FEV₁ were obtained.

### Eucapnic Voluntary Hyperpnea Challenge

The EVH challenge was performed according to the method described by Anderson and Brannan.²⁴ Briefly, subjects inhaled a dry-air mixture containing 5% CO₂ at room temperature for 6 min. The target ventilation was 30 × FEV₁, FEV₁ was measured before the test and at 3, 5, 10, 15, 20, 25, and 30 min after EVH. At each time interval, FEV₁ was measured twice, and if there was a >10% difference between the FEV₁ at each attempt, a third FEV₁ was performed. We used both the lowest and the highest of the two reproducible measurements after the test to calculate the lowest post-challenge value (therefore generating two sets of data), to verify the impact of these different methods to calculate the maximal decrease in FEV₁. In keeping with IOC recommendations, we used the higher of the two reproducible values to discuss the prevalence of EIB to EVH, as previously suggested.²²

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Subjects had a diagnosis of EIB when a decrease in FEV₁ ≥ 10% from baseline was recorded and sustained over 5 min after EVH. After the EVH challenge was performed, FEV₁ had to return to at least 90% of baseline before the methacholine challenge was done; this usually took between 30 and 60 min.

**Methacholine Challenge**

AHR to methacholine was measured using the tidal-breathing method. After baseline measurements of FEV₁ and FVC, each subject inhaled saline (0.9%) followed by doubling concentrations of methacholine between 0.03 and 128 mg/mL to obtain a 20% decrease in FEV₁. Methacholine aerosols were generated by a Wright nebulizer with an output of 0.13 mL/min and were inhaled for 2 min at 5-min intervals. FEV₁ was measured 30 and 90 s after each inhalation and every 2 minutes until it started to increase. An acceptable-quality FEV₁ was obtained at each time point; otherwise the FEV₁ maneuver was repeated. AHR was defined as a PC₂₀ ≤ 4 mg/mL, according to the WADA and IOC-MC guidelines, and for athletes taking ICS for at least 1 month, a positive response was a PC₂₀ of ≤ 16 mg/mL. The impact of a methacholine challenge PC₂₀ cutoff ≤ 16 mg/mL on the prevalence of AHR was also studied and compared with EVH.

**Questionnaire**

A questionnaire regarding past and current respiratory conditions and exercise-induced respiratory symptoms (wheezeing, cough, phlegm production, and chest tightness), family history of asthma and allergies, and training and sport habits was administered. We used a questionnaire translated and adapted from the European Community Health Survey, as previously described.

**Statistical Analysis**

Data were expressed as mean ± SD or percentage values. Analysis of variance was used to compare the three groups. Subjects with a PC₂₀ > 128 mg/mL were assigned a PC₂₀ of 128 mg/mL for statistical analysis. Statistical results from this parameter were expressed with the log-transformed values. Post hoc comparisons were performed using the Tukey/Kramer technique. Contingency tables were used to compare the prevalence of AHR or EIB in all three groups and the prevalence of exercise-induced symptoms in the two groups of athletes. The results were considered significant at P values ≤ 0.05. Data were analyzed using the statistical package program SAS, version 9.1.3 (SAS Institute Inc.; Cary, NC).

**RESULTS**

**Subjects’ Characteristics**

The characteristics of the subjects included in the study are presented in Table 1. Swimmers (11 synchronized swimmers, 32 swimmers, and two divers) and winter sport athletes (seven biathletes, 22 cross-country skiers, and 16 speed-skaters training outdoors) were competing at national to Olympic levels. Eleven percent of swimmers and 9% of winter sport athletes had asthma diagnosed during their childhood before beginning their sport career. All athletes taking ICS for > 1 month had also been prescribed short-acting β₂-agonists on demand, except for one swimmer, who used a long-acting β₂-agonist (formoterol).

