Developmental changes in response to subatmospheric pressure loading of the upper airway

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Marcus, Carole L., Janita Lutz, Audrey Hamer, Philip L. Smith, and Alan Schwartz. Developmental changes in response to subatmospheric pressure loading of the upper airway. J. Appl. Physiol. 87(2): 626–633, 1999.—Children snores less than adults and have fewer obstructive apneas, suggesting a less collapsible upper airway. We therefore hypothesized that the compensatory upper airway responses to subatmospheric pressure loading decrease with age because of changes in upper airway structure and ventilatory drive. We measured upper airway upstream pressure-flow relationships during sleep in 20 nonsnoring, nonobese children and adults. Measurements were made by correlating maximal inspiratory airflow with the level of nasal pressure applied via a mask. The slope of the upstream pressure-flow curve ($S_{PF}$) was used to characterize upper airway function. We found that $S_{PF}$ was flatter in children than in adults ($8 \pm 5$ vs. $30 \pm 18$ ml s$^{-1}$ cmH$_2$O$^{-1}$, $P<0.002$) and that $S_{PF}$ correlated with age ($r=0.62$, $P<0.01$) and body mass index ($r=0.63$, $P<0.01$). The occlusion pressure in 100 ms during sleep was measured in six children and two adults; it correlated inversely with $S_{PF}$ ($r=-0.80$, $P<0.02$). We conclude that the upper airway compensatory responses to subatmospheric pressure loading decrease with age. This is associated with increased body mass index, even in nonsnor ing, nonobese subjects. Ventilatory drive during sleep plays a role in modulating upper airway responses.

ventilatory control; sleep-disordered breathing; critical pressure; normalized differences in body size may partly explain the developmental differences in upper airway structure or upper airway muscles.

A major structural factor that can affect upper airway collapsibility is obesity, which is a well-described risk factor for the development of the obstructive sleep apnea syndrome (OSAS) in children (20) and adults. Because children tend to be thinner than adults (13), differences in body size may partly explain the decreased upper airway collapsibility noted in normal children compared with adults. Previous studies have shown that the structural properties of the upper airway can be evaluated by determining the relationship between nasal pressure ($P_N$) and inspiratory flow with use of the Starling resistor model of upper airway function (22, 30). According to this model, under conditions of flow limitation, maximal inspiratory flow ($V_{\text{Imax}}$) is determined by the pressure changes upstream (nasal) to a collapsible locus of the upper airway and is independent of the downstream (tracheal) pressure generated by the diaphragm. The critical closing pressure ($P_{\text{crit}}$) occurs at the x-intercept of the pressure-flow curve, i.e., the pressure at which there is zero flow due to upper airway closure. In an isolated Starling resistor model, $V_{\text{Imax}}$ is determined by $P_{\text{crit}}$ and the resistance of the upper airway upstream to the site of collapse. Therefore, the mechanical properties of the upper airway leading to airflow obstruction can be evaluated by determining $P_{\text{crit}}$ and upstream resistance.

Neuromuscular factors are also important in maintaining upper airway stability. The upper airway muscles are accessory muscles of ventilation and, as such, are affected by changes in ventilatory drive. Because children have a higher ventilatory drive than adults (10, 31, 35), this may partly explain the differences in upper airway function. One of the neuromuscular factors thought to be important in the maintenance of upper airway patency is the reflex response to subatmospheric pressure. Previous studies have shown increases in upper airway neuromuscular activity in response to drops in $P_N$ during wakefulness in adults; this is attenuated during sleep (4). The effects of these reflex responses on upper airway patency have not been systematically examined but can be further evaluated using the Starling resistor model. In an isolated Starling resistor model, the sensitivity of the upstream pressure-flow relationship is represented by the slope of the pressure-flow curve ($S_{PF}$). The resistance of the upstream segment of the upper airway is the reciprocal of the $S_{PF}$. However, in the living organism the $S_{PF}$ is affected not only by mechanical and structural factors (the degree of "stiffness" of the upper airway), but also by reflex neural mechanisms. Thus the $S_{PF}$ is a useful tool for the comprehensive evaluation of upper airway function.

