Ventilatory Response and Drive of Asthmatic Children to Alveolar Hypoxia

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Summary

Hypoxic ventilatory responses and 100-msec inspiratory occlusion pressures (P_{100s}) were measured at constant alveolar PCO_2 (normocapnia) in 13 asthmatic [12.5 ± 1.0 (S.E.) years] and in 12 normal children (13.3 ± 0.6 years) to determine the appropriateness of the asthmatics' minute ventilation and ventilatory (inspiratory) drive, respectively. Most asthmatics were well controlled with continuous drug therapy and exhibited only mild pulmonary abnormalities at the time of testing. Hypoxia-induced increases in minute ventilation were quantitated in terms of A-values per m^2 body surface area. An A-value describes, in numerical terms, the slope of the hyperbolic ventilatory response to progressive alveolar hypoxia. Larger A-values denote greater increases in ventilation. The A-values were not significantly different between the asthmatic (105 ± 14) and normal children (123 ± 24). The occlusion pressures were significantly different, however, and were 2.3 ± 0.2 cm H_2O (sub-atmospheric) for the asthmatics and 1.5 ± 0.1 cm H_2O for the normal children at an alveolar $PO_2 = 80$ mm Hg, and 7.7 ± 0.9 and 5.2 ± 0.8 cm H_2O for the respective groups at an alveolar $PO_2 = 40$ mm Hg ($P < 0.05$). These findings indicate that asthmatic children with minimal pulmonary abnormalities maintain a normal ventilatory response to alveolar hypoxia by increasing their ventilatory drive, whereas adult asthmatics have been reported to have less than a normal increase in ventilatory drive and hence a diminished ventilatory response during hypoxic exposure.

Speculation

Although the mechanism(s) which diminishes the hypoxic ventilatory response and drive in asthmatic adults, but not in asthmatic children, is not known, it may relate to hypoxic exposures or advancing age.

The development of the inspiratory occlusion technique, which measures the pressure developed against an occluded airway during the initial part of inspiration, has provided a convenient method for measuring the ventilatory (inspiratory) drive (35) while the more traditional measurement of minute ventilation is made simultaneously. Decreased minute ventilation, in the presence of a normal or elevated drive, indicates that the reduced ventilation is not neural in origin but is due to poor pulmonary mechanics. Using these techniques, investigators recently have shown that adult asthmatics maintain a normal resting ventilation by increasing their inspiratory drive (1, 12). The ventilatory drive in asthmatic adults showed a less-than-normal increase to progressive hypoxia, however, and both minute ventilation and ventilatory drive were significantly decreased from that of normal adults at an alveolar PO_2 of 40 mm Hg (12). In order to determine whether similar abnormalities existed in the hypoxic ventilatory responses (HVRs) of the pediatric age group, we studied asthmatic children (7-17 years). Minute ventilation and ventilatory drive were measured during progressive hypoxia to determine whether diminished increases in these parameters were inherent abnormalities in

all asthmatics or whether such abnormalities developed with advancing age and prolonged asthma.

MATERIALS AND METHODS

SUBJECTS

Thirteen perennially asthmatic children under good clinical control and 12 normal children of similar mean ages and body surface areas (BSA) participated in this study which was approved by the institution's Human Ethics Committee. The anthropometric characteristics of the participants are summarized in Tables 1 and 2. The asthmatic children were ambulatory, full-time residents at our asthma treatment center in Denver (altitude = 1610 m) and were selected at random for the study as part of their routine clinical evaluation. The mean duration of illness in the patients was 8.9 years with a range of 3-16.5 years. As few as four, but as many as 30 emergency room visits or hospitalizations were documented for the asthmatic children and two had experienced acute respiratory failure. Eleven of the 13 asthmatic children were on theophylline-containing drugs (mean = 23 ± 3 (S.E.) mg/kg/day) whereas the remaining two were on no drug therapy at the time of testing. Seven of those on theophylline-containing drugs were also receiving steroids; one patient was on oral steroids, two were on inhaled steroids and four were on both oral and inhaled steroids (Table 1). The normal children were included in the study after informed, written consent was obtained from them and their parents, and after it had been determined that they were free from allergic, respiratory, and cardiac diseases. To eliminate the possible effects of genetic factors (4, 25), residency at altitude (32), and physical conditioning (3) on HVRs, only the following were accepted for the study: one individual per family, individuals who had not lived at an altitude above 1610 m, and individuals engaging in non-endurance physical activities.

VENTILATORY RESPONSE MEASUREMENTS TO PROGRESSIVE HYPOXIA

The children came to the laboratory 3 h after their last light meal and began by relaxing in a comfortable, semi-recumbent position (blood donor chair) for 10 min before going onto the breathing apparatus. The participants watched television with the sound coming through headphones before and while measurements were made.

Partial pressures of end-tidal O_2 and CO_2 were measured with a mass spectrometer (Perkin-Elmer MGA, Pomona, CA) and served as indices of alveolar gases (P_AO_2 , P_ACO_2). In order to remove any possible hypoxic stimulus to breathing while determining baseline (resting) ventilation and steady-state (S-S) P_ACO_2 , the subjects were given 60% O_2 ($P_iCO_2 = 0$ mm Hg) to breathe. After this hyperoxic mixture had been breathed for at least 3 min, resting ventilation and S-S P_ACO_2 (normocapnia) were determined over a 2-min period. After a 5-min break, the subjects began breathing from a bag-in-box rebreathing system for HVR measurements (23). The bag initially contained a volume

Table 1. Asthmatic children: anthropometric, ventilatory and occlusion pressure data

Subject	Sex	Age Yr	Asthma ² yr	BSA ³ m ²	Steady-State ⁴ P _A CO ₂ mm Hg	A-Value ⁵ per m ²	$\Delta\dot{V}_E^5$ liter/min per m ²	Occlusion Pressure ⁶ in cm H ₂ O at P _A O ₂ s of				+Meds ⁷
								80	60	50	40	
1	M	8.3	6	0.93	33.5	168	18.5	0.78	2.51	4.50	7.23	
2	M	15.2	13.5	1.67	33.2	129	14.2	2.31	4.14	5.90	8.45	t
3	F	14.6	13	1.52	31.4	29	3.2	1.74	2.00	2.15	2.34	to
4	F	16.6	16.5	1.87	33.8	105	11.6	2.26	3.46	4.88	6.86	t
5	M	12.6	12	1.32	30.8	88	9.7	2.60	4.28	6.26	8.99	ti
6	F	16.4	11.5	1.53	38.3	122	13.5	1.75	4.36	6.78	10.20	ti
7	M	15.1	10	1.52	33.6	59	6.5	1.46	1.98	2.62	3.50	
8	F	13.6	10.5	1.37	32.5	123	13.6	1.98	3.22	4.52	6.28	toi
9	F	13.5	3	1.43	31.0	159	17.5	3.01	5.50	7.80	11.66	toi
10	M	13.7	3	1.36	30.7	68	7.5	2.89	4.38	5.50	7.00	toi
11	F	8.0	6.5	1.05	29.3	189	20.8	4.27	7.11	9.82	13.87	toi
12	F	8.3	7	0.88	29.9	52	5.7	2.53	3.46	4.22	5.32	t
13	M	7.0	3.5	0.93	29.0	68	7.5	2.14	3.56	5.24	7.85	t
Means		12.5	8.9	1.34	32.1	105	11.6	2.29	3.84	5.40	7.66	
± S.E.		1.0	1.2	0.09	0.7	14	1.5	0.24	0.39	0.56	0.87	
P values ⁸		NS		NS	P < 0.05	NS	NS	P < 0.05	P < 0.05	P < 0.05	P < 0.05	

¹ Two asthmatics had experienced acute respiratory failure.² Duration of asthma to nearest half yr³ BSA = body surface area in square meters.⁴ Steady-state alveolar PCO₂ measured during hyperoxia.⁵ Hypoxic ventilatory responses quantitated in terms of A-values and ventilatory increase in liter/min per m².⁶ Occlusion pressures measured at alveolar PO₂s of 80, 60, 50 and 40 mm Hg were sub-atmospheric.⁷ Medications were: t = theophylline containing drug, O = oral steroid, i = inhaled steroid.⁸ P values for comparison of above means with means for normal children given in Table 2, NS = not significant.

Table 2. Normal children: anthropometric, ventilatory and occlusion pressure data

Subject	Sex	Age yr	BSA m ²	Steady-State P _A CO ₂ mm Hg	A-Value per m ²	$\Delta\dot{V}_E$ liter/min per m ²	Occlusion Pressures in cm H ₂ O at P _A O ₂ s of			
							80	60	50	40
14	M	13.8	1.61	32.0	71	7.8	0.91	1.36	1.73	2.34
15	F	12.4	1.49	36.0	71	7.8	1.78	2.52	3.10	3.84
16	M	9.6	1.06	35.1	349	38.5	1.76	4.40	7.50	10.90
17	F	11.6	1.15	32.0	93	10.3	1.62	3.06	4.64	7.10
18	M	15.6	1.73	34.9	183	20.2	1.62	2.60	3.50	4.77
19	F	11.5	1.27	34.7	101	11.1	2.03	2.80	3.58	4.70
20	F	12.3	1.40	33.2	77	8.5	1.32	1.72	2.44	3.54
21	M	14.1	1.56	36.0	85	9.4	1.16	1.76	2.54	3.64
22	M	13.6	1.35	34.1	72	7.9	1.14	1.56	2.07	2.96
23	F	17.9	1.44	33.6	118	13.0	0.68	1.50	2.86	4.76
24	F	13.0	1.44	36.2	70	7.7	1.47	2.20	3.04	4.18
25	M	13.8	1.26	36.0	181	20.0	2.50	4.45	6.55	9.57
Mean ¹		13.3	1.40	34.5	123	13.6	1.50	2.49	3.63	5.19
± S.E.		0.6	0.06	0.4	24	2.6	0.14	0.30	0.51	0.76

¹ Means from normal children are compared with the means from asthmatic children (Table 1). See the bottom of Table 1 for an explanation of symbols and P values.

of 28% O₂ and 72% N₂ which allowed the P_AO₂ to fall approximately 6 mm Hg/min during the test and the responses were terminated about 10 min later when P_AO₂ had reached 40 mm Hg. The S-S P_ACO₂ level previously determined for a given subject was maintained constant for his/her HVR measurements by varying the rate at which gas from the rebreathing bag was circulated through CO₂ absorber (23). Subjects recovered on ambient air for 5–10 min after their first HVR before the next response was measured. Breath-by-breath volume signals from a rolling-seal spirometer (Ohio, Houston, TX) and alveolar gas signals from the mass spectrometer were processed by a data acquisition system (HealthGarde, Salt Lake City, UT) to give 15 sec averages for expired ventilation in liters/minute (liter/min) (BTPS), and alveo-

lar PO₂ and PCO₂ in mm Hg. These parameters were displayed on a cathode ray terminal during a response and printed out afterwards. HVRs were quantitated both in terms of liter/min ventilatory increase and A-value. The computer calculated A-values using the relationship introduced by Weil *et al.* (33): $\dot{V} = \dot{V}_E^* + A/(P_{A}O_2 - K)$. An A-value is a slope parameter which describes the hypoxic ventilatory response; the larger A-values denote greater increases in ventilation. An A-value of 100 measured over the P_AO₂ range of 100–40 mm Hg, for example, would indicate a 11 liter/min ventilatory increase, whereas an A-value of 200 would indicate a 22 liter/min increase. In the relationship, $\dot{V}_E^*$ is the extrapolated ventilation at an infinitely high P_AO₂, and the constant K (32 mm Hg), is the P_AO₂ at which ventilation

theoretically approaches infinity (33). Inasmuch as HVRs in adults have shown a positive correlation to both height and weight (11), the responses of our subjects were standardized by dividing ventilation by BSA. The conclusions of the study would not have been altered if ventilation had not been divided by BSA.

Two HVRs were measured with the $P_A\text{CO}_2$ maintained at the resting, normocapnic level. When the smaller of the HVRs differed from the larger by more than 30% a third response was measured and the data from similar responses were averaged. The mean coefficient of variation for the accepted responses was 16%.