**Prevalence of AHR and/or EIB According to Sport Authorities’ Criteria**

One swimmer withdrew from the study without performing the EVH challenge. Five swimmers, four winter sport athletes, and three controls were considered negative to EVH because they reached a decrease in FEV₁ of at least 10% at one time point only, as well as one subject in each group who reached a 10% decrease at two nonconsecutive time points. All subjects with a positive EVH had an FEV₁ decrease of at least 10% for a sustained 5 min. When considering the highest of the two reproducible measurements after the test to calculate the lowest post-EVH value and obtain the maximal decrease in FEV₁, the prevalence of EIB on EVH or AHR (as defined by a methacholine challenge PC₂₀ ≤ 4 mg/mL or ≤ 16 mg/mL in athletes on ICS) was significantly higher in swimmers compared with winter sport athletes and controls (60% vs 29% and 17%, respectively) (P < 0.005) (Table 2).

When considering the lowest of the two reproducible measurements at each time point after EVH to calculate the lowest post-EVH value and obtain the maximal decrease in FEV₁, the prevalence of EIB to EVH was significantly higher in the three groups compared with the prevalence previously used when considering the higher of the two reproducible measurements (P < 0.05). Using this former method of calculation, the prevalences of EIB to EVH were 75% in swimmers, 40% in winter sport athletes, and 33% in controls. The prevalence remained significantly higher in swimmers compared with controls (P < 0.05).

According to the WADA and IOC-MC criteria, the prevalence of EIB assessed with EVH using this method

![Table 1—Subject Characteristics](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/22089/)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Swimmers (n = 45)</th>
<th>Winter Sport Athletes (n = 45)</th>
<th>Control Subjects (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>13 (29)</td>
<td>26 (58)</td>
<td>14 (47)</td>
</tr>
<tr>
<td>Age, y</td>
<td>20 ± 4</td>
<td>18 ± 2</td>
<td>21 ± 2</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>21 ± 2</td>
<td>22 ± 2</td>
<td>21 ± 3</td>
</tr>
<tr>
<td>Atopy</td>
<td>34 (76)</td>
<td>33 (73)</td>
<td>23 (77)</td>
</tr>
<tr>
<td>Years of training</td>
<td>12 ± 4ᵃᵇ</td>
<td>9 ± 4ᵇ</td>
<td>4 ± 3</td>
</tr>
<tr>
<td>Hours of training per week</td>
<td>28 ± 8ᵇ</td>
<td>15 ± 7ᵇ</td>
<td>3 ± 3</td>
</tr>
<tr>
<td>Physician-diagnosed asthma</td>
<td>11 (24)</td>
<td>13 (29)</td>
<td>...</td>
</tr>
<tr>
<td>Current inhaled β₂-agonists</td>
<td>5 (11)</td>
<td>10 (22)</td>
<td>0</td>
</tr>
<tr>
<td>Current ICS</td>
<td>2 (4)</td>
<td>6 (13)</td>
<td>0</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>119 ± 16ᵇ</td>
<td>109 ± 10</td>
<td>105 ± 14</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>133 ± 16ᵇ</td>
<td>116 ± 13</td>
<td>112 ± 14</td>
</tr>
</tbody>
</table>

All values are expressed as means ± SD or No. (%). ICS = inhaled corticosteroids.

ᵃ P < .001 compared with control subjects.
ᵇ P < .001 compared with winter sport athletes.
and/or methacholine challenge (PC_{20} ≤ 4 mg/mL) remained significantly higher in swimmers compared with winter sport athletes and controls (82% vs 47% and 33%, respectively) (P < .0001).

There was a negative correlation between the methacholine challenge PC_{20} and the lowest FEV_1 value observed after the EVH test in swimmers, winter sport athletes, and in the entire population, whatever the reproducible measurement chosen at each time point after EVH to calculate the lowest post-EVH value (the lowest or highest) (Fig 1). In the whole group of athletes, the correlation between methacholine challenge PC_{20} and the lowest FEV_1 value observed after the EVH test was r = −0.50, P < .0001.

