

# Polysomnographic Values In Children Undergoing Puberty: Pediatric Vs. Adult Respiratory Rules in Adolescents

Ignacio E. Tapia, MD<sup>1</sup>; Laurie Karamessinis, CCRC<sup>1</sup>; Preetam Bandla, MD<sup>1</sup>; Jingtao Huang, PhD<sup>1</sup>; Andrea Kelly, MD<sup>2</sup>; Michelle Pepe, RPSGT<sup>1</sup>; Brian Schultz, RPSGT<sup>1</sup>; Paul Gallagher, MA<sup>3</sup>; Lee J. Brooks, MD<sup>1</sup>; Carole L. Marcus, MBBCh<sup>1</sup>

<sup>1</sup>Sleep Center; <sup>2</sup>Division of Endocrinology, and <sup>3</sup>Division of Biostatistics and Epidemiology, The Children's Hospital of Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, PA

**Study Objectives:** Polysomnographic respiratory events in children should be scored using pediatric respiratory rules. However, due to a lack of data on adolescents, recently revised rules allow children aged 13–18 years to be scored by adult or pediatric criteria. To clarify which criteria to use, we describe the evolution of respiratory events with Tanner stage, and we compare events in children aged 13–18 years with the new American Academy of Sleep Medicine adult and pediatric respiratory rules.

**Design:** Cross-sectional

**Setting:** Academic hospital

**Participants:** Healthy subjects aged 8–18 years recruited for research purposes

**Interventions:** Physical examination to determine Tanner stage, overnight polysomnogram, and determination of sex hormones.

**Results:** Sixty-eight subjects (Tanner 1–5) were studied, mean age [SD] = 13 ± 3 years, median apnea hypopnea index (AHI) = 0.1 (range: 0–1.2)/h. The median percentages of total sleep time (TST) with SpO<sub>2</sub>

< 92% were 0.1 (0–4.2)%, and with end-tidal CO<sub>2</sub> > 50 torr was 0.1 (0–88.6)%. Thirty-two subjects were aged 13–18 years, (Tanner 3–5). The difference between AHI scored by pediatric (median = 0 [0–0.9]/h) and adult (median = 0 [0–0.5]/h) criteria was statistically significant (P = 0.043), but not clinically relevant.

**Conclusions:** Respiratory events in normal children aged 8–18 years are rare and unrelated to Tanner stage. Adult or pediatric respiratory rules can be used for scoring polysomnograms in asymptomatic subjects approaching adulthood. Further studies are needed in symptomatic children within this age group.

**Keywords:** Adolescents, apnea, hypopnea

**Citation:** Tapia IE; Karamessinis L; Bandla P; Huang J; Kelly A; Pepe M; Schultz B; Gallagher P; Brooks LJ; Marcus CL. Polysomnographic values in children undergoing puberty: pediatric vs. adult respiratory rules in adolescents. *SLEEP* 2008;31(12):1737-1744.

POLYSOMNOGRAPHY IS THE GOLD STANDARD FOR THE ASSESSMENT OF CHILDREN WITH SUSPECTED SLEEP DISORDERED BREATHING.<sup>1-3</sup> BECAUSE OF well-recognized differences in epidemiology<sup>4</sup> and pathophysiology<sup>5-9</sup> of sleep disordered breathing in children and adults, respiratory events in children should be scored using pediatric respiratory criteria.<sup>10</sup> However, there is little information as to which respiratory rules should be used for scoring polysomnograms in adolescents between 13 and 18 years of age. Even the recently published “American Academy of Sleep Medicine manual for the scoring of sleep and associated events” states that there is no consensus for this age group.<sup>3</sup>

Adolescence is a dynamic transition process from childhood to adulthood. It is characterized by simultaneous but asynchronous development that starts with puberty, the onset of which is variable,<sup>11-14</sup> and ends with adulthood.<sup>15</sup> Therefore, it is reasonable to infer that respiratory polysomnographic scoring criteria and normal reference values would transition from pediatric to adult during adolescence.

We present this cross-sectional study primarily aimed at examining the evolution of respiratory events with Tanner stage in a population of 68 children aged 8–18 years, recruited as part of a research study directed at investigating the effects of pu-

berty on upper airway dynamics during sleep.<sup>16</sup> Because of the lack of data regarding which respiratory rules to use in children aged 13–18 years, we further analyzed a subset of 32 subjects within this age group to identify a possible rationale for the use of pediatric or adult scoring criteria in children approaching adulthood. We rescored the respiratory events of these subjects according to the new American Academy of Sleep Medicine guidelines for children and adults.

## MATERIALS AND METHODS

### Subjects

Subjects were selected from a population of asymptomatic, healthy children recruited by means of advertisement to investigate the effects of puberty on upper airway dynamics during sleep at The Children's Hospital of Philadelphia during a 2-year period (2004–2006).<sup>16</sup> Healthy, non-snoring males between 9 and 18 years old and females between 8 and 18 were included. The age criteria were designed to recruit adolescents with Tanner stages 1–5.<sup>11-13,15</sup> Exclusion criteria included significant medical conditions, significant medications, history of upper airway surgery, family history of obstructive sleep apnea syndrome, and a body mass index > 95th percentile. The Institutional Review Board of The Children's Hospital of Philadelphia approved the study. Informed consent was obtained from 18-year-old subjects and the parents guardians of subjects younger than 18, as well as assent from those subjects younger than 18 years.

All subjects underwent a physical examination to determine Tanner stage, followed by a polysomnogram. Tanner stage was

Submitted for publication February, 2008

Accepted for publication July, 2008

Address correspondence to: Carole L. Marcus, MBBCh, The Children's Hospital of Philadelphia, Pulmonary Division, 5th floor Wood, 34th & Civic Center Blvd, Philadelphia, PA 19104; Tel: (267) 426-5842; Fax: (215) 590-3500; E-mail: marcus@email.chop.edu

corroborated with serum hormone levels, which were obtained first thing in the morning following the polysomnogram, to minimize circadian variability. Ultra-sensitive luteinizing hormone was obtained in all subjects, follicular stimulating hormone and estradiol in females, and testosterone in males.

### Polysomnogram

Subjects were studied in the sleep laboratory at The Children’s Hospital of Philadelphia as previously described.<sup>17</sup> Polysomnography data were digitally recorded using Somnostar Alpha (SensorMedics, Yorba Linda, CA) or Rembrandt (Medcare, Buffalo, NY). The electroencephalogram was recorded using 4 scalp electrodes (C3/A2, C4/A1, O1/A2, and O2/A1), and the right and left electrooculograms were recorded via 2 electrodes at the lateral canthi. Muscle tone of the chin was measured by submental electromyography. Oxyhemoglobin saturation (SpO<sub>2</sub>) was measured by pulse oximetry (Masimo Rad-9, Irvine, CA), set at 2-sec averaging. Nasal pressure was measured by cannula (Pro-Tech, Mukilteo, WA). As a back-up, oronasal airflow was measured by an oronasal thermistor (Pro-Tech, Mukilteo, WA). End-tidal CO<sub>2</sub> was measured by sidestream sample (Novamatrix Medical Systems, Wallingford, CT). Movements of the chest and abdomen were measured by respiratory inductive plethysmography (SensorMedics, Yorba Linda, CA). The electrocardiograph was recorded by a modified lead I. Leg movements were recorded by electromyographic leads placed over the anterior tibialis muscles of both legs.

Sleep architecture, arousals from sleep, respiratory variables, and periodic limb movements were determined using the American Academy of Sleep Medicine new criteria.<sup>3</sup> In brief, arousals were defined as an abrupt shift in EEG frequency  $\geq 3$  sec duration, preceded by a period  $\geq 10$  sec of stable sleep. During REM sleep, a concurrent increase in submental electromyography  $\geq 1$  second was required. The arousal index represented the number of arousals per hour of sleep. Respiratory events were scored with pediatric respiratory rules. For each type of respiratory event (central apnea, obstructive apnea, mixed apnea, hypopnea, and respiratory effort related arousal), an index that represented the number of events per hour of sleep was calculated. Respiratory effort related arousals were scored using a nasal pressure sensor, as recommended by *The AASM Manual for the Scoring of Sleep and Associated Events*.<sup>3</sup> The apnea/hypopnea index (AHI) included the sum of all obstructive and mixed apneas, hypopneas, and respiratory effort related arousals divided by total sleep time (TST). The total duration of time with SpO<sub>2</sub> below 92% was expressed as a percentage of TST. The total duration of time with end-tidal CO<sub>2</sub> > 50 torr was expressed as a percentage of TST. We excluded SpO<sub>2</sub> and end-tidal CO<sub>2</sub> measurements associated with poor waveforms or artifacts. The periodic limb movement index was the number of periodic limb movements per hour of sleep.

In addition, all the respiratory events of subjects with ages between 13 and 18 years old were rescored by one of the authors (I.T.) using the new respiratory rules for adults of *The AASM Manual for the Scoring of Sleep and Associated Events*,<sup>3</sup> and results were compared. The main difference between the apnea scoring criteria is the duration of the event. Specifically, an event must last  $\geq 10$  sec to be scored as an apnea using adult

**Table 1**—Racial Distribution by Tanner Stage

	Tanner Stage					Total
	1	2	3	4	5	
African American (N)	5	6	3	9	9	32
Caucasian (N)	6	1	3	7	7	24
Asian (N)	2	2	0	3	0	7
Mixed (N)	2	1	1	0	1	5
Total	15	10	7	19	17	68

rules. The respiratory rules for children mandate that an event must last  $\geq 2$  missed breaths to meet the apnea criteria, regardless of its duration in seconds. The adult rules give 2 options for scoring hypopneas; both require the duration of the event to be  $\geq 10$  sec. The recommended option establishes that at least a 30% drop in nasal pressure and at least 4% in oxyhemoglobin saturation from baseline are necessary to meet the hypopnea criteria. The alternative is identical to pediatric criteria, except for the duration of the event. The pediatric rules dictate that a  $\geq 50\%$  drop in nasal pressure and a  $\geq 3\%$  in oxyhemoglobin saturation from baseline or an associated arousal are needed to score an event as a hypopnea. We used both adult hypopnea rules.

### Data Analysis

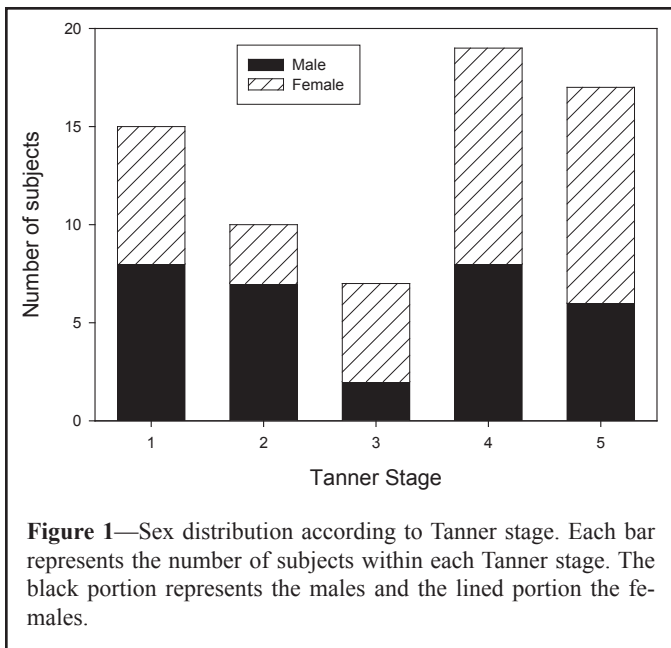
The statistical analysis was performed with SigmaStat 3.0 (Systat Software Inc., San Jose, CA). The distribution of continuous data was tested with the Kolmogorov-Smirnov test. The data that passed this normality test are presented as mean  $\pm$  standard deviation (SD). The data that failed this normality test are presented as median and range. Differences in AHI, central apnea index, hypopnea index, and obstructive apnea index between pediatric and adult respiratory scoring rules were examined using the paired signed rank test. One-way ANOVA was used to compare  $\geq 3$  groups with a normal distribution (i.e., arousal index distribution according to Tanner stages). A post hoc analysis, when appropriate, was performed with the Bonferroni *t*-test. The Kruskal-Wallis One-way ANOVA Ranks test was utilized to compare  $\geq 3$  groups without a normal distribution (i.e., AHI distribution according to Tanner stages). A post hoc analysis, when appropriate, was performed with the Dunn’s test. Associations between 2 variables were examined using Pearson or Spearman correlation coefficients, depending on normalcy of distribution of the data. A P value < 0.05 was required for significance.

## RESULTS

### All subjects

#### Study Group Characteristics

Sixty-eight subjects (37 female, 54%) were recruited. The mean age of the group was  $13.2 \pm 2.8$  years, with a range between 8.1 and 18.7 years. The racial distribution, by Tanner stage, is shown in Table 1. Most subjects were African American or Caucasian. Three of the Caucasian subjects (of Tanner stages 1, 4, 5) were of Hispanic ethnicity. Tanner staging was consistent



with hormone levels in 97% of subjects (the remaining 3% were assigned using clinical Tanner staging). The sex distribution according to Tanner stage is shown in Figure 1. As expected, older subjects had more advanced Tanner stages (Table 2).

### Sleep Architecture

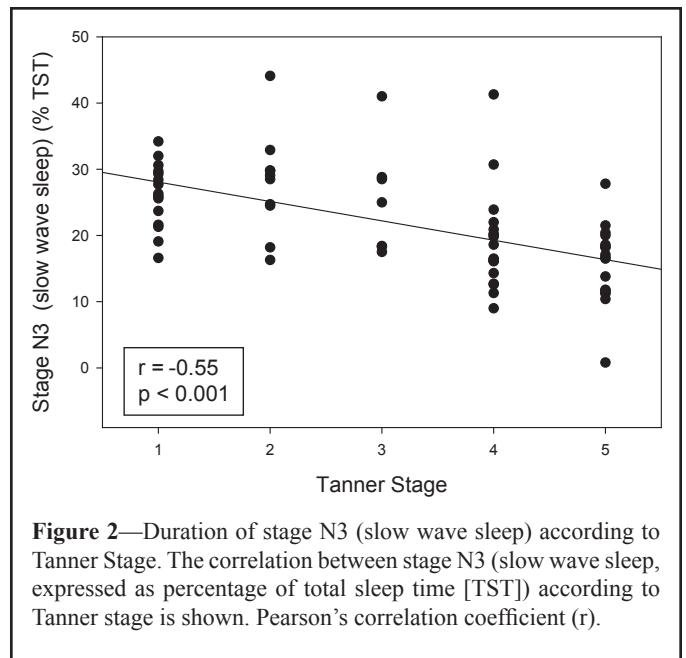
Sleep architecture according to Tanner stage is shown in Tables 2 a and b. Adolescents of Tanner stages 4-5 had less percentage of stage N3 (slow wave sleep) than subjects with Tanner stages 1-2 (Figure 2). Conversely, subjects of Tanner stages 4-5 had a greater percentage of stage N2 sleep than subjects of Tanner stages 1-2. There were no differences in regards to sleep efficiency, sleep latency, REM latency, arousal index, or percentage of stage R (REM) among Tanner stages.

### Respiratory Events

Respiratory events according to Tanner stage are presented in Table 3. Central apneas were rare across the Tanner stages. The central apnea index for all the groups ranged between 0–1.5/hour. Only 1 subject had a mixed apnea. Obstructive events were scarce, and did not differ between Tanner stages. The median apnea/hypopnea index for the entire study group was 0.1/hour. Respiratory effort related arousals were determined in the 66 of 68 subjects who had accurate nasal pressure measurements throughout the night. Only 1 subject (a 10-year-old male, Tanner stage 2) had 1 respiratory effort related arousal.

The respiratory rate during sleep stage N1, N2, N3, and R is shown in Table 3. The respiratory rate during NREM and REM sleep did not change with Tanner stage. The mean respiratory rate for the entire group was  $16.5 \pm 2.1$  breaths/min during NREM sleep, and  $16.9 \pm 2.3$  breaths/min during REM sleep.

Sixty-four of 68 subjects had accurate end-tidal CO<sub>2</sub> measurements during the study. The median percentage of total sleep time > 50 torr and peak end-tidal CO<sub>2</sub> for the entire group was 0.1% and 49 torr, respectively. Five outliers had end-tidal CO<sub>2</sub> > 50 torr more than 25% of the total sleep time; their per-



centage of total sleep time > 50 torr ranged between 39% and 88.6% with peak end-tidal CO<sub>2</sub> between 52 and 59 torr.

The median percentage of total sleep time < 92% for the entire group was 0.1%, and the median nadir SpO<sub>2</sub> was 93%.

There were no significant gas exchange differences among Tanner stages.

### Periodic Limb Movements

Periodic limb movements during sleep were infrequent. Only 22 subjects had periodic limb movements, and of those, only 2 (a 14-year-old female [Tanner stage 4] and a 10-year-old male [Tanner stage 1]) had a periodic limb movement index > 5/h. The periodic limb movement index for the group ranged between 0 and 13.1/h. The median periodic limb movement index was 0/hour. There was a statistically significant difference between Tanner stages in regard to the periodic limb movement index. However, after adjusting the P value to account for the multiple pairwise comparisons, none of the pairwise tests were statistically significant.

### 13–18 Year Old Subset

#### Respiratory Events

We further analyzed the respiratory events of the subjects between 13–18 years old ( $N = 32$ ; Tanner stages 3–5, mean age  $15.8 \pm 1.4$  years). The results are shown in Table 5. Sixteen subjects had central apneas, with a median duration of 12.2 (5.7–21) sec; the median central apnea index was 0.06 (0–0.6)/h. Since all of our subjects were normal and asymptomatic, only 15 of them had obstructive events. All 15 subjects had hypopneas, with a median duration of 15.5 (6–24.8) sec. Two subjects also had obstructive apneas, with a mean duration of 13.7 sec. The median apnea hypopnea index was 0 (0–0.9)/h. Of 32 subjects, 31 had accurate nasal pressure measurements; no subject in this age group had respiratory effort related arousals.

**Table 2a**—Sleep Architecture and Periodic Limb Movements During Sleep (PLMS) According to Tanner stage. Data with Normal Distribution. Values are Displayed as mean  $\pm$  SD.

	Tanner Stage					P value
	1	2	3	4	5	
Number of patients	15	10	7	19	17	
Age (years)	10.1 $\pm$ 0.9	10.9 $\pm$ 0.9	12.3 $\pm$ 1.3	14.7 $\pm$ 1.8	16.1 $\pm$ 1.8	<0.001
Arousal index (N/hour)	11.5 $\pm$ 4.4	9.4 $\pm$ 3.4	10.4 $\pm$ 3.2	9.5 $\pm$ 3.4	10.6 $\pm$ 4.0	0.532
Stage N1 (% TST)	6.8 $\pm$ 3.7	4.5 $\pm$ 2.3	5.3 $\pm$ 2.9	6.7 $\pm$ 4.0	6.9 $\pm$ 5.6	0.545
Stage N2 (% TST)	48.2 $\pm$ 4.2	49.7 $\pm$ 7.3	52.3 $\pm$ 8.6	56.6 $\pm$ 7.2	59.7 $\pm$ 7.9	<0.001
Stage N3 (% TST)	26.1 $\pm$ 4.9	27.8 $\pm$ 7.8	25.4 $\pm$ 8.4	18.9 $\pm$ 7.3	15.7 $\pm$ 6.0	<0.001
Stage R (% TST)	18.9 $\pm$ 4.4	17.4 $\pm$ 5.0	17.0 $\pm$ 6.4	17.7 $\pm$ 4.5	17.8 $\pm$ 5.7	0.922

TST, total sleep time. Stage N3 (slow wave sleep) decreased with increased Tanner stage. Consequently, stage N2 increased with Tanner stage. Since older subjects were in more advanced Tanner stages, this represents the well recognized reduction of stage N3 with age.

**Table 2b**—Sleep Architecture and Periodic Limb Movements During Sleep (PLