

Expiratory flow limitation during exercise in prepubescent boys and girls: prevalence and implications

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Submitted 4 February 2009; accepted in final form 26 February 2010

Swain KE, Rosenkranz SK, Beckman B, Harms CA. Expiratory flow limitation during exercise in prepubescent boys and girls: prevalence and implications. *J Appl Physiol* 108: 1267–1274, 2010. First published March 4, 2010; doi:10.1152/jappphysiol.00123.2009.—The purpose of this study was to compare the prevalence and implications of expiratory flow limitation (EFL) during exercise in boys and girls. Forty healthy, prepubescent boys (B; $n = 20$) and girls (G; $n = 20$) were tested. Subjects completed pulmonary function tests and an incremental cycle maximal oxygen uptake ($\dot{V}O_{2\max}$) test. EFL was recorded at the end of each exercise stage using the % tidal volume overlap method. Ventilatory and metabolic data were recorded throughout exercise. Arterial oxygen saturation (Sp_{O_2}) was determined via pulse oximetry. Body composition was determined using dual-energy X-ray absorptiometry. There were no differences ($P > 0.05$) in height, weight, or body composition between boys and girls. At rest, boys had significantly higher lung volumes (total lung capacity, $B = 2.6 \pm 0.5$ liters, $G = 2.1 \pm 0.5$ liters) and peak expiratory flow rates ($B = 3.6 \pm 0.6$ l/s; $G = 1.6 \pm 0.3$ l/s). Boys also had significantly higher $\dot{V}O_{2\max}$ ($B = 46.9 \pm 5.9$ ml·kg lean body mass⁻¹·min⁻¹, $G = 41.7 \pm 6.6$ ml·kg lean body mass⁻¹·min⁻¹) and maximal ventilation ($B = 49.8 \pm 8.8$ l/min, $G = 41.2 \pm 8.3$ l/min) compared with girls. There were no sex differences ($P > 0.05$) at $\dot{V}O_{2\max}$ in VE/VCO_2 , end-tidal P_{CO_2} , heart rate, respiratory exchange ratio, or Sp_{O_2} . The prevalence ($B = 19/20$ vs. $G = 18/20$) and severity ($B = 58 \pm 7\%$ vs. $G = 43 \pm 8\%$ tidal volume) of EFL was not significantly different in boys compared with girls at $\dot{V}O_{2\max}$. A significant relationship existed between % EFL at $\dot{V}O_{2\max}$ and the change in end-expiratory lung volume from rest to maximal exercise in boys ($r = 0.77$) and girls ($r = 0.75$). In summary, our data suggests that EFL is highly and equally prevalent in prepubescent boys and girls during heavy exercise, which led to an increased end-expiratory lung volume but not to decreases in arterial oxygen saturation.

expiratory limitation; healthy children; dynamic hyperinflation

SEX DIFFERENCES EXIST in the structure and function of the respiratory system that may, in theory, affect gas exchange and ventilation during exercise. For example, adult men have larger diffusion surfaces and lung volumes compared with height-matched adult women (38). Furthermore, Mead (28) suggested that sex differences in pulmonary function at rest may be primarily explained by smaller airways relative to lung size (dysanapsis) in women compared with men. It is likely that these differences contribute to greater gas exchange disturbance (16, 17) and expiratory flow limitation (EFL), with attendant dynamic lung hyperinflation and increased respiratory discomfort (breathlessness) during exercise in women (12, 26, 33). In normal, healthy, untrained men, a large reserve exists for increases in ventilation during exercise (18). How-

ever, due to smaller airways relative to lung size, women experience significant EFL during heavy exercise that limits (or mechanically constrains) further increases in tidal volume (V_T) expansion and therefore exercise ventilation (12, 26).

Sex differences also exist in children that may affect gas exchange and the ventilatory response to exercise. For the same stature, boys have larger lungs than girls, resulting in a larger number of total alveoli and a larger alveolar surface area for gas exchange (38). Boys also have higher aerobic capacity [maximal oxygen uptake ($\dot{V}O_{2\max}$)] and maximal ventilation ($\dot{V}_{E\max}$) compared with girls, even with similar lean body mass (LBM) (10). Given these differences in pulmonary structure and aerobic capacity, there may be differences in the presence and/or severity of EFL during exercise between boys and girls.

It has been recently shown by Nourry et al. (31, 32) that the majority of prepubescent children (~70%), both trained and untrained, experience EFL during exercise, due to smaller airways relative to lung size, and excessive ventilation compared with the metabolic demands during exercise. These studies reported that the prevalence of EFL was similar between trained and untrained children, regardless of higher ventilation demonstrated by trained children. However, regulation of dynamic operating lung volumes, including end-expiratory lung volume (EELV) and end-inspiratory lung volume (EILV), was different between groups, since trained children regulated breathing at a higher EELV than untrained children. Specific factors contributing to the presence of EFL in a larger population, including sex differences in EFL, have not yet been determined in children.

Therefore, the purpose of this study was to determine the prevalence, severity, and physiological consequences of EFL in prepubescent girls and boys during heavy exercise. Based on previous reports, we hypothesized that in prepubescent children during heavy exercise 1) EFL would be present in the majority of both boys and girls, 2) the degree of EFL would be greater in girls than in boys due to smaller lungs and airways in girls, 3) those subjects with the most EFL would demonstrate the greatest dynamic lung hyperinflation and exercise-induced arterial desaturation.

METHODS

Forty healthy prepubescent children (20 girls, 20 boys), ages 7–11 years, were recruited and volunteered as subjects. All subjects were free of asthma or disease and demonstrated normal lung function as measured by standard pulmonary function tests. Children were prepubescent and were in the first stage of maturation, as defined by Tanner stage I (37). Subjects were characterized by physical activity habits via a physical activity questionnaire (39) and categorized as competitively active (60 min/day of moderate-intensity physical activity and participating in a competitive sports team; boys, $n = 12$; girls, $n = 8$), recreationally active (60 min/day of moderate-intensity physical activity; boys, $n = 5$; girls = 8), or inactive (boys, $n = 3$;

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girls, $n = 4$). None of the subjects were involved in swim training. Each subject had a parent or guardian present to provide medical history information and informed consent. All research components were reviewed and approved by the Institutional Review Board of Human Subjects at Kansas State University, Manhattan, KS.