We hypothesized that the pediatric upper airway was better able to compensate for a subatmospheric pressure load than the adult upper airway because of differences in upper airway structure or upper airway neuromuscular responses to the load. We therefore examined the developmental differences in upper airway function among normal individuals during sleep. Specifically, we determined the influence of subatmospheric pressure on the maintenance of upper airway patency across the age spectrum. Responses to subatmospheric pressure were examined by delineating the
upstream pressure-flow relationships for each individual.

**METHODS**

Nonsnorers were recruited from the general community. All subjects underwent baseline polysomnography to ensure that they were normal. On a separate night, pressure-flow measurements during sleep and occlusion pressure in 100 ms ($P_{0.1}$) during wakefulness and sleep were determined.

Study group. The study group consisted of healthy children (old enough to cooperate with testing) and adults. Subjects with habitual (nightly) snoring or obesity (defined as a body mass index (BMI) $\geq 30$ kg/m$^2$) were excluded. Children with a history of tonsillectomy and/or adenoidectomy were excluded, because OSA5 is now a common indication for adenotonsillectomy (27). All children had visible tonsillar tissue on examination. Because tonsillectomies and adenoidectomies were performed so commonly in the past, this exclusion criterion was not applied to the adult group. Informed consent was obtained from each subject, as well as from the parents/legal guardians of the children. The study was approved by the Institutional Review Board of Johns Hopkins University.

Baseline polysomnography. Polysomnographic studies were performed overnight. During polysomnography, the following parameters were measured and recorded continuously using a computerized polysomnography system (Alice 3, Healthdyne, Marietta, GA): electroencephalogram (C3/A2, O1/A2); right and left electrooculogram; submental electromyogram (EMG); tibial EMG; electrocardiogram; chest and abdominal wall motion (piezoelectric transducers); oronasal airflow (3-pronged thermistor); end-tidal PCO$_2$, measured at the nose by infrared capnometer (model N-1000, Nellcor, Van Nuys, CA); arterial O$_2$ saturation by pulse oximetry (model N-1000; Nellcor) and oximeter pulse waveform. Subjects were also monitored and recorded on videotape with an infrared video-camera and were continuously observed by a polysomnography technician. Sleep architecture, arousals from sleep, and cardiorespiratory parameters were analyzed using standard techniques (2, 3, 26, 33). Subjects with an apnea index $\geq 5$/h were excluded.

Pressure-flow measurements. Pressure-flow measurements were obtained during a separate, overnight polysomnogram, as previously described. Routine polysomnographic parameters were measured as described above, except measurements were recorded on a polygraph recorder (model 78E, Grass, Quincy, MA). To measure airflow, the patient breathed through a snug-fitting nasal continuous positive airway pressure (CPAP) mask (Respironics, Murrysville, PA) attached to a heated pneumotachometer (Hans Rudolph, Kansas City, MO) and transducer (Validyne Engineering, Northridge, CA). $P_N$ was measured within the mask with use of a differential pressure transducer referenced to atmosphere. End-tidal PCO$_2$ was measured via a port on the mask. A thermistor was placed at the mouth to detect oral breathing. $P_N$ was altered in a positive or a negative (subatmospheric) direction by use of CPAP (Respironics), one of which had been modified to provide subatmospheric pressure. The subject was allowed to fall asleep on a low level of positive pressure (2–4 cmH$_2$O), sufficient to abolish inspiratory airflow limitation. Inspiratory airflow limitation was considered to occur when airflow failed to increase, despite increasing respiratory effort, as demonstrated by the characteristic flow waveform. The characteristic waveform pattern consists of increasing inspiratory flow followed by a midinspiratory plateau (7, 22). $P_N$ was then lowered in 2-cmH$_2$O increments until upper airway obstruction occurred, the patient aroused from sleep, or a maximum pressure of $-20$ cmH$_2$O had been applied. Measurements were performed during non-rapid-eye-movement sleep, preferentially during slow-wave sleep (SWS). When measurements during SWS were not possible (because of sleep stage transitions or lack of deep sleep in the laboratory situation), measurements were performed during stage 2 sleep. For purposes of comparison, measurements were performed during SWS and stage 2 sleep in nine subjects; the SWS measurements were used for the final analysis. Pressure-flow curves were constructed by plotting maximal inspiratory airflow ($V_{\text{Imax}}$) of flow-limited breaths against $P_N$. $P_N$ vs. inspiratory airflow curves were fitted by least-squares linear regression. $P_{\text{crit}}$ was defined as the x-axis intercept of the regression line ($V_{\text{Imax}} = 0$). Many of the children did not demonstrate flow limitation, even at markedly subatmospheric pressures (Fig. 1B). In these cases, the x-intercept could not be determined without extreme extrapolation, and consequently $P_{\text{crit}}$ could not always be determined. Therefore, $S_{PF}$ was used to characterize the upper airway response. $P_{0.1}$ measurements. $P_{0.1}$ was measured during wakefulness at the beginning of the study and then again during stage 2 sleep after the pressure-flow measurements. The respiratory