Prevalence of Exercise-Induced Respiratory Symptoms

Because most controls performed only occasional physical activity, we only report this group’s exercise-induced respiratory symptoms for descriptive purposes (Table 2). Fifty-three percent of swimmers and 71% of winter sport athletes reported having exercise-induced symptoms during the previous 12 months (Table 2). Cough was the only symptom that was significantly more frequently reported in winter sport athletes than in swimmers (P < .005).

### Table 2—Response to EVH or Methacholine Challenge and Report of Exercise-Induced Respiratory Symptoms Among Athletes and Controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Swimmers (n = 45)</th>
<th>Winter Sport Athletes (n = 45)</th>
<th>Controls (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVH challenge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive EVH</td>
<td>17 (39)^a</td>
<td>11 (24)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Maximum decrease in FEV_1, %</td>
<td>13 ± 8^b</td>
<td>9 ± 9</td>
<td>8 ± 4</td>
</tr>
<tr>
<td>Ventilation, L/min</td>
<td>103 ± 13</td>
<td>128 ± 31^c</td>
<td>98 ± 27</td>
</tr>
<tr>
<td>Ventilation, % MVV</td>
<td>80 ± 12</td>
<td>97 ± 15^d</td>
<td>78 ± 13</td>
</tr>
<tr>
<td>Report of exercise-induced</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>respiratory symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>14 (31)^d</td>
<td>29 (64)^b</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>10 (22)</td>
<td>15 (33)^c</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Phlegm production</td>
<td>16 (36)</td>
<td>18 (40)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>Chest tightness</td>
<td>12 (27)</td>
<td>13 (29)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Methacholine challenge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PC_{20} ≤ 4 mg/mL</td>
<td>21 (47)^c</td>
<td>8 (18)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>PC_{20} &gt; 4 and ≤ 16 mg/mL</td>
<td>14 (31)^d</td>
<td>7 (15)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>PC_{20} &gt; 16 mg/mL</td>
<td>10 (22)^b</td>
<td>30 (67)</td>
<td>21 (70)</td>
</tr>
</tbody>
</table>

All values are expressed as mean ± SD or No. (%) unless otherwise noted. EVH = eucapnic voluntary hyperpnea; MVV = maximal voluntary ventilation; PC_{20} = provocative concentration inducing a 20% decrease in FEV_1. See Table 1 for expansion of other abbreviation.

The prevalence of symptomatic AHR and/or EIB was not significantly different between the two groups of subjects (P = .16). Asymptomatic AHR and/or EIB was significantly higher in swimmers compared with winter sport athletes (P < .05) (Fig 2). However, among athletes without a diagnosis of AHR and/or EIB, winter sport athletes reported exercise-induced respiratory symptoms more often than swimmers (P < .01).

**Prevalence of AHR According to Various Methacholine Challenge PC_{20} Cutoffs**

Swimmers had a significantly higher prevalence of AHR than winter sport athletes and controls for the two methacholine challenge cutoffs (P < .0001) (Table 2). The distribution of athletes positive to EVH and methacholine challenge according to the chosen cutoff is represented in Figure 3.
The two swimmers taking ICS had a methacholine challenge PC_{20} \leq 4 \text{ mg/mL} and a positive EVH. Among the six winter sport athletes on ICS, 17% had a positive EVH and 83% had a methacholine challenge PC_{20} \leq 16 \text{ mg/mL}, 50% having a methacholine challenge PC_{20} \leq 4 \text{ mg/mL}. One winter sport athlete on ICS did not fill the IOC-MC and WADA criteria.

Among athletes with a PC_{20} \leq 4 \text{ mg/mL} or \leq 16 \text{ mg/mL} for athletes on ICS, 67% of swimmers and 63% of winter sport athletes reported exercise-induced respiratory symptoms. Among athletes with a PC_{20} between 4 and 16 mg/mL, 43% of swimmers and 100% of winter sport athletes reported exercise-induced respiratory symptoms (P < .05), and 36% of swimmers, 50% of winter sport athletes, and 25% of controls had a positive EVH test. Among subjects with a PC_{20} > 16 mg/mL, 44% of swimmers and 62% of winter sport athletes reported exercise-induced respiratory symptoms (P = .35).