Experimental design. Subjects reported to the laboratory on two separate occasions. A parent or guardian was present at both sessions. During *session 1*, height and weight were recorded using a calibrated eye-level physical scale with height rod (Detecto, Webb City, MO). Subjects were then familiarized with the equipment and procedures. After several practice trials, standard pulmonary function measurements were performed using an automated pulmonary function testing system in accordance with recommended techniques (discussed below). Subjects then completed a symptom-limited incremental cycle exercise test to determine maximal oxygen uptake ($\dot{V}O_{2max}$) (discussed below). A second exercise test at constant work load (105% $\dot{V}O_{2max}$) was performed following 15 min of rest to verify $\dot{V}O_{2max}$. During the second visit, each subject underwent a DXA (dual-energy X-ray absorptiometry) scan to determine body composition. This measurement was made to determine whether body fat or LBM was contributing to sex differences.

Body composition. Total body composition was measured by use of a whole body DXA system (version 5.6, GE Lunar, Milwaukee, WI). Instructions were to lie as still as possible during the scanning procedure. DXA scanning has been validated and uses two X-ray beams with differing energy levels to find differences in absorption and therefore LBM, body fat percentage, and body fat distribution (15).

Pulmonary function tests. Total lung capacity (TLC), maximal inspiratory pressure ($P_{I_{max}}$), maximal expiratory pressure ($P_{E_{max}}$), maximal flow-volume loops (MFVL), and lung diffusing capacity (DL_{CO}) were assessed before exercise testing (SensorMedics 229 Metabolic Cart, SensorMedics, Yorba Linda, CA). Diffusing capacity of the lung was measured from normalized alveolar volume (DL_{CO}/V_A) before exercise using a test gas mixture of 0.3% acetylene, 0.3% carbon monoxide, 0.3% methane, 21% O_2 , with balance of N_2 using the intra-breath exhalation technique. TLC was determined using the nitrogen wash-out technique. $P_{I_{max}}$ was measured at residual volume (RV), and $P_{E_{max}}$ was measured at TLC. All tests were performed in triplicate, with the average value used in analysis.

$\dot{V}O_{2max}$. An incremental exercise test to exhaustion was performed using a cycle ergometer (Ergometer 800S, Sensor Medics, Yorba Linda, CA) to determine $\dot{V}O_{2max}$. Subjects were given consistent and complete instructions explaining the protocol of the test to ensure maximal volitional effort. Before testing, a 3-liter calibration syringe was used to calibrate the flow sensor. Known gas concentrations that spanned the range of expected measurements were used to calibrate gas analyzers. Resting metabolic measurements were taken for 3 min. Subjects then began with a warm-up for ~2 min at a work rate of 20 W, pedaling between 50–60 revolutions/min. Subjects were instructed to maintain this pedaling speed while the work rate was increased by 10 W each minute. Subjects remained seated throughout the test. After the warm-up period and following each minute of an exercise stage, subjects reported a rate of perceived exertion (RPE) and dyspnea value based on the modified Borg scale. However, we found that our children had a difficult time understanding and/or reporting their perceptions during exercise. Therefore, we have not included this analysis in our results. Heart rate (HR) was monitored throughout the test via a four-lead ECG interfaced to the metabolic software. The sensor from a pulse oximeter (Datex-Ohmeda, 3900P, Madison, WI) was secured to the left earlobe to estimate arterial oxygen saturation (Sp_{O_2}). The pulse oximeter was self calibrated before each test. The pulse oximeter supplied a visual pulse waveform to ensure adequate blood perfusion throughout the test. Sp_{O_2} values were averaged over the last minute of each exercise stage. Subjects continued to exercise until reaching volitional exhaustion (<16 min). Verbal encouragement was provided throughout the test. The $\dot{V}O_{2max}$ test concluded when subjects could not maintain a pedal frequency of

>50 revolutions/min for five consecutive revolutions. Metabolic and ventilatory data were assessed continuously through breath-by-breath analysis (SensorMedics 229 Metabolic Cart, SensorMedics, Yorba Linda, CA). Data was averaged over a 20-s period near the end of each minute of exercise and several breaths before the inspiratory capacity (IC) maneuver (see below).

Following the $\dot{V}O_{2max}$ test, subjects rested for 15 min and then performed a constant load (105% $\dot{V}O_{2max}$) exercise test until exhaustion to verify $\dot{V}O_{2max}$ (34). Work rate for the test was determined from the final work rate (Watts) during the incremental test. Subjects were given a warm-up period of 90 s pedaling 50 revolution/min at 20 W. Work rate was increased until reaching calculated work rate (~30 s), and subjects were instructed to maintain 50 revolutions/min until volitional fatigue.

Determination of EFL and V_T regulation. EFL was determined by recording V_T loops during incremental exercise using a bidirectional flow sensor together with the gas analyzer. After a full explanation and demonstration to each subject, satisfactory technique and reproducibility of the IC maneuvers ($\pm 5\%$) were obtained during the familiarization day at rest and also during exercise. The software in this system allows for quality control checks (both during and after the test) to ensure proper (and consistent) IC efforts at rest and during exercise. Each subject performed three to four maximal flow-volume loop maneuvers before and immediately following exercise, and the largest loop (postexercise) was used in analysis. Postexercise maximal flow rates (e.g., forced expiratory flow of 25–75%, forced expiratory flow of 50%) were ~3% larger for both boys and girls, with no difference ($P > 0.05$) between sexes. At the end of each exercise stage, following 5–10 tidal breaths, an IC maneuver was performed from functional residual capacity (FRC) to determine placement of V_T for each exercise stage. We assumed that TLC did not change significantly during exercise (19). A breath was considered typical if it had similar volume and flow characteristics to the other breaths before the IC maneuver. The metabolic cart used in our study also automatically corrects for drift that occurs when there are differences between inspiratory and expiratory volumes. EFL was defined as present when the intersection of the exercising V_T loop and the maximal flow volume loop was $\geq 5\%$ (6, 32). The change in regulation of V_T within FVC during exercise was recorded as EELV and EILV. EELV and EILV were expressed as ratios of expiratory reserve (ERV) and inspiratory reserve volume (IRV) relative to forced vital capacity (FVC; ERV/FVC, IRV/FVC). During analysis, approximately five breaths before the IC maneuver during exercise were monitored to track any changes in breathing regulation.