![Fig. 1](https://example.com/fig1.png)

**Fig. 1.** A: maximal inspiratory flow ($V_{\text{Imax}}$) vs. nasal pressure ($P_N$) for a 42-yr-old woman. As $P_N$ became more negative, $V_{\text{Imax}}$ decreased. Critical pressure ($P_{\text{crit}}$) is $-21$ cmH$_2$O, and slope of upstream pressure-flow curve is 22 ml·s$^{-1}$·cmH$_2$O$^{-1}$. B: $V_{\text{Imax}}$ vs. $P_N$ for a 6-yr-old boy. $V_{\text{Imax}}$ was maintained, despite increasingly subatmospheric $P_N$; thus $P_{\text{crit}}$ could not be determined. Slope of upstream pressure-flow curve is 2 ml·s$^{-1}$·cmH$_2$O$^{-1}$.**
Table 1. Study group characteristics

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<tr>
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<th>Children (≤16 yr)</th>
<th>Adults (≥18 yr)</th>
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<tbody>
<tr>
<td>Age, yr</td>
<td>11 ± 3</td>
<td>31 ± 12*</td>
</tr>
<tr>
<td>Range</td>
<td>6–15</td>
<td>17–53</td>
</tr>
<tr>
<td>Males</td>
<td>6 (67%)</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>20 ± 2</td>
<td>23 ± 3†</td>
</tr>
<tr>
<td>Range</td>
<td>16–22</td>
<td>17–29</td>
</tr>
<tr>
<td>Apnea hypopnea index, no./h</td>
<td>0.2 ± 0.3</td>
<td>0.7 ± 1.1</td>
</tr>
<tr>
<td>SpO₂ nadir, %</td>
<td>95 ± 1</td>
<td>95 ± 3</td>
</tr>
<tr>
<td>Peak end-tidal Pco₂, Torr</td>
<td>48 ± 3</td>
<td>45 ± 6</td>
</tr>
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Values are means ± SD unless otherwise specified; values in parentheses are percentages. BMI, body mass index; SpO₂, arterial O₂ saturation measured by pulse oximetry. *P < 0.001; †P < 0.01.

circuit was designed so that the patient could be switched from the \( P_{\text{crit}} \) to the \( P_{0.1} \) circuit by changing a connection at the mask outlet. Because some subjects aroused during this procedure, \( P_{0.1} \) measurements during sleep could not always be obtained. For \( P_{0.1} \) measurements the patient wore a nasal mask attached to a pneumotachometer and pressure transducers, as described above. No CPAP or negative pressure was applied; the circuit was exposed to atmospheric pressure only. A balloon valve (Hans Rudolph) was attached to the inspiratory limb of the circuit. A one-way valve was attached to the expiratory limb. During exhalation, the balloon valve was inflated rapidly and quietly via remote control. The mask pressure during the 1st ms of inspiration was recorded; then the valve was opened rapidly to prevent arousal. Five measurements were made for each trial, and the mean value was used.

Statistical analysis. Values are means ± SD unless otherwise specified. The correlation between factors was determined by linear regression. Differences were compared between groups by use of the unpaired \( t \)-test (continuous variables) and \( \chi^2 \) analysis (categorical variables). The difference in \( S_{PF} \) during SWS and stage 2 sleep for the same individual was compared using the paired \( t \)-test.

RESULTS

Study population. Twenty-nine subjects were recruited. Two were excluded because of abnormalities on baseline polysomnography (one had an apnea index of 8 and one had an arrhythmia), three declined the second part of the study, and four (all adults) failed to sleep adequately during the pressure-flow measurements. Therefore, 20 subjects (9 children and 11 adults) successfully completed the protocol. Subject characteristics are shown in Table 1. As expected, adults had a greater BMI than children (13). BMI was \( >25 \) kg/m² in only two subjects. Although no subject had a history of habitual snoring, mild, intermittent snoring was noted in four subjects (3 children and 1 adult) during polysomnography.