INSPIRATORY OCCLUSION PRESSURES

A two-way Rudolph respiratory valve (Hans Rudolph, Kansas City, MO), modified by us with a diaphragm, which occluded the inspiratory side when pressurized, was used in the study. The occlusion was applied to the inspiratory side of the valve during expiration by pressing a remote button. Release of the occlusion occurred automatically 250–400 msec after the onset of inspiration. Inspiratory occlusion pressures were measured with a differential pressure transducer (Validyne, Northridge, CA) approximately every 30 sec but at irregular intervals during a HVR so the subjects could not predict when an occlusion would occur. The pressure changes were recorded at a paper speed of 100 mm/sec with 20 msec time lines (Electronics for Medicine, White Plains, NY). Inspiratory occlusion pressures (P_{100} s) were measured manually from the records as the change (decrease) in pressure between 30 and 130 msec after the beginning of inspiration (the starting point varied somewhat depending on the position of a time line). With this procedure, occasional base-line noise or distortions were avoided without compromising the measurement. The pressure tracings rose linearly to beyond 200 msec and a subject could not sense an occlusion and alter inspiration in less than 200 msec (35).

Occlusion pressures at specific $P_A\text{O}_2$ s were calculated for each subject using a curve-fitting model of P_{100} versus $P_A\text{O}_2$ which resulted in the highest correlation coefficient. The parabolic, power and hyperbolic models gave the best results. The mean correlation coefficient (r) was 0.76 for the accepted curves and an average of 18 points was included in the analysis of each response.

ARTERIAL PO_2 MEASUREMENTS

Arterial blood was drawn from the radial artery of 12 asthmatics for PO_2 measurements on the day prior to the HVR measurements. The asthmatic children breathed a 13% O_2 and 87% N_2 gas mixture during the sampling procedure. Alveolar PO_2 was monitored simultaneously with a mass spectrometer which allowed alveolar-arterial PO_2 differences [(A-a) PO_2] to be determined.

PULMONARY FUNCTION EVALUATIONS

Because the asthmatic children were familiar with the laboratory, their pulmonary functions were determined just before the measurement of their ventilatory responses. The pulmonary functions of the normals were determined on a day prior to the measurement of their ventilatory responses, so that time could be taken to familiarize them with the laboratory and breathing equipment. From the spirometric tests, we obtained vital capacity and its subdivisions, forced expired volume in one sec and the maximal mid-expiratory flow rate. Airway resistance (R_{aw}) and functional residual capacity (FRC) were determined with a constant-volume body plethysmograph by the methods of DuBois *et al.* (6, 7). Specific conductance was calculated from R_{aw} and the simultaneously measured thoracic gas volume. Residual volume and total lung capacity were calculated from FRC and the subdivisions of the vital capacity.

DATA ANALYSES

Paired t tests and one way analysis of variance were used to analyze the data (5). The level of statistical significance accepted was 0.05 or less.

RESULTS

The pulmonary function measurements of the asthmatic and normal children are summarized in Table 3. Mean values for vital capacity, forced expired volume in one sec, maximal mid-expiratory flow rate and specific conductance were not significantly different between groups. The mean residual volume, functional residual capacity and total lung capacity were significantly greater in the asthmatic than in the normal children, however. The mean (A-a) PO_2 was determined for 12 of the asthmatic children and was 1.6 ± 0.7 (S.E.) mm Hg when the mean $P_A\text{O}_2$ was 40 mm Hg. The (A-a) PO_2 was greater than 3 mm Hg at an alveolar PO_2 of 40 mm Hg in only two of the 12 asthmatics in whom it was measured.

Ventilation ($\dot{V}_E$) and P_{100} are plotted versus alveolar PO_2 in Figure 1. The P_{100} s are all sub-atmospheric but the negative sign (–) has been deleted from the data in the figure and tables. As the alveolar PO_2 was progressively decreased from 100 to 40 mm Hg, $\dot{V}_E$ increased from 5.5 to 24 liter/min (BTPS) which is comparable to an A-value of 168. Over this same hypoxic range the P_{100} “increased” from about 2 to 13 cm H_2O .

Tables 1 and 2 summarize the anthropometric, ventilatory and P_{100} data obtained from the asthmatic and normal children. The mean ages and BSA were not significantly different for the two groups. The mean resting S-S $P_A\text{CO}_2$ value during the hyperoxic period was significantly ($P < 0.05$) lower for the asthmatics, (32.1 ± 0.7 mm Hg), than for the normal children (34.5 ± 0.4 mm Hg). Hyperoxic, resting ventilation was not significantly different between the groups and was 6.6 ± 0.6 liter/min per m^2 for the asthmatics and 6.1 ± 0.3 liter/min per m^2 for the normals. The means for the hypoxia-induced ventilatory responses, expressed in terms of A-values/ m^2 , were 105 ± 14 for the asthmatics and 123 ± 24 for the normals; these A-values were not significantly

