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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: a 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 FEV₁ of greater than 10%.

Measurements and Main Results: Ten participants (17.8%) had a significant drop in FEV₁. 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

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 VO2, and
respiratory exchange ratio greater than 1.0
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, FEV1, FEV1/FVC
ratio, forced expiratory flow between 25
and 75% of FVC (FEF25–75%), 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, FEV1, FEF25–75% 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 FEV1 by 10% or greater from
pre-exercise value (16). We employed
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an abnormal response to exercise as EIB by
a decrease in FEV1 by 10% or greater from
pre-exercise value (16).

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

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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 FEV₁ (r = 0.98; 95% CI = 0.97–0.99), and less strongly for FEF₂₅–₇₅% (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 FEV₁ 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 FEV₁. 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.

### 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 FEV₁, stricter criteria have been proposed, with a threshold of a 15–20% FEV₁ 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 FEV₁, 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 with 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 FEV₁ 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...
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 FEV₁. In contrast to the ATS steady WR exercise protocol, the ramp test was designed to measure peak \( V_{\text{O}_2} \) 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 while having normal responses after the ATS exercise test. Although the ramp protocol has been widely used in assessing peak \( V_{\text{O}_2} \), 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 FEV₁ 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 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.

![Figure 1. Percent change of FEV₁ 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; \( \times \) symbol indicates subjects who responded to ramp only; square symbol indicates subjects who responded to both ramp and ATS.](image-url)
Table 2. Work rate and physiologic variables during exercise with the ATS challenge and ramp testing

<table>
<thead>
<tr>
<th>Variables</th>
<th>Abnormal FEV₁</th>
<th>Normal FEV₁</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work rate, watts</td>
<td>136.6 ± 49.1</td>
<td>182.0 ± 64.2</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>184.1 ± 10.4</td>
<td>187.0 ± 10.1</td>
</tr>
<tr>
<td>VO₂, ml/min/kg</td>
<td>35.8 ± 7.1</td>
<td>38.9 ± 8.9</td>
</tr>
<tr>
<td>VE, L/min/kg</td>
<td>1.49 ± 0.19</td>
<td>1.45 ± 0.40</td>
</tr>
<tr>
<td>RR</td>
<td>56.3 ± 13.7</td>
<td>48.8 ± 12.3</td>
</tr>
<tr>
<td>RER</td>
<td>1.12 ± 0.10</td>
<td>1.17 ± 0.07</td>
</tr>
</tbody>
</table>

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 FEV₁ (n = 5); normal FEV₁ (n = 51).
†Ramp challenge: abnormal FEV₁ (n = 7); normal FEV₁ (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 FEV₁ 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 VO₂ 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.

References