Upstream pressure-flow measurements. Typical pressure-flow curves are shown in detail for an adult (42 yr old; Fig. 1A) and a child (6 yr old; Fig. 1B), and the pressure-flow curves for all the individual subjects are shown in Fig. 2. The configuration of the pressure-flow curve was different for the children. As \( P_N \) became increasingly subatmospheric, children were able to maintain upper airway patency and had little decrease in inspiratory flow. Thus the slope of the pressure-flow curve was flat, and \( P_{\text{crit}} \) (the x-intercept) could not be determined. Therefore, \( S_{PF} \) was used to characterize upper airway function.

In contrast to the children, most adults showed a progressive decline in inspiratory flow with decreasing \( P_N \). The mean \( S_{PF} \) was 8.4 ± 4.9 and 30.0 ± 17.6 ml·s⁻¹·cmH₂O⁻¹ for children and adults, respectively (\( P < 0.002 \)). \( S_{PF} \) was <20 ml·s⁻¹·cmH₂O⁻¹ in all the children but in only three (27%) of the adults. The mean correlation coefficient for \( P_N \) vs. \( V_{\text{Imax}} \) was 0.54 ± 0.25 for the children and 0.80 ± 0.23 for the adults (\( P < 0.05 \)).

The pressure-flow measurements were obtained during SWS in 16 subjects and in stage 2 sleep in two subjects. Two other subjects changed state during the pressure-flow measurements (one from SWS to stage 2, and one from stage 2 to SWS). Nine subjects underwent repeated measurements during SWS and stage 2 sleep; there was no significant difference in \( S_{PF} \) between the two states.

\( S_{PF} \) increased significantly with age (\( r = 0.62, P < 0.01 \); Fig. 3) and BMI (\( r = 0.63, P < 0.01 \); Fig. 4). As expected, BMI correlated with age (\( r = 0.73, P < 0.01 \)).
For the children the correlation between BMI and $S_{PF}$ was 0.01 \(\text{[not significant (NS)]}\); for the adults it was 0.51 \((P < 0.05)\ NS)\). There was no significant difference in $S_{PF}$ between male and female subjects: 19.6 ± 17 and 22 ± 18 ml·s\(^{-1}\)·cmH\(_2\)O\(^{-1}\), respectively. However, the correlation between $S_{PF}$ and either age or BMI was stronger in female than in male subjects (Table 2).

$P_{0.1}$ measurements. $P_{0.1}$ measurements were obtained in 17 (85\%) of the subjects during wakefulness; technically adequate measurements were not obtained in 3 children. There was no correlation between $P_{0.1}$ during wakefulness and $S_{PF}$ \((r = 0.28, P = \text{NS})\). Most subjects aroused from sleep when the respiratory circuit was changed, and therefore $P_{0.1}$ measurements during sleep were possible in only eight subjects (6 children and 2 adults). There was a strong inverse correlation between $P_{0.1}$ during sleep and $S_{PF}$ \((r = -0.80, P < 0.02; \text{Fig. 5})\).

Table 2. Correlation coefficient for $S_{PF}$ and gender

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<thead>
<tr>
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<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td>Age vs. $S_{PF}$</td>
<td>0.55</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI vs. $S_{PF}$</td>
<td>0.51</td>
<td>0.77</td>
</tr>
<tr>
<td>$P_{0.1}$ vs. $S_{PF}$</td>
<td>-0.77*</td>
<td>-1.00†</td>
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$S_{PF}$, slope of upstream pressure-flow curve; $P_{0.1}$, occlusion pressure in 100 ms. *\(n = 5\); †\(n = 3\).

