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Vigorous Exercise Can Cause Abnormal Pulmonary Function in Healthy Adolescents

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Abstract

Rationale: Although exercise-induced bronchoconstriction is more common in adolescents with asthma, it also manifests in healthy individuals without asthma. The steady-state exercise protocol is widely used and recommended by the American Thoracic Society (ATS) as a method to diagnose exercise-induced bronchoconstriction. Airway narrowing in response to exercise is thought to be related to airway wall dehydration secondary to hyperventilation. More rigorous exercise protocols may have a role in detecting exercise-induced bronchoconstriction in those who otherwise have a normal response to steady-state exercise challenge.

Objectives: The objective of this study was to determine the effect of two different exercise protocols—a constant work rate protocol and a progressive ramp protocol—on pulmonary function testing in healthy adolescents. We hypothesized that vigorous exercise protocols would lead to reductions in lung function in healthy adolescents.

Methods: A total of 56 healthy adolescents (mean age, 15.2 ± 3.3 [SD] years) were recruited to perform two exercise protocols: constant work rate exercise test to evaluate for exercise-induced bronchoconstriction (as defined by ATS) and standardized progressive ramp protocol. Pulmonary function abnormalities were defined as a decline from baseline in FEV_1 of greater than 10%.

Measurements and Main Results: Ten participants (17.8%) had a significant drop in FEV_1. Among those with abnormal lung function after exercise, three (30%) were after the ATS test only, five (50%) were after the ramp test only, and two (20%) were after both ATS and ramp tests.

Conclusion: Healthy adolescents demonstrate subtle bronchoconstriction after exercise. This exercise-induced bronchoconstriction may be detected in healthy adolescents via constant work rate or the progressive ramp protocol. In a clinical setting, ramp testing warrants consideration in adolescents suspected of having exercise-induced bronchoconstriction and who have normal responses to steady-state exercise testing.

Keywords: exercise physiology; exercise testing; exercise-induced bronchoconstriction

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Exercise-induced bronchoconstriction (EIB) is a reversible airway narrowing that occurs after rigorous exercise. Exercise can trigger a transient bronchoconstriction and reduction in pulmonary function variables in healthy individuals even without a history of asthma (1). Early detection of EIB in children is encouraged to minimize the potential limitation that bronchoconstriction could have on daily physical activity. The dynamic assessment of pulmonary function through exercise testing is gaining popularity in its utility in detecting early functional deficits, possibly due to early lung disease; however, exercise challenges for the study of EIB are not standardized, leading to wide ranges in reported prevalence (2). In general, EIB affects 8–17% of the population of individuals without asthma (3, 4), with higher rates of up to 90% in the population of individuals with asthma (5) and 30–70% in elite athletes (6). Identifying the presence of EIB in otherwise healthy adolescents allows clinicians to address treating these respiratory limitations to optimize their patients' potential for an active lifestyle.

Exercise challenge testing with pulmonary function measurements is recognized as an important diagnostic tool in identifying EIB. The bronchoconstrictive effect found after exercise depends on the individual reaching near the limit of physiologic response to exercise. The exercise challenge protocols, as defined by the American Thoracic Society (ATS) and the European Respiratory Society, use steady work rates (WRs) as the mainstay of the exercise protocol (7, 8), and therefore may not fully capture all cases of EIB. The ramp test was designed for subjects to reach the peak level in exercise capacity using progressively increasing WR, whereas the ATS test was designed to elicit 80–90% of the subject's predicted peak heart rate (PHR) for 6–8 minutes on a treadmill. The parameters of interest in the ramp test are usually the physiological response to exercise, whereas those of interest in the ATS test are the average response to stable WR after the first 3 minutes of exercise. As such, De Fuccio and colleagues (9) have pointed out that using the progressive maximal exercise protocol can be as useful as the constant WR test in diagnosing EIB in susceptible subjects.

The goal of this study was twofold: first, to evaluate the degree of postexercise lung function abnormalities, falling within the ATS pulmonary function criteria for EIB, in healthy adolescents with no prior history of asthma; and second, to determine whether these results obtained from the ATS constant exercise protocol are consistent with those obtained from the progressive ramp protocol. We hypothesized that these exercise tests, the ATS challenge protocol and the ramp exercise protocol, may lead to reductions in pulmonary function variables even in normal adolescents without a history of asthma.

Methods

The University of California, Irvine Institutional Review Board approved this study, and informed written assent and consent were obtained from all participants and their parents or guardians. Participants were recruited from Children's Hospital of Orange County clinics and by flyers from local schools and athletic programs in Orange County, California. Each participant underwent a careful history and physical examination with standard questions regarding wheezing, respiratory difficulty, recurrent cough, or asthma symptoms (10). We included only those without a history of known illnesses, including asthma, and those who were not on any medications. Moreover, we excluded adolescents with a history of wheezing, chronic or recurrent cough, inhaler use in the 5 years before the study, or history suggesting exercise intolerance, and those who could not complete one or both of the exercise protocols. Anthropometric data were determined before exercise testing with calibrated scales and stadiometers. A standardized questionnaire was used to estimate pubertal status (11). Body mass index (BMI) for age percentiles was determined using current U.S. Centers for Disease Control and Prevention growth charts.

Participants reported to the University of California, Irvine Institute for Clinical and Translational Science Applied Physiology–Human Performance Laboratory for two visits on separate days. On visit 1, the participants performed a standardized ATS exercise test designed to diagnose EIB in adolescents. We used an electronically braked, servo-controlled cycle ergometer. Throughout the challenge, WR was adjusted to maintain heart rate (HR) within the target range of between 80 and 90% of the PHR to achieve a steady state. PHR, defined as 220 beats per minute minus the age, was achieved within the first several minutes of the exercise challenge, and the participants continued to exercise at that WR for at least 4–6 minutes, according to the ATS guidelines (12).

Participants returned within 1 month, but no earlier than 2 weeks for the second visit to perform the ramp test (13). Participants began the test with a warm-up stage by cycling at 0 watts for 2–3 minutes. Each participant performed a ramp-type progressive cycle ergometer with steadily increasing WR. The WR was increased at a rate according primarily to age: for participants less than 12 years old, the rate was increased by 10–15 watts/min, and for those greater than 12 years old, the rate was increased by 20–25 watts/min. The participants were vigorously encouraged during the high-intensity phase of the exercise protocol to continue to exercise. Each participant was instructed to raise his or her hand when they could no longer continue, at which time the resistance was immediately reduced to zero watts and participants pedaled without resistance. Participants were actively encouraged to maintain a constant pedaling rate of at least 60 rpm, and a pedometer was always kept in full view of the participant.

During both the ATS exercise challenge and the ramp test, gas exchange variables were measured breath by breath (Vmax229; SensorMedics, Yorba Linda, CA). The apparatus was calibrated against standard commercial gas mixtures before each test. HR was continuously monitored with a three-lead electrocardiogram (SensorMedics). PHR, peak $\dot{V}O_2$, and respiratory exchange ratio greater than1.0 as an adjunct measurement, were obtained and reflect the participant's maximal effort.

Spirometry was performed (Ergoline 800S; SensorMedics metabolic system) before exercise and at 5, 10, 15, 20, and 30 minutes after each exercise test. At each time point, three maximal maneuvers were performed and the FVC, FEV_1, FEV_1/FVC ratio, forced expiratory flow between 25 and 75% of FVC ($FEF_{25-75\%}$), and peak expiratory flow rate (PEFR) with the best efforts were recorded. No more than four maneuvers were performed at each time point to avoid respiratory muscle fatigue. All participants had heart and lung auscultation before and after exercise. Additional auscultation was performed if there were decrements in lung function or symptoms of possible asthma.

FVC, FEV_1, $FEF_{25-75\%}$, and PEFR have been used to evaluate the pulmonary response to exercise (14–16). We employed the criteria set forth by ATS (16) to define an abnormal response to exercise as EIB by a decrease in FEV_1 by 10% or greater from pre-exercise value (7).

For both the ATS and ramp tests, the percent change of pulmonary function was calculated as proportion of change from baseline to the lowest postexercise over-baseline level. Pearson's correlation (r) was calculated to evaluate the consistency between the ATS challenge and the ramp test on the baseline pulmonary function testing (PFT) and the percent change of PFT. The corresponding 95% confidence interval (CI) was obtained using Fisher's z transformation (17). The two-sample *t* test was applied to evaluate physiologic response to exercise challenge between subjects with and without EIB for both ATS and ramp tests. Data are presented with mean and SD or frequency and percentage. All analyses were performed with SAS 9.1 (SAS Institute, Cary, NC), and the significant level was set at 0.05.

Results

A total of 56 adolescents (29 male; mean age = 15.2 ± 3.3 years; mean BMI % = 52.0 ± 5.5%) were included in this study (Table 1). A total of 14 participants were early pubertal (6 girls), 29 were late pubertal (14 girls), and 13 were in middle puberty (7 girls). Eight participants had a BMI percentile over 85%; 59% of the participants were white, 21.4% were Hispanic, 16.1% were Asian, and 3.6% were African American.

In Table 1, the mean level of baseline PFT from both ATS and ramp tests are presented for boys and girls separately. Baseline PFT between the two exercise visits correlated strongly for FVC (r = 0.98; 95% CI = 0.97–0.99) and FEV_1 (r = 0.98; 95% CI = 0.97–0.99), and less strongly for $FEF_{25–75\%}$, (r = 0.88; 95% CI = 0.81–0.93) and PEFR (r = 0.87; 95% CI = 0.78–0.92). The correlation of percent change of PFT between the two exercise tests was low: between 0.10 and 0.26.

The average duration for the ATS exercise challenge was 10.2 (±0.7) minutes and the average work load was 103.1 (±42.6) watts, whereas the average duration for the ramp test was 9.9 (±1.4) minutes and the average work load was 86.1 (±32.4) watts.

Ten participants (17.8%) had at least one abnormal FEV_1 result, as seen in Figure 1: three (5.3%) after ATS test only, five (8.9%) after ramp test only, and two (3.5%) after both ATS and ramp tests; 16 participants showed a decrease in PEFR of 15% or more without a significant decline in FEV_1. There was no specific time for the reduction in PFT after exercise. The majority of declines occurred between 5 and 20 minutes after exercise. Review of the flow–volume loops before and after exercise did not reveal any limitation of the inspiratory flow in any responder, which makes the presence of variable extrathoracic airway obstruction unlikely. Table 2 shows the physiologic response to the ATS exercise challenge (the average during the stable stage after 3 minutes of exercise) and ramp test (the maximal values during the last 2 minutes of exercise) between the groups with and without EIB.

Table 1. Participants' anthropometric and baseline pulmonary function testing characteristics

Characteristics	Male (*n* = 29)	Female (*n* = 27)
Anthropometric characteristics		
Age, yr	15.2 ± 3.4	14.4 ± 3.3
Height, cm	168.4 ± 17.1	157.8 ± 12.8
Weight, kg	61.8 ± 23.7	51.7 ± 15.4
BMI, kg/m^2	21.1 ± 4.7	20.4 ± 4.0
BMI Percentile, %	52.0 ± 29.4	53.1 ± 28.9
Baseline PFT at ATS test		
FVC, L	4.3 ± 1.5	3.2 ± 0.6
FEV_1, L	3.6 ± 1.2	2.8 ± 0.6
$FEF_{25–75\%}$, L/min	3.9 ± 1.3	3.3 ± 1.1
PEFR, L/min	6.7 ± 2.1	5.3 ± 1.3
Baseline PFT at RAMP test		
FVC, L	4.3 ± 1.5	3.2 ± 0.7
FEV_1, L	3.7 ± 1.2	2.8 ± 0.7
$FEF_{25–75\%}$, L/min	3.9 ± 1.3	3.4 ± 1.2
PEFR, L/min	7.4 ± 2.3	5.8 ± 1.4

Definition of abbreviations: ATS = American Thoracic Society; BMI = body mass index; $FEF_{25–75\%}$ = forced expiratory flow between 25 and 75% of FVC; PEFR = peak expiratory flow rate; PFT = pulmonary function testing.
Data presented as mean ± SD.