Table 3. Pulmonary function measurement

	VC ¹	FEV ₁	MMEF	SGaw	RV	FRC	TLC
Asthmatics	123	110	87	72	150	132	130
±S.E.	4	7	10	5	16	7	4
Normals	111	106	104	81	95	107	107
±S.E.	4	4	8	7	11	4	4
P value	NS	NS	NS	NS	<0.05	<0.05	<0.05

¹ Abbreviations are as follows: VC = vital capacity; FEV₁ = forced expired volume in one sec; MMEF = maximal mid-expiratory flow rate; SGaw = specific airway conductance; RV = residual volume; FRC = functional residual capacity; and TLC = total lung capacity; NS = not significant. Pulmonary functions given as % predicted (22, 34).

Fig. 1. Ventilation (●) and inspiratory occlusion pressures (▲) increase in a hyperbolic manner for the subject as alveolar PO_2 is decreased. The above data are from a single, isocapnic, hypoxic ventilatory response whereas the summary data in Tables 1 and 2 are means from two similar responses after the ventilatory responses have been adjusted for body surface area. The coordinate for occlusion pressure (P_{100}) in this figure is shifted downward from the coordinate for ventilation ($\dot{V}_E$) to avoid overlapping of the data points.

different. The mean increases in minute ventilation ($\Delta \dot{V}_E$) were also not significantly different between groups.

The P_{100S} at P_{AO_2S} of 80, 60, 50 and 40 mm Hg were significantly greater for the asthmatics and were 2.29 ± 0.24 ; 3.84 ± 0.39 ; 5.40 ± 0.56 and 7.66 ± 0.87 cm H_2O , respectively. In the normal subjects, the P_{100S} were 1.50 ± 0.14 ; 2.49 ± 0.30 ; 3.63 ± 0.51 and 5.19 ± 0.76 cm H_2O at the same P_{AO_2S} . The ventilation/ P_{100} ratio was calculated for the subjects also. This ratio appears to be an index of ventilatory efficiency and reflects the volume of respiratory gas which was ultimately inspired/minute per cm H_2O pressure developed at the onset of inspiration (1). The ratios indicated that the asthmatics were less efficient than were the normals at any given PO_2 between 80 and 40 mm Hg. For example, the mean ventilation/ P_{100} ratio was 2.8 ± 0.3 liter/min per cm H_2O at P_{AO_2S} of 50 mm Hg for the asthmatic children and 4.3 ± 0.6 liter/min per cm H_2O for the normal children ($P < 0.02$).

Although the mean inspiratory flow (20, 21) ($\dot{V}_I$ = tidal volume/duration of inspiration) is not thought to be a reliable index of inspiratory drive in individuals with abnormal pulmonary mechanics, it was also determined in our subjects to compare with P_{100} measurements. The $\dot{V}_I$ s were slightly greater, indicating increased inspiratory drive, in the asthmatics than in the normals but the differences were not statistically significant. At P_{AO_2S} of 80 and 40 mm Hg the values were 0.41 ± 0.03 , and 0.95 ± 0.07 liter/sec for the asthmatics; and 0.34 ± 0.02 , and 0.82 ± 0.08 liter/sec respectively for the normals.

DISCUSSION

This study has shown that although there was no significant difference between the mean ventilatory responses of asthmatic and normal children to acute hypoxia, the ventilatory drive (P_{100}) necessary to achieve the same ventilatory response was significantly greater in the asthmatic children. This indicates that asthmatic children usually compensate satisfactorily for abnormalities in pulmonary mechanics and that they maintain an appropriate HVR by increasing ventilatory drive. Our findings conflict with those reported for adult asthmatics by Hudgel and Weil (13) and Hudgel *et al.* (12) who reported that adult asthmatics have both decreased ventilatory and P_{100} responses for a given degree hypoxia.

Similar to what Hudgel *et al.* (12) reported, the normoxic P_{100S} of our asthmatic children were not correlated with their FRCs. On the other hand, the normoxic P_{100S} of the normal children were negatively correlated ($P < 0.05$) with their FRCs as reported by Shaffer *et al.* (27). The FRC has been shown to increase in normal subjects as the O_2 content of the inspired gas is decreased (9). Consequently, the neural stimulus needed to produce a certain pressure is increased in a given subject as his/her FRC becomes larger because the muscle fibers of the diaphragm are already somewhat shortened (18). The occlusion pressures would reflect over-all inspiratory drive and effort in cases where the FRC has changed but P_{100} would not be an accurate index of respiratory neural output (18). Since the asthmatic children in our study were relatively hyperinflated compared to normal children (Table 3), their P_{100S} , if anything, would presumably underestimate their respiratory neural output.