Statistics. SigmaStat statistical software (Janel Scientific Software) was used for data analysis. Data is expressed as means \pm SD. Differences between sexes were determined using ANOVA. Relationships were determined by Pearson's product moment correlation. Significance was set at $P < 0.05$ for all analyses.

RESULTS

Subject characteristics. Subject characteristics are presented in Table 1. The boy-to-girl ratio was equal (20 girls, 20 boys). No significant differences were found in anthropometric data or body composition between boys and girls. Medical history information provided by a parent or guardian confirmed that all subjects were in Tanner maturation stage 1 (37).

Metabolic and ventilatory data. Table 1 shows baseline lung volumes and resting pulmonary function. Baseline pulmonary function test results were not significantly different from predicted values for prepubescent children (22). All variables were significantly higher in boys than in girls, with the exception of forced expiratory volume in 1 s (FEV_1)/FVC.

Exercise data. Data collected during exercise and at $\dot{V}O_{2max}$ are shown in Table 2. At $\dot{V}O_{2max}$, relative and absolute oxygen

Table 1. Subject characteristics and pulmonary function

	Boys (n = 20)			Girls (n = 20)		
	Means ± SD	Predicted†	Range	Means ± SD	Predicted†	Range
Age, yr	9.8 ± 0.6		8.2–11.0	9.5 ± 0.9		7.6–11.4
Weight, kg	34.3 ± 7.8		26.0–55.6	32.9 ± 12.2		24.8–78.2
Height, cm	140.0 ± 5.5		132.1–149.9	136.3 ± 7.2		125.7–151.1
Lean body mass, %	77.3 ± 9.5		57.3–88.4	74.5 ± 9.9		48.4–87.5
Body fat, %	19.6 ± 10.4		7.9–42.8	22.7 ± 10.5		9.1–50.5
BSA, cm ²	1,382 ± 165		1,139–1,708	1,271 ± 198		1,038–1,769
BMI, kg/m ²	17.5 ± 3.7		21.1–27	17.4 ± 4.7		13.9–34.2
TLC, liters	2.6 ± 0.5*	2.7 ± 0.4	1.9–3.5	2.1 ± 0.5	2.1 ± 0.4	1.4–2.9
FVC, liters/s	2.2 ± 0.3*	2.2 ± 0.3	1.7–2.9	1.9 ± 0.4	1.8 ± 0.4	1.4–2.8
RV, liters	0.4 ± 0.3*	0.4 ± 0.2	0.1–1.2	0.2 ± 0.2	0.2 ± 0.2	0.1–0.7
FRC, liters	0.9 ± 0.3*	0.9 ± 0.2	0.4–1.9	0.7 ± 0.3	0.7 ± 0.3	0.2–1.3
IC, liters	1.7 ± 0.3*	1.6 ± 0.2	1.2–2.3	1.4 ± 0.3	1.5 ± 0.2	1.1–2.0
DLCO, mmHg·l ⁻¹ ·min ⁻¹	15.9 ± 3.0*		11.7–23.8	12.1 ± 3.2		7.6–20.1
PEF, liters/s	3.6 ± 0.7*		2.3–4.8	2.9 ± 0.6		1.8–4.3
FEV ₁ , liters/s	1.9 ± 0.2*	2.0 ± 0.2	1.6–2.5	1.6 ± 0.3	1.6 ± 0.3	1.3–2.4
FEV ₁ /FVC, %	85.3 ± 6.5	86.2 ± 5.9	76–96	82.4 ± 6.9	82.4 ± 5.8	64–89
FEF _{50%} , liters/s	2.3 ± 0.5*		1.3–3.1	1.9 ± 0.5		1.0–3.0
FEF _{25–75%} , liters/s	2.1 ± 0.4*		1.4–2.8	1.7 ± 0.4		0.8–2.7
P _I max, cmH ₂ O	83.7 ± 25.9*		33–125	72.1 ± 24.9		28–119
P _E max, cmH ₂ O	72.9 ± 17.4*		43–119	64.8 ± 20.5		32–110
MVC, liters/min	76.0 ± 2.1*		64–100	64.1 ± 2.2		52–96

FVC, forced vital capacity; PEF, peak expiratory flow; FEV₁, forced expiratory volume in 1 s; FEF_{50%}, forced expiratory flow at 50%; FEF_{25–75%}, forced expiratory flow between 25–75%; P_Imax, maximal inspiratory pressure; P_Emax, maximal expiratory pressure; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; IC, inspiratory capacity; DLCO, lung diffusing capacity, MVC, maximal ventilatory capacity (FEV₁ × 40). †Predicted equations from Knudson et al. (22) *Significantly higher in boys ($P < 0.05$).

uptake ($\dot{V}O_2$), minute ventilation ($\dot{V}E$), CO₂ uptake ($\dot{V}CO_2$), and work rate were significantly higher in boys compared with girls. Maximal ventilation as a percentage of maximal voluntary capacity was similar ($P > 0.05$) between sexes (boys = 65.5 ± 6.1%; girls = 64.4 ± 5.7%). There was no difference ($P > 0.05$) in $\dot{V}O_{2max}$ between the incremental test (boys = 35.4 ± 7.5 ml·kg⁻¹·min⁻¹; girls = 29.5 ± 6.6 ml·kg⁻¹·min⁻¹) and the constant load test at 105% $\dot{V}O_{2max}$ (boys = 33.2 ± 8.3 ml·kg⁻¹·min⁻¹; girls = 27.9 ± 6.1 ml·kg⁻¹·min⁻¹). There were also no significant differences in V_T , breathing frequency, ventilatory equivalents ($\dot{V}E/\dot{V}O_2$, $\dot{V}E/\dot{V}CO_2$), HR, or RER at $\dot{V}O_{2max}$ between boys and girls. There were no differences ($P > 0.05$) between sexes in any measured variable during rest or submaximal exercise. Oxygen saturation (SpO₂) was maintained within 3% of resting values in all subjects throughout exercise and was not different ($P > 0.05$) between boys and girls.