Discussion

Proper management of EIB in children is essential for participation in daily play and sports. Exercise protocols have been set forth by ATS guidelines, and the standardization of these methodologies has enabled further investigations into defining EIB (7). These studies have encompassed comparing surrogates for exercise testing using direct and indirect bronchoprovocation measures in populations of individuals with asthma, and in healthy or elite athlete populations. In the present study, we focused on healthy adolescents without asthma who developed EIB after the ATS steady WR protocol, the progressive ramp protocol, or both. Overall, 17.8% of patients without asthma were diagnosed with EIB, which falls within previous estimates of EIB in healthy populations (3). Although we used the ATS definition of EIB with 10% or greater decline in FEV_1, stricter criteria have been proposed, with a threshold of a 15–20% FEV_1 drop in pediatric and elite athlete populations and for field exercise challenges (18). As our study aimed to detect smaller changes in airway response to two different protocols, we elected to use the 10% cutoff for FEV_1, which is the standard value (19).

PEFR was widely used in past studies investigating airway response to exercise challenges (15, 20), but have fallen out of favor due to high within-subject variability (21, 22). We found a significant portion of the pulmonary function changes after exercise were within PEFR only. Because PEFR is an effort-dependent measurement, these changes were attributable to postexercise fatigue. Surprisingly, there were five subjects who had a significant drop in FEV_1 without a corresponding decrease in PEFR. Three of those subjects did exhibit a drop in PEFR without reaching an abnormal threshold, whereas the other two subjects actually showed a slight increase in PEFR after exercise. These discrepancies support avoiding the use of PEFR as a measurement of EIB.

Of particular significance were the five subjects with abnormal lung function after the ramp protocol only, as seen in Figure 1. The proposed mechanism underlying EIB is

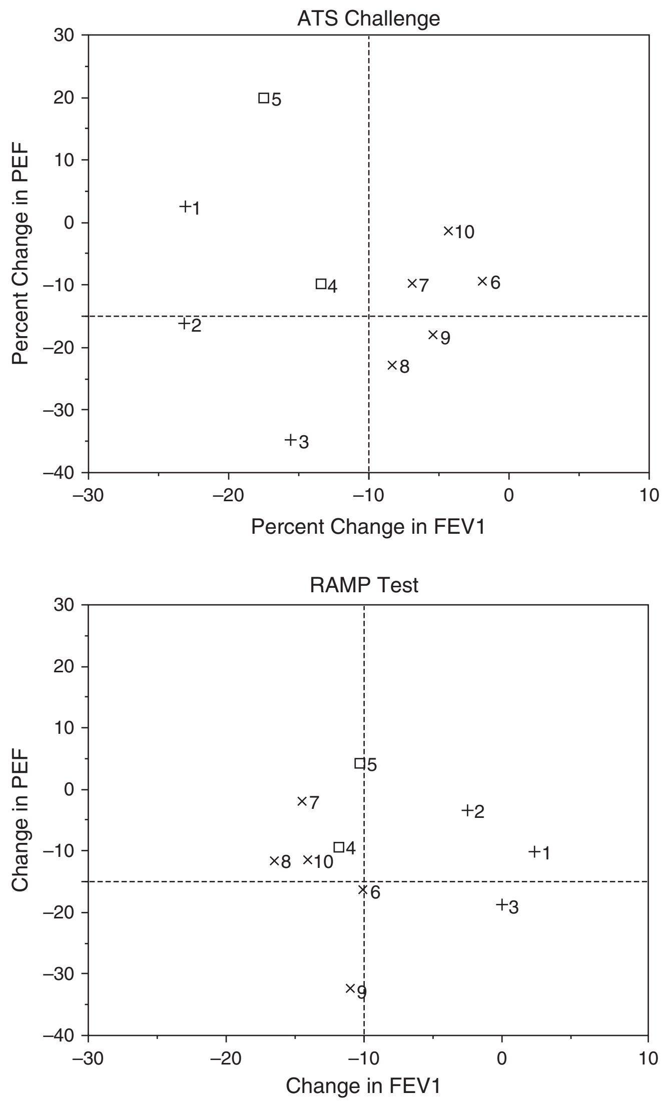

Figure 1. Percent change of FEV_1 and peak expiratory flow (PEF) from baseline to lowest postexercise value after American Thoracic Society (ATS) and ramp protocols in subjects with exercise-induced bronchoconstriction (EIB). Subjects are labeled by *numbers*; *plus symbol* indicates subjects who responded to ATS only; *X symbol* indicates subjects who responded to ramp only; *square symbol* indicates subjects who responded to both ramp and ATS.

related to airway dehydration and resultant osmotic shifts during hyperventilation (23, 24). Carlsen and colleagues (25) showed that higher exercise loads corresponded with larger declines in FEV_1. In contrast to the ATS steady WR exercise protocol, the ramp test was designed to measure peak $\dot{V}O_2$ and required maximum effort on behalf of the participant. This rigorous protocol showed that maximum ventilation rate was approximately 1.5 L/min/kg, whereas the average ventilation during the stable stage in the ATS exercise protocol was around 1.1 L/min/kg. In addition, three patients who responded to the ATS challenge did not have abnormal lung function after the ramp test. Regardless, these findings agree with the ATS recommendations that multiple studies may need to be done to detect EIB.

In children, EIB is often the first manifestation of asthma (26), and we did find a substantial number of children with no history of asthma responding to vigorous exercise with a mild degree of EIB. In comparing ATS to ramp exercise protocols, we illustrated that both studies are able to detect occurrences of EIB. EIB testing using ATS guidelines is a clearly stated and justified method that does not depend on participation effort and subjectivity. By standardizing temperature, humidity, HR, and ventilation, the ATS exercise protocol permits unbiased intersubject comparison of pulmonary function after exercise. Furthermore, epidemiological studies evaluating for EIB have also shown it to be a test with high reproducibility (27). However, because it does not require maximum effort, milder cases of EIB that would only manifest in response to maximum exercise may not be identified.

In contrast, the ramp protocol drives subjects to reach their maximum effort and presumably highest tolerated HR and ventilation. This rigorous exertion unmasked five patients with EIB who showed a drop in FEV_1 after the ramp test while having normal responses after the ATS exercise test. Although the ramp protocol has been widely used in assessing peak $\dot{V}O_2$, it is not as well studied as the ATS exercise test for diagnosing EIB. Further evaluation of the ramp protocol as a diagnostic test for EIB may be difficult, owing to its subjective criteria. Other parameters, such as percentage of maximum HR, could predict the participants' efforts, but exercise intensity may not necessarily be consistent between participants. However, previous studies have shown that children involved in active play do not sustain moderate levels of exercise for prolonged periods of time (28). Instead, their activity fluctuates from being at rest to rapid acceleration of short bouts of high-intensity exercise. Ramp testing may be advantageous by reflecting this natural play in children, and would warrant further investigation in future studies to evaluate EIB.

Despite these drawbacks, clinicians suspecting EIB in patients with normal lung function with ATS exercise testing should consider ramp testing as the next step. For clinicians, evaluating EIB requires testing that favors high sensitivity. In research, pharmaceutical testing needs more specific methods to differentiate treatment effects of various drugs, for which a stricter cutoff FEV_1 drop of 15–20% should be substituted for a more accurate diagnosis of EIB. Similarly, PEFR should not be included as an outcome, due to its variability.

In this study, participants underwent full forced maneuvers before and after exercise to evaluate all pulmonary function

Table 2. Work rate and physiologic variables during exercise with the ATS challenge and ramp testing

Variables	Abnormal FEV_1	Normal FEV_1
ATS challenge (average during stable stage after the first 3 min of exercise)*		
Work rate, watts	77.2 ± 37.2	117.6 ± 48.1
HR, bpm	170.5 ± 3.4	168.2 ± 7.8
$\dot{V}O_2$, ml/min/kg	29.1 ± 6.0	28.2 ± 6.7
$\dot{V}E$, L/min/kg	1.08 ± 0.22	0.97 ± 0.22
RR	42.0 ± 9.7	36.9 ± 8.9
RER	1.0 ± 0.06	1.0 ± 0.05
Ramp test (maximal during the last 2 min of exercise)†		
Work rate, watts	136.6 ± 49.1	182.0 ± 64.2
HR, bpm	184.1 ± 10.4	187.0 ± 10.1
$\dot{V}O_2$, ml/min/kg	35.8 ± 7.1	38.9 ± 8.9
VE, L/min/kg	1.49 ± 0.19	1.45 ± 0.40
RR	56.3 ± 13.7	48.8 ± 12.3
RER	1.12 ± 0.10	1.17 ± 0.07

Definition of abbreviations: ATS = American Thoracic Society; HR = heart rate; RER = respiratory exchange ratio; RR = respiratory rate.
Data presented as mean ± SD.
*ATS challenge: abnormal FEV_1 ($n = 5$); normal FEV_1 ($n = 51$).
†Ramp challenge: abnormal FEV_1 ($n = 7$); normal FEV_1 ($n = 49$).

parameters. Full maneuvers are not recommended, as repeated testing could contribute to respiratory muscle fatigue and could account for the significant decline in peak flow testing (16) and lower postexercise FEV_1 results. For the ramp tests, we asked participants to raise their hands when they were unable to continue exercise to indicate termination of the study. Although our purpose of determining volitional fatigue was fulfilled for this study, including Borg scoring would have been helpful to evaluate their perception of exertion as an additional determination of exercise effort (29). Future studies would warrant the addition of Borg scores as a means to judge the effectiveness of the ramp protocol on each participant. Although none of the participants reported allergy symptoms, we did not have any objective measurements, such as serum IgE or allergy

Presently, there is no single test that detects all occurrences of EIB. This is one of the first studies to assess exercise associated PFT abnormalities in children without asthma and compare responses between the ATS and ramp exercise protocols. Given that any pulmonary limitation during or after exercise may play a role in exacerbating obesity in otherwise healthy children, early assessment of EIB would be especially helpful. Future studies are warranted to explore the role of the ramp protocol in EIB diagnostic testing, and may be considered as a next step after a normal ATS exercise challenge in clinical practice.

Conclusions

We observed that exercise-associated PFT abnormalities occurred in a surprisingly large number of healthy adolescents with no history of asthma. Two very different protocols, the ATS exercise challenge and a ramp progressive exercise test, led to mild reductions in PFT with no pattern or common set of mechanisms that we could identify. The advantage of using the progressive ramp over the steady-state protocol for bronchoconstriction is that assessment of fitness via peak $\dot{V}O_2$ may be performed in addition to evaluating for EIB. Thus, a single test could potentially identify EIB and fitness levels simultaneously. However, this study reveals that both the steady-state and progressive ramp protocols should be considered in evaluating EIB in healthy individuals, as EIB may manifest in one test, but not the other. More studies are needed to understand the pathogenesis of EIB in healthy children, with further assessment of how individual factors impact the detection of EIB from ATS steady-state and ramp exercise.

Practical Implications

- Adolescents without asthma may show changes in pulmonary function after exercise.
- These changes in pulmonary function occur after either steady WR protocols or progressive ramp protocols.
- Using both exercise protocols can better detect EIB in healthy adolescents. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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