Although the mechanism(s) for decreased HVRs in adults is not specifically known, there has been suggestive evidence that the cause might be sustained chronic hypoxemia or repeated exposures to severe hypoxia. This evidence has come from studies on long-time high-altitude residents and natives (26, 29, 32) and from studies on patients with chronic heart (8, 30) and lung disease (10, 15). The work of McFadden and Lyons (19) has shown that asthmatics tend to have low arterial PO_2 whenever their asthma was exacerbated. Thus hypoxemia appears to be the common denominator in adult asthmatics and in the others who have acquired diminished HVRs.

Our data on children do not show that age *per se* or that the duration of illness correlate with any reduction in HVR. Hudgel

et al. (12) were likewise unable to correlate the duration of illness with the reduction of HVR in adult asthmatics. A corollary to the difference in the HVRs of asthmatic children and asthmatic adults has been observed to occur at altitude, however. Adults who had lived for several years at 3,100 m exhibited decreased HVRs, whereas 10-year-old children of the same altitude did not (2, 32).

Even though no group differences in HVR were demonstrated between asthmatic and normal children, there were some asthmatics who had reduced responses. Three out of the 13 asthmatics had A-values of 59 or less and ventilatory increases of 6.5 liter/min or less. These values were clearly less than the lowest values observed in the normal children (Tables 1 and 2). The two asthmatic children who had experienced respiratory failure had the smallest and largest HVR in their group. The incidence of poor responders to alveolar hypoxia may have increased if the asthmatic children had been pre-selected as those suspected of having decreased HVRs.

Aside from the obvious difference in age between our patients and those of Hudgel *et al.*, two other differences of potential significance should be considered. Some of the adults had more severe pulmonary abnormalities than did the asthmatic children (13). It is interesting, however, that the adult asthmatics did not compensate for their airway obstruction during hypoxic exposure by increasing ventilatory drive as other asthmatics have been shown to do when challenged with hypercapnia and inspiratory resistance combined (14). It is also important to note that the asthmatic adults studied by Hudgel *et al.* (12, 13) were taken off their medications for at least 6 h prior to being studied whereas our asthmatic children received their regularly scheduled medications on the day of testing. Consequently, the normal HVRs of our patients could be attributed, at least, in part, to drug therapy. Theophylline-containing drugs have been reported by Lakshminarayan *et al.* (17) and Sanders *et al.* (24) to augment HVR but whether long-term theophylline therapy exerts a similar effect on HVR is not known. Five of the asthmatic children on theophylline were also on prednisone. The effect of adrenocorticosteroid therapy on HVR is difficult to predict even though Hudgel and Weil (13) showed a correlation between adrenocorticosteroids dosage and the magnitude of HVR in adult asthmatics. Some of the effect of adrenocorticosteroids on the HVR of asthmatics would be secondary as it is administered primarily to improve pulmonary mechanics. Progesterone, or an analog of progesterone, is currently administered to hypercapnic or hypoxic patients when an increase in ventilation is desirable (16, 28, 31).

When A-values are determined on the basis of alveolar PO_2 rather than arterial PO_2 , the HVRs can be significantly overestimated whenever there is an abnormally large (A-a) PO_2 . In order for the HVRs of the asthmatics in Table 1 to be significantly less than the HVRs of the normals, the asthmatics' values would need to be reduced about 20% from what they are. Our calculations indicate that the (A-a) PO_2 at an alveolar PO_2 of 40 mm Hg would need to be 3 mm Hg greater in the asthmatic children than in the normal children for such a reduction in the HVR values to occur. The mean (A-a) PO_2 for the asthmatic children, however, was 1.6 mm Hg at an alveolar PO_2 of 40 mm Hg which is not significantly large to explain the normal HVR observed in the asthmatic children. In addition, the interpretation of HVR and P_{100} data from adult asthmatics was similar whether the level of hypoxic stimulus was quantitated as alveolar PO_2 or arterial oxygen saturation (12).

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