DISCUSSION

This study examined the inspiratory airflow response to changes in upper airway subatmospheric pressure across the age spectrum. We found a greater change in flow for a given change in pressure in adults. In contrast, children showed little change in flow in response to changes in upper airway pressure; i.e., children were able to maintain upper airway patency, despite increasingly subatmospheric $P_N$. Thus the $S_{PF}$ correlated with age. To determine the mechanism of the...
between upper airway (P_{crit}) becomes greater than pressure surrounding the collapsible segment of the upper airway (i.e., hypopharyngeal) from the collapsible segment, the resistance of which is pressure-flow curve. In this model of the upper airway, inspiratory pressure at the nares is atmospheric pressure swings. Under these circumstances, R_N and P_{crit} determine V_{\text{Imax}} as described by the following equation: \( V_{\text{Imax}} = (P_N - P_{crit})/R_N \). Airflow will become zero (i.e., the airway will occlude) when P_N falls below P_{crit}. Thus P_{crit} and R_N can be used to characterize the flow response to changes in P_N. This is analogous to using the slope and x-intercept of the minute ventilation-PCO_2 curve to characterize the sensitivity of the ventilatory response to hypercapnia. In the present study, we found a flattening of the S_PF in children. This precluded the determination of P_{crit}, because airway collapse did not occur even at maximal subatmospheric P_N. We therefore evaluated the S_PF, which represents the conductance of the upper airway (1/R_N). We found a lower S_PF in children than in adults. This could be due to structural or neuromuscular factors.

Because BMI increases with age (13), this increase in subatmospheric P_{crit} was so low, this could not be confirmed experimentally. Alternatively, the response could theoretically be explained by an increase in upstream resistance, because the pediatric airway is smaller than the adult airway. This is unlikely, because there was an ~100-fold difference between the S_PF and the predicted normative values for total pulmonary conductance (36). Although total pulmonary conductance is measured under different conditions (i.e., during wakefulness while the subjects breathe at atmospheric pressure), it seems improbable that technical differences could account for such a huge difference. Therefore, it is likely that dynamic changes in upper airway neuromuscular activation played an important role in the preservation of V_{\text{Imax}}.

The upper airway has pressure receptors that are sensitive to changes in inspiratory pressure. Previously, it has been shown that the application of subatmospheric pressure during wakefulness results in activation of the upper airway muscles, as demonstrated by EMG (4). However, during sleep in adults, EMG activation often does not occur, and the airway tends to collapse (4, 30). We have now shown that the application of subatmospheric pressure to the pediatric upper airway, in contrast to the adult upper airway, results in preservation of airflow, presumably secondary to upper airway neuromuscular activation.

![Fig. 6. Starling resistor model of upper airway. Upper airway is represented as a tube with a collapsible segment. Segments upstream (nasal) and downstream (hypopharyngeal) from collapsible segment have fixed diameters and resistances (R_N and R_{HP}) and pressures (P_N and P_{HP}), respectively. Collapse occurs when pressure surrounding airway (P_{crit}) becomes greater than pressure within airway.](http://jap.physiology.org/)

{10.2203.33.3 on April 20, 2017}
Neuromuscular factors are known to be important in maintaining upper airway stability. This is demonstrated most obviously by the fact that obstructive apnea occurs only during sleep. If OSAS was due purely to anatomic factors, obstruction would occur during wakefulness and sleep. Studies using denervation of airway dilating muscles or postmortem measurements have shown that, when upper airway muscle function is decreased or absent, the airway is more prone to collapse (5, 38). Thus children with abnormal upper airway neuromotor control, such as children with muscular dystrophy (18) or cerebral palsy (19), often develop OSAS. On the other hand, stimulation of the upper airway muscles decreases collapsibility (31, 32). The present study suggests that the upper airway in children responds to a subatmospheric pressure load by neuromuscular activation, thereby preventing airway collapse. This reflex appears to be more effective in children than in adults.