EFL. Figure 1 shows the prevalence of EFL in boys and girls from rest throughout exercise expressed in absolute and relative $\dot{V}O_{2max}$ values. Substantial increases in EFL were observed in both sexes at $\dot{V}O_2$ of ~20–30 ml·kg⁻¹·min⁻¹ or 60–80% $\dot{V}O_{2max}$. There were no significant differences between boys and girls at any given $\dot{V}O_2$ or percent of $\dot{V}O_{2max}$. EFL was present in 95% of boys (19 of 20) and 90% of girls (18 of 20) at $\dot{V}O_{2max}$. There was no difference ($P > 0.05$) in severity of EFL between boys (58 ± 7% of V_T) and girls (43 ± 8% of V_T) at $\dot{V}O_{2max}$. We were also interested in determining whether the amount of EFL was related to $\dot{V}E_{max}$, $\dot{V}O_{2max}$, or TLC. Figure 2 shows $\dot{V}E_{max}$ and percent EFL at $\dot{V}O_{2max}$. There was no relationship ($P > 0.05$) between these variables. Furthermore, both boys and girls were divided into an upper and lower 50th percentile based on $\dot{V}O_{2max}$ (Fig. 3A) and TLC (Fig. 3B). There were no significant differences in EFL between subjects with low $\dot{V}O_{2max}$ (boys = 29.6 ml·kg⁻¹·min⁻¹; girls = 24.3 ml·kg⁻¹·min⁻¹) and high $\dot{V}O_{2max}$ (boys = 41.3 ml·kg⁻¹·min⁻¹; girls = 34.7

ml·kg⁻¹·min⁻¹). There was no relationship ($P > 0.05$) between $\dot{V}O_{2max}$ and % EFL at $\dot{V}O_{2max}$ ($r = 0.21$). There were also no significant differences in EFL between boys and girls with low TLC (boys = 2.2 ± 1.1 liters; girls = 1.7 ± 1.6 liters) and high TLC (boys = 2.9 liters; girls = 2.6 liters). There was no relationship ($P > 0.05$) between TLC and % EFL at $\dot{V}O_{2max}$ ($r = 0.24$).

Regulation of V_T . Individual and mean changes in EELV, as reflected by ERV/FVC from rest to maximal exercise in boys and girls, are represented in Figs. 4 and 5. Table 3 shows IC, ERV/FVC, and IRV/FVC during exercise. The onset of changes in EELV during submaximal exercise were highly variable between subjects and did not always correspond to the onset of EFL. There was no difference ($P > 0.05$) between sexes in IC or ERV/FVC for a given ventilation during exercise. Twelve of 20 boys (60%) and 18 of 20 girls (90%) increased ERV/FVC from rest to $\dot{V}O_{2max}$. There was a significant increase in ERV/FVC with the average increase of 21.3 ± 4.9% in boys and 25.6 ± 3.4% in girls. Figure 6 shows the relationship between % EFL at $\dot{V}O_{2max}$ and the change in ERV/FVC from rest to maximal exercise in boys and girls. In agreement with our third hypothesis, those subjects who experienced EFL also demonstrated the greatest increase in ERV/FVC. There was a significant relationship between these variables in both boys ($r = 0.77$) and girls ($r = 0.75$), indicating that those subjects with the greatest severity of EFL at $\dot{V}O_{2max}$ had the greatest increase in EELV (dynamic hyperinflation) at $\dot{V}O_{2max}$.

DISCUSSION

The purpose of this study was to determine the sex-based differences in prevalence and implications of EFL during exercise in healthy, prepubescent children. Our major findings support our first hypothesis that EFL would be present in the majority of prepubescent boys and girls during heavy exercise,

Table 2. Ventilatory and metabolic data during exercise

	40% $\dot{V}_{O_{2max}}$	60% $\dot{V}_{O_{2max}}$	80% $\dot{V}_{O_{2max}}$	100% $\dot{V}_{O_{2max}}$	Range
\dot{V}_{O_2} ml·kg ⁻¹ ·min ⁻¹					
Boys	14.5 ± 2.7	21.6 ± 4.2	28.3 ± 5.9	35.4 ± 7.5*	20.7–47.3
Girls	12.3 ± 2.4	18.2 ± 4.4	24.8 ± 5.7	29.5 ± 6.6	17.4–39.8
\dot{V}_{O_2} , ml·kg LBM ⁻¹ ·min ⁻¹					
Boys	19.3 ± 2.8	28.7 ± 3.4	37.4 ± 4.9	46.9 ± 5.9*	36.3–59.3
Girls	17.9 ± 2.9	26.2 ± 4.7	33.3 ± 5.6	41.7 ± 6.6	26–52.2
\dot{V}_{O_2} , l/min					
Boys	0.5 ± 0.1	0.7 ± 0.1	1.0 ± 0.1	1.2 ± 0.2*	0.9–1.5
Girls	0.4 ± 0.1	0.6 ± 0.1	0.8 ± 0.2	0.9 ± 0.2	0.6–1.4
V_E , l/min					
Boys	18.2 ± 3.6	25.8 ± 3.5	35.7 ± 4.2	49.8 ± 8.8*	32.7–69.9
Girls	16.3 ± 2.7	23.8 ± 4.4	32.6 ± 6.6	41.2 ± 8.3	26.3–52.7
V_T , liters					
Boys	0.6 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	0.7–1.3
Girls	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.2	0.8 ± 0.2	0.5–1.4
Fb, breaths/min					
Boys	30.3 ± 7.8	36.1 ± 6.9	45.4 ± 6.4	57.6 ± 12.3	26–76
Girls	31.1 ± 6.2	37.9 ± 9.3	46.8 ± 11.5	53.5 ± 13.1	34–88
\dot{V}_{CO_2} , l/min					
Boys	0.4 ± 0.1	0.7 ± 0.1	0.9 ± 0.2	1.2 ± 0.2*	0.9–1.6
Girls	0.3 ± 0.1	0.5 ± 0.1	0.8 ± 0.2	0.9 ± 0.2	0.5–1.5
V_E/\dot{V}_{CO_2}					
Boys	44.1 ± 9.8	40.9 ± 8.2	39.6 ± 4.0	41.1 ± 3.9	34–49
Girls	51.2 ± 8.7	45.6 ± 8.8	44.4 ± 6.2	43.4 ± 5.5	34–53
V_E/\dot{V}_{O_2}					
Boys	40.9 ± 12.0	38.7 ± 9.3	38.1 ± 4.2	41.3 ± 4.2	33–50
Girls	45.9 ± 9.2	45.3 ± 12.5	43.7 ± 7.7	43.4 ± 5.9	28–52
PET _{O₂} , Torr					
Boys	99.2 ± 4.9	100.9 ± 3.2	104.8 ± 3.1	109.7 ± 3.6	100.3–115.0
Girls	101.2 ± 4.0	104.4 ± 3.7	107.5 ± 3.3	109.8 ± 4.9	92.8–114.2
PET _{CO₂} , Torr					
Boys	39.1 ± 3.7	39.2 ± 3.1	38.2 ± 2.6	35.5 ± 2.5	31.6–40.7
Girls	37.4 ± 2.7	37.5 ± 2.7	36.5 ± 2.8	35.7 ± 3.2	31.2–44.5
HR, beats/min					
Boys	121.2 ± 12.3	138.8 ± 13.8	158.0 ± 17.1	174.4 ± 23.1	123–204
Girls	125.4 ± 12.5	149.5 ± 16.7	172.2 ± 14.2	183.4 ± 16.6	147–205
SpO ₂ , %					
Boys	98.9 ± 0.9	98.3 ± 1.3	97.9 ± 1.6	96.7 ± 3.4	94–99
Girls	99.5 ± 0.6	98.9 ± 0.8	98.2 ± 1.5	97.7 ± 1.3	95–99
RER					
Boys	0.8 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	1.0 ± 0.1	0.9–1.1
Girls	0.9 ± 0.1	0.9 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	0.8–1.1
Work, W					
Boys	30.5 ± 8.9	53 ± 11.7	75.0 ± 12.4	97.5 ± 15.2*	60–120
Girls	25.2 ± 5.9	46.5 ± 9.9	65.1 ± 11.5	80.5 ± 18.1	50–110

Values are means ± SD. \dot{V}_{O_2} , oxygen uptake; V_E , minute ventilation; V_T , tidal volume; \dot{V}_{CO_2} , carbon dioxide output; PET_{O₂}, end-tidal partial pressure oxygen; PET_{CO₂}, end-tidal partial pressure carbon dioxide; SpO₂, arterial oxygen saturation (boys, $n = 20$; girls, $n = 20$). *Significantly different from girls ($P < 0.05$).

which would lead to increased EELV. However, contrary to our second hypothesis, we were surprised with the extremely high prevalence of EFL in both boys and girls. We have also shown, for the first time, that there was no difference in the prevalence of EFL between sexes. Similar prevalence of EFL occurred despite boys having larger lungs and aerobic capacity than girls, even when the means were similar for height, weight, and body composition. In agreement with our third hypothesis, the subjects with the greatest EFL also demonstrated the greatest dynamic hyperinflation. Our results also indicated that EFL during exercise could not be predicted based on aerobic capacity, exercise ventilation, or TLC. Last, despite the high prevalence of EFL and contrary to our hypothesis, there was minimal arterial oxygen desaturation throughout exercise, even in those subjects with the greatest EFL.

Prevalence of EFL. The high prevalence of EFL in our subjects is consistent with previous literature that reports significant EFL in both trained (30) and untrained prepubescent children (31). Nourry et al. (31) studied 24 children (11 untrained, 13 trained) to determine EFL and V_T regulation. Results indicated that trained children breathed at a higher lung volume during exercise, yet the proportion of trained and untrained children who experienced EFL (8 of 11 untrained, 9 of 13 trained) was not significantly different. In 2006, Nourry et al. (32) conducted a study that evaluated breathing patterns and flow-volume loops to analyze ventilatory constraints in 18 healthy, untrained prepubescent children. EFL occurred in 10 of 18 subjects. Flow-limited children regulated breathing in dissimilar patterns compared with nonflow-limited children, and there was no association of EFL with age, size, body mass, fat mass percentage, or body mass index. We found similar

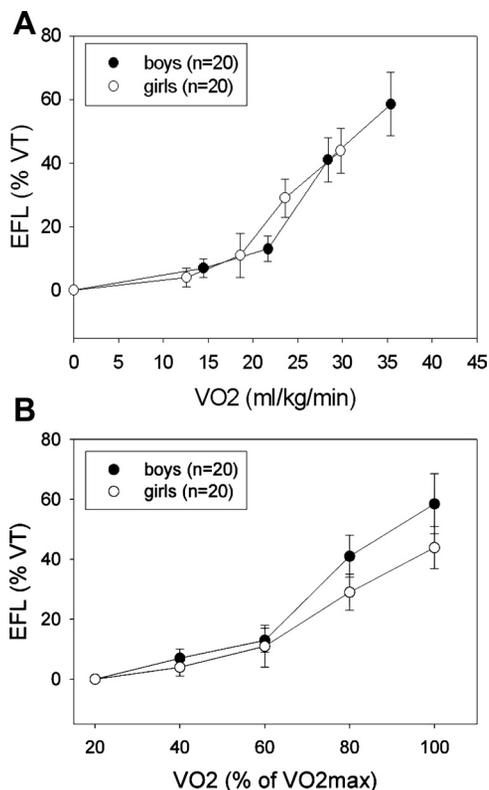


Fig. 1. Degree of expiratory flow limitation (EFL) in boys and girls during exercise expressed in absolute (A) and relative (B) values. There were no differences ($P > 0.05$) between sexes at any exercise intensity in EFL.

results even when we included girls and those with wider ranges of aerobic capacities and body composition in our research design.

Certain adult populations experience EFL during exercise, including highly fit individuals, older adults, and pulmonary disease patients, primarily due to a conflict between capacity of the pulmonary system and metabolic demands of exercise (5, 19, 20, 26). Several differences in ventilatory response to exercise exist between children and adults that may explain potentially higher prevalence of EFL in children. First, children have smaller airways relative to lung size compared with adults (28). Second, children ventilate out of proportion to metabolic demand during heavy exercise (8, 11). It has been documented

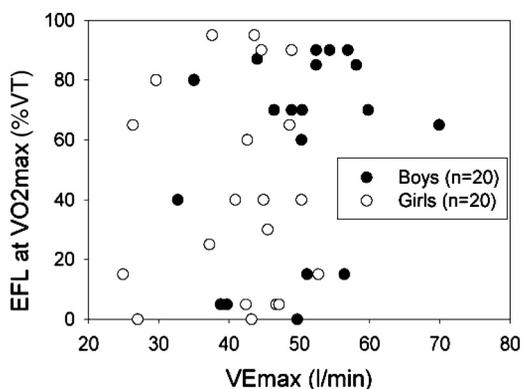


Fig. 2. Relationship between maximal ventilation ($\dot{V}_{E_{max}}$) and EFL at maximal O_2 uptake ($\dot{V}_{O_{2max}}$). There is no correlation between $\dot{V}_{E_{max}}$ and EFL at $\dot{V}_{O_{2max}}$.

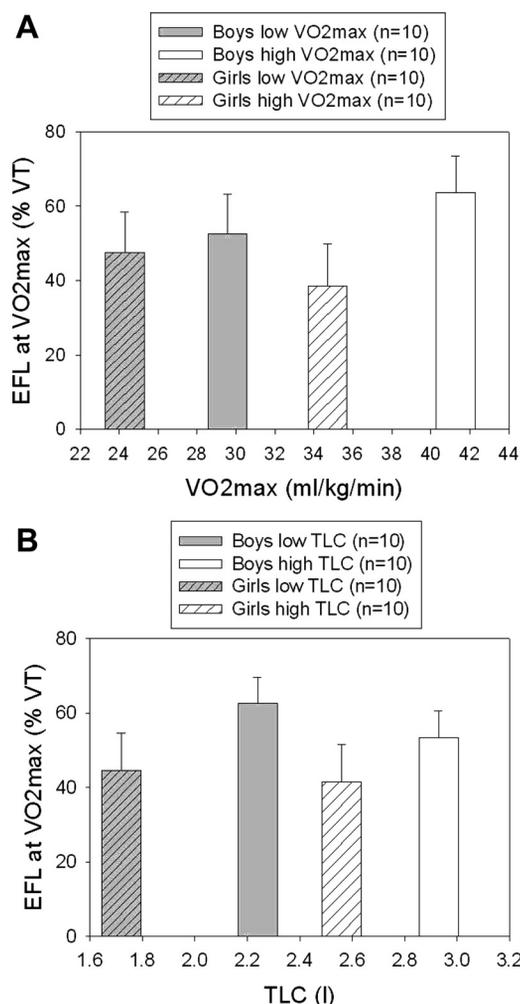


Fig. 3. Expiratory flow limitation vs. $\dot{V}_{O_{2max}}$ (A) and total lung capacity (TLC; B). There was no significant difference ($P > 0.05$) between groups in the amount of EFL at $\dot{V}_{O_{2max}}$ relative to aerobic capacity ($\dot{V}_{O_{2max}}$) or TLC. There was also no relationship ($P > 0.05$) between these variables.

that ventilation in children is higher than adults at rest (24) and during exercise (1, 4). Our data support this premise that ventilation is higher in children during exercise. Compared with adults (36), our subjects demonstrated significantly higher ventilatory equivalents for O_2 and CO_2 , a reflection of “excessive” ventilation relative to exercise demand. The higher ventilatory equivalent combined with smaller lung volumes than adults in our study might suggest children’s increased susceptibility to EFL during exercise. This premise obviously requires further testing as the prevalence and severity of EFL in the healthy adult population has not been established.

Sex differences in EFL during exercise. McClaran et al. (27) and Guenette et al. (12) reported that adult women experience a significant amount of EFL during heavy exercise, primarily due to smaller lung size and lower peak expiratory flow rates than age-matched adult men. These studies indicate adult women use a larger percentage of ventilatory reserve during exercise than men. To our knowledge, there have been no previous reports that have directly compared EFL during exercise between prepubescent boys and girls. Prepubescent boys have larger lungs (38) and larger lung volumes at rest (3, 40) than girls. Also consistent with adults, boys have greater venti-

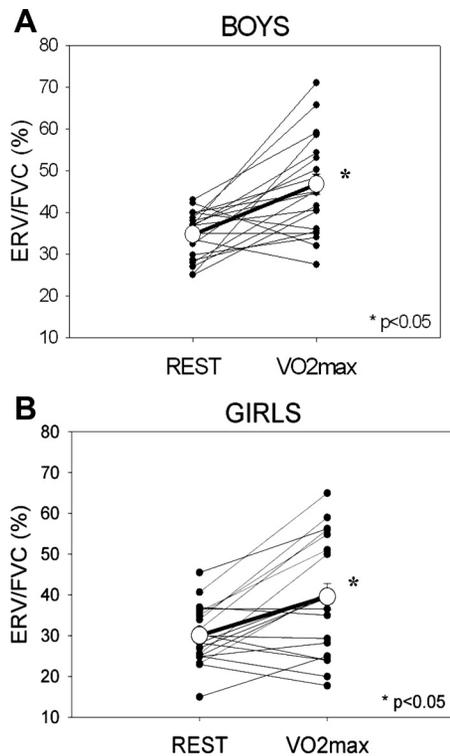


Fig. 4. Mean changes in expiratory residual volume (ERV)/forced vital capacity (FVC) vs. ventilation during exercise in boys and girls. There was no difference ($P > 0.05$) between sexes.

lation and V_T measures (3, 36) compared with prepubescent girls. Given that girls have smaller lungs relative to body size and lower ventilation during exercise, we predicted that EFL would be greater in girls. We were surprised to find the prevalence and severity of EFL during exercise similar between boys and girls. Our data does suggest, however, that the balance between metabolic demand and pulmonary capacity in determining EFL is different between boys and girls (see below).

Prepubescent boys have higher exercise V_E , V_T , and $\dot{V}O_{2max}$ compared with girls (2, 36). Because boys have larger lung capacity, they may be able to generate higher ventilation levels than girls without experiencing ventilatory constraints. However, we found no relationship between V_E , lung capacity

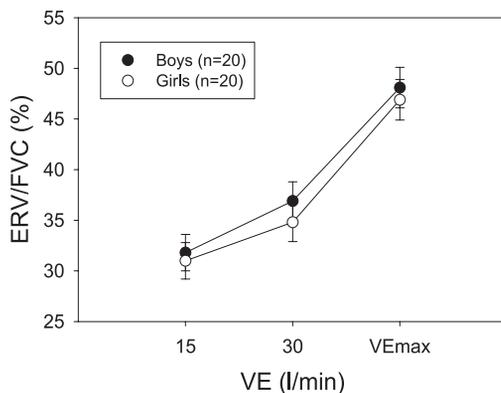


Fig. 5. Individual and mean change in ERV/FVC from rest to $\dot{V}O_{2max}$ in boys (A) and girls (B). Significant increases occurred from rest to $\dot{V}O_{2max}$ in ERV/FVC in both boys and girls.

Table 3. ERV/FVC and IRV/FVC during exercise

	40% $\dot{V}O_{2max}$	60% $\dot{V}O_{2max}$	80% $\dot{V}O_{2max}$	100% $\dot{V}O_{2max}$
IC, liters				
Boys	0.83 ± 0.13	0.85 ± 0.19	0.99 ± 0.14	1.25 ± 0.17
Girls	0.62 ± 0.18	0.65 ± 0.17	0.69 ± 0.19	0.96 ± 0.16
ERV/FVC, %				
Boys	31.8 ± 1.3	32.7 ± 1.9	37.9 ± 2.4	48.1 ± 1.8
Girls	29.7 ± 1.4	30.8 ± 2.4	32.8 ± 2.0	45.9 ± 2.1
IRV/FVC, %				
Boys	31.6 ± 2.1	31.0 ± 3.1	21.3 ± 2.2	11.0 ± 2.2
Girls	33.5 ± 1.8	32.4 ± 2.2	25.1 ± 2.6	12.9 ± 2.6

IC inspiratory capacity; ERV expiratory reserve volume; FVC forced vital capacity; IRV inspiratory reserve volume.

(TLC), and the amount of EFL in either boys or girls, suggesting that different mechanisms underlie the similar prevalence rates of EFL in prepubescent children. In summary, Fig. 7 shows mean data from our subjects depicting the similarity in the amount of EFL in boys and girls. Notice the difference in how EFL is experienced. Specifically, in age- and body size-matched boys and girls, girls experience EFL primarily due to smaller maximal flow-volume loop (MFVL) compared with boys. Significantly smaller lung volumes and maximal expiratory flows cause girls to be more susceptible to mechanical constraints of ventilation. Conversely, boys demonstrate a much larger MFVL than girls but experience EFL primarily due to higher metabolic demand ($\dot{V}O_{2max}$).

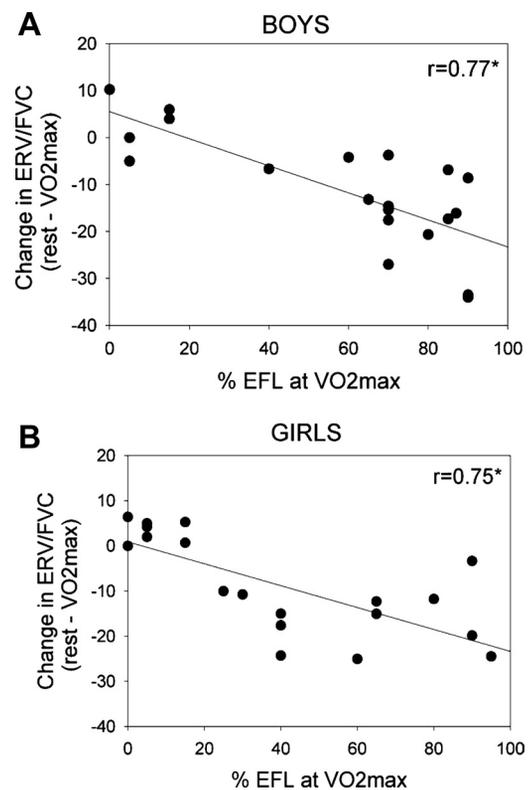


Fig. 6. Relationship between the change in ERV/FVC from rest to $\dot{V}O_{2max}$ to expiratory flow limitation in boys (A) and girls (B). Of the boys and girls who demonstrated EFL, the subjects who exhibited the most EFL had the largest increase in end-expiratory lung volume (dynamic hyperinflation) during exercise. *Significant difference ($P < 0.05$).

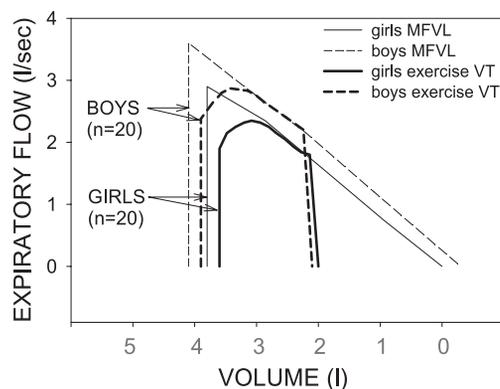


Fig. 7. Summary of maximal flow-volume loops and exercising tidal volume loops for boys and girls.

Regulation of V_T during exercise. Guenette et al. (12) noted that, although there were no differences in breathing regulation during submaximal exercise between men and women, at maximal exercise women had significantly higher EELV when normalized to FVC. Highly fit men and women who reach very high levels of ventilation during maximal exercise were used in this study, which may or may not have affected the amount of EFL that was present. Just as there was no difference in the amount of EFL between boys and girls in our study, there was also no difference in the regulation of V_T in boys and girls at rest or at maximal exercise. Also, the large variability of physical activity habits in the children in our study gave us a broad activity continuum to examine V_T regulation and EFL, which is representative of this population.

In healthy adult populations, EFL during exercise is associated with regulating V_T at increased lung volumes (27). Few studies have investigated EFL in children, but a recent study from Nourry et al. (32) shows dissimilar breathing patterns between those who did and those who did not experience EFL. Surprisingly, flow-limited children had significantly lower EELV, as estimated by ERV/FVC, and higher EILV, as estimated by IRV/FVC, compared with nonflow-limited children during peak exercise. Similarly, we used dynamic EELV, estimated by ERV relative to FVC (ERV/FVC), to determine V_T regulation. Our data contradict these previous results, however, and agree with adult evidence by showing a strong relationship between % EFL during exercise and increased ERV/FVC. We are not aware of any factors to suggest that V_T regulation should be different between children and adults.

Consequences of EFL. There are likely several physiological consequences attributed to the high prevalence of EFL during exercise in our subjects. The increase in EELV that occurs with EFL (18, 25) decreases optimal inspiratory muscle length and increases the work and oxygen cost of breathing. During maximal exercise, most of the children in our study breathed at high lung volumes, indicating the tidal breath was placed near the top of the pressure-volume relationship where lung compliance is decreased, and work of breathing likely increased. Furthermore, in adults, increased minute ventilation has been associated with increased work of breathing in men (7, 29). Guenette et al. (12) introduced the concept of evaluating this relationship in women given their smaller vital capacities relative to height-matched men. Beyond light-intensity activity, women increase their minute ventilation “out of propor-

tion” to men; in fact, beyond 90 l/min, the work of breathing was twice as high in women as in men (12), which has recently been shown to reflect greater resistive work rather than elastic work in women (13). Given the similarities in structure between women and children, it would be expected that the excessive ventilation also seen in children would suggest a higher work of breathing in children compared with adults.

Significant EFL and ventilatory constraints could also affect gas exchange. To our knowledge, there are very few studies that have evaluated exercise-induced arterial hypoxemia (EIAH) or arterial desaturation in healthy, active children (23, 30). Due to ethical concerns, pulse oximetry rather than temperature-corrected arterial blood samples are typically used in children. In the study by Nourry et al. (30), significant arterial desaturation occurred in 7 of 24 prepubescent children. There was a significant association of EIAH with lower FVC and breathing reserve in hypoxemic subjects matched for physical activity. In our study, although significant EFL was observed in both boys and girls, ventilation, pulmonary O_2 diffusing capacity, and pulmonary capillary red blood cell transit time were apparently sufficient to prevent Sa_{O_2} from falling significantly. Our subjects did not experience any relative alveolar hypoventilation (Table 2) that would also contribute to EIAH (15). The apparent difference between our study and the results of others could potentially be due to the physical activity habits of the subjects. The subjects in the Nourry et al. (30) study were highly active with $\dot{V}_{O_{2max}}$ values that were higher than with our subjects. EIAH is common in adults who undergo regular training (9), and training-induced augmentation of aerobic demands may contribute to the onset of EIAH in children. Notwithstanding the above, even our subject with the highest $\dot{V}_{O_{2max}}$ did not demonstrate arterial desaturation at maximal exercise.

Limitations

We used the tidal breath within the maximal voluntary flow volume loop (obtained immediately after exercise) to estimate the onset and degree of EFL experienced during exercise. During voluntary forced expiratory maneuvers, high pleural pressures may compress intrathoracic gas. When flow rate and volume are measured at the airway opening, this measurement of volume displacement will underestimate the true dimensions of the maximal expiratory flow-volume envelope (27). Thus we may have overestimated the onset and/or severity of EFL during exercise. However, previous studies utilizing an independent measurement of the maximal transpulmonary pressure (P_{max}) during expiration showed close agreement during heavy and maximal exercise between the severity of EFL as estimated from the tidal vs. maximal flow-volume envelope with that determined from the proximity of the tidal expiratory pressure to the P_{max} (19).

Also, the unfortunate lack of RPE and dyspnea ratings during exercise limits our understanding of subject perception in response to EFL. Future studies should examine these measurements to determine additional factors that may affect exercise tolerance.

In conclusion, our results confirm that EFL is common in healthy, prepubescent boys, and we have shown for the first time that the prevalence is also high in girls, regardless of height, weight, or body composition. Differences exist between boys and girls in metabolic demand and pulmonary capacity,

the combined effects of which cause the prevalence of EFL to be high and similar. However, ventilatory constraints in pre-pubescent children do not lead to arterial oxygen desaturation, despite a high (and similar) prevalence of EFL in both boys and girls. Although our study indicates similar prevalence rates of EFL in boys and girls, ventilatory constraints are more prevalent in adult women compared with adult men. As children mature into adults, there seems to be dissimilar growth-related changes in the pulmonary system seen between sexes. Further investigation would be worthwhile to track children through adolescence to determine the prevalence and implications of these documented ventilatory constraints into adulthood.

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