**DISCUSSION**

Using the IOC-MC criteria, we found that 60% of swimmers and 29% of winter sport athletes had AHR or EIB, and therefore could be allowed to use certain types of asthma medication. Interestingly, our study underlines that the elite swimmer population is characterized by a high prevalence of symptomatic and asymptomatic AHR and/or EIB, whereas winter sport athletes often report exercise-induced cough but with a prevalence of AHR and/or EIB similar to controls. Furthermore, among athletes with a methacholine challenge PC_{20} between 4 and 16 mg/mL, all winter sports athletes and 43% of swimmers were symptomatic, whereas 36% of swimmers, 50% of winter sport athletes, and 25% of controls had a positive EVH test (using the highest of two reproducible FEV_{1} post-EVH) suggesting a diagnosis of EIB. Our observations raise the following questions: (1) Should a systematic screening for EIB be done in athletes, especially swimmers? (2) Should athletes with a methacholine challenge PC_{20} between 4 and 16 mg/mL with exercise-induced symptoms be considered to have asthma? Furthermore, this study stresses the need to specify the method used to calculate response to EVH to allow adequate comparison of the results with other studies.

Using the highest value among two reproducible values at each time point to calculate the maximal FEV_{1} decrease after EVH, we found 39% of swimmers having EIB on EVH and 47% having AHR according to the WADA criteria of a methacholine challenge PC_{20} \leq 4 \text{ mg/mL} or \leq 16 \text{ mg/mL} for athletes taking ICS for \geq 1 month. These rates corroborate the results other investigators have reported in swimmers.\textsuperscript{15-17} Pedersen et al\textsuperscript{18} found a similar prevalence of EIB of 31% in nonallergic female swimmers, and Castricum et al\textsuperscript{17} reported a prevalence of 50% of EIB to EVH in elite swimmers, without previously diagnosed asthma. It is interesting to note that despite the high prevalence of atopy in our subjects and the inclusion of subjects previously diagnosed with asthma we did not observe an increased prevalence of EIB compared with previous reports.

Figure 3. Relationship between EVH challenge response and airway responsiveness to methacholine, according to the chosen methacholine challenge PC_{20} cutoff. Athletes on ICS for at least 1 month, having a positive EVH test and a methacholine challenge PC_{20} \leq 16 \text{ mg/mL}, were included in the group of athletes having a positive EVH and a methacholine challenge PC_{20} \leq 4 \text{ mg/mL}. MCh = methacholine challenge. See Figure 1 legend for expansion of other abbreviations.
In our study, the prevalence of EIB in swimmers was significantly higher compared with controls. We may wonder if EVH is too sensitive for swimmers or does not reflect swimming-induced bronchoconstriction. The absence of reported exercise-induced respiratory symptoms in swimmers may be due to a lack of bronchoconstriction during swimming, possibly related to the protective effect of warm and humid ambient air or to the bronchoprotective role of CO2 during swimming, as it has been previously hypothesized by Donnelly. A positive diagnosis of EIB to EVH in swimmers could reflect the damage to the airway epithelium provoked by chlorine derivatives exposure, but its clinical significance remains to be examined. Further studies are therefore needed to confirm the above hypothesis, which is supported by a study showing that 55% of the swimmers evaluated had a positive EVH, whereas only 3% of those had EIB after swimming.

In our study, winter sport athletes had a prevalence of 24% of EIB to EVH, similar to controls and to the overall prevalence found in athletes. Interestingly, 44% of winter sport athletes reported exercise-induced symptoms but had no AHR. We also observed that all winter sport athletes with a PC20 between 4 and 16 mg/mL reported exercise-induced respiratory symptoms, compared with 67% in those with a PC20 ≤ 4 mg/mL and 60% in those with a PC20 > 16 mg/mL. The discrepancy between the prevalence of AHR and reported exercise-induced symptoms has been documented by Rundell et al and is often attributed to a poor perception of airflow dysfunction by athletes. Others have observed that cold-air inhalation can induce respiratory symptoms in the absence of asthma or AHR. It has also been shown that hyperventilation with cold or dry air resulted in cough when high ventilatory rates were reached, without requiring underlying AHR. Thus, exercise-induced symptoms, particularly cough, may simply result from the cooling and drying of the airways and the concomitant release of inflammatory mediators, especially in winter sport athletes. Mechanical stress may also be implicated, resulting in the deformation of airway receptors, followed by the release of mediators such as prostaglandins from the bronchi, stimulation of airway C-fibers, and finally induction of cough.

With regard to the method used to calculate the response to EVH, we may consider that when the FEV1 is changing rapidly, the lowest value of each measurement could reflect the maximal response if the expiratory maneuver is of good quality. With regard to methacholine, we did use the lowest value, but it has been shown that using the highest or lowest value at each postdosing time point does not significantly change the results. However, according to our present analysis, using the highest or lowest value of FEV1 at each time point posttest to estimate the maximal decrease in this parameter makes a difference in the determination of prevalence of EIB to EVH test.

We found that either 39% or 75% of swimmers had a positive response to EVH according to the methods used. The choice of the FEV1 among two reproducible measures (the highest or the lowest) at each time point after EVH is often not mentioned in the methods section of current reports and guidelines, but different methodologies may have been used. This stresses the need for standardization of the methods, and we suggest the use of the highest of the reproducible measures done at each time point post-EVH to determine such response. The prevalence of EIB to EVH may be overestimated when selecting the lowest of these posttest values, and to our knowledge, standardization of this test has been done using the highest value.

Because 24% of swimmers with AHR or EIB were asymptomatic, our study raises the question of a systematic screening for EIB in athletes, especially swimmers. Furthermore, the significance of a methacholine PC20 between 4 and 16 mg/mL in athletes needs to be further studied to determine if there is a necessity to increase the cutoff value for future international events, although the significance of such PC20 may differ from one category of athletes to another. In this regard, bronchial provocation challenge should be done in symptomatic winter sport athletes to avoid the opposite problem of overdiagnosing EIB. The significance of a positive EVH challenge should also be studied in swimmers.

Acknowledgments

Authors contributions: Dr Boulet: contributed to conceiving the study, performing the tests, drafting the manuscript, and reading and approving the final manuscript.
Dr Turmel: contributed to conceiving the study, performing the tests, and reading and approving the final manuscript.
Dr Boulet: contributed as the main investigator of the study; he helped with the conception of the study, performed the medical examination of all subjects, helped to draft the manuscript, and read and approved the final manuscript.

Financial/nonfinancial disclosures: The authors have reported the following conflicts of interest: Dr Boulet has served on advisory boards for AstraZeneca, Altana, GlaxoSmithKline, Merck Frosst, and Novartis; has received lecture fees from 3M, Altana, AstraZeneca, GlaxoSmithKline, Merck Frosst, and Novartis; has received sponsorship for investigator-generated research from AstraZeneca, GlaxoSmithKline, Merck Frosst, and Schering; has received research funding for participating in multicenter studies from 3M, Altana, AsthmaTx, AstraZeneca, Boehringer-Ingelheim, Dynavax, Genentech, GlaxoSmithKline, IVAX, MedImmune, Merck Frosst, Novartis, Roche, Schering, Topigen, and Wyeth; has received support for the production of educational materials from AstraZeneca, GlaxoSmithKline and Merck Frosst; has served as adviser for the Conseil du Médicament du Québec Member of the Quebec Health Region Compensation Board Respiratory Committee; and has served as chair of the Canadian Thoracic Society Guidelines Dissemination and Implementation Committee.
and as co-leader of the Therapeutics Theme of the Canadian AllerGen Network of Centers of Excellence. He holds the Laval University Chair on Knowledge Transfer, Prevention and Education in Respiratory and Cardiovascular Health, and is a Member of the asthma committee of the World Allergy Organisation. Drs Bougault and Turmel have reported no conflicts.

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REFERENCES