What causes the upper airway neuromotor activation? Many factors regulate upper airway function, including central ventilatory drive, chemoreceptor afferents, upper airway pressure and flow receptors, pulmonary mechanoreceptors, posture, and sleep state. In the present study, we used \( P_{0.1} \) as a marker for central ventilatory drive and showed an inverse correlation between \( P_{0.1} \) and \( S_{PF} \). This suggests that central drive played a role in preserving upper airway patency. However, the use of \( P_{0.1} \) as a marker for central ventilatory drive can be criticized. \( P_{0.1} \) is an index of ventilatory drive to the pump muscles and does not necessarily indicate drive to the upper airway muscles. In fact, animal studies suggest that the diaphragm and upper airway muscles may respond differently to negative pressure (24). The relevance of these animal model studies to humans is unclear, because anesthetized rabbits develop central apnea in response to subatmospheric pressure, whereas this effect was not seen in any of our study subjects. It is known that the upper airway muscles, being accessory muscles of respiration, are affected by ventilatory drive. For example, the upper airway muscles are activated by hypoxemia and hypercapnia. In addition, upper airway muscles are activated by the administration of a pressure load. Previous studies have shown increases in upper airway neuromuscular activity in response to subatmospheric pressure during wakefulness in adults that are attenuated during sleep (4). A number of studies suggest that the upper airway activation in response to pressure loading is centrally mediated. 1) The response of humans to upper airway loading during sleep is very different from the response during wakefulness (4, 14), suggesting a role for the higher central nervous system centers. 2) Functional magnetic resonance imaging studies show activation of central nervous system centers in response to upper airway loading (11). 3) The EMG responses of the upper airway muscles to hypercapnia and inspiratory loading are similar (25). These studies suggest that ventilatory drive plays a role in the upper airway response to subatmospheric pressure. This is confirmed by the present study, in which the \( P_{0.1} \) during sleep correlated inversely with the degree of inspiratory flow limitation. This finding suggests that the central ventilatory drive plays a key role in maintaining upper airway patency during sleep. In the present study, \( P_{0.1} \) was measured primarily in children; thus this finding may not apply to adults. However, other studies have shown that children have a higher ventilatory drive than adults (10, 21, 35), which is consistent with their decreased \( S_{PF} \). The fact that the \( S_{PF} \) correlated with \( P_{0.1} \) during sleep but not during wakefulness demonstrates that deficits in ventilatory drive may be sleep state specific.

A number of factors may have influenced the age-related changes in \( S_{PF} \) in addition to the ventilatory drive. We found that \( S_{PF} \) correlated with BMI, an index of obesity. Obesity is a common risk factor for OSAS, and weight loss results in a fall in \( P_{crit} \) in obese patients with obstructive apnea (29). Thus structural factors are also determinants of inspiratory airflow during sleep. This is supported by studies demonstrating a lower passive closing pressure of the upper airway in anesthetized children than in adults (15, 16). It is also possible that there is an independent, age-related effect on upper airway function. \( S_{PF} \) correlated with age and BMI. Because BMI is well known to correlate with age (13), multiple linear regression could not be performed, and the relative contribution of each factor could not be determined (1). Thus the study design did not allow us to definitively determine the mechanism for the age-related changes in upper airway function. However, the fact that \( S_{PF} \) did not correlate with BMI in the pediatric age group suggests that the role of structural factors in children is limited.

The action of sex hormones may also have influenced the age-related differences in upper airway function. In this study, age, BMI, and \( P_{0.1} \) played a greater role in determining \( S_{PF} \) in female than in male subjects, suggesting that additional, unstudied factors play a role in men. One such factor may be testosterone-induced changes in the morphology of the male upper airway. In adults, OSAS is twice as common in men as in women (39); the administration of exogenous testosterone may result in OSAS (28) and increase the airway closing pressure (6), and obstructive apnea may recur in adolescent males who were successfully treated during childhood (12). All these factors suggest a role for testosterone in promoting upper airway collapse. This effect would be absent or diminished in prepubertal/pubertal males.

Limitation of methods. We recognize that additional factors could potentially play a role in determining age-related differences in upper airway pressure responses, including developmental changes in upper airway morphology and chest wall mechanics. \( P_{0.1} \) measurements can be affected by a number of factors, including age-related changes in chest wall compliance and the time constant (37). However, it would not be expected that these mechanical factors would differ significantly between school-aged subjects and adults.

Clinical relevance. In contrast to adults, normal children snore infrequently and rarely have obstructive...
apneas during sleep (23). This is consistent with the better preservation of upper airway patency in response to subatmospheric pressure noted in the present study. Whereas adults with OSAS tend to have repetitive obstructive apneas, children with OSAS frequently manifest a pattern of persistent, partial upper airway, rather than discrete, apneas (3). Thus the pattern of upper airway muscle recruitment in children with OSAS (17) may be different from that in adults; in children, upper airway muscle activation may be greater, thereby preventing total airway occlusion.

We found that $P_{\text{T}}$ was affected by ventilatory drive and BMI. This correlates with clinical findings: clinically, subtle changes in ventilatory control have been noted in patients with OSAS, and OSAS is related to obesity in children (20) and adults.

Conclusion. In conclusion, this study has shown that the upper airway response to subatmospheric pressure loads in normal, healthy subjects is modulated by age, ventilatory drive during sleep, and body size. Further studies are needed to delineate the role played by each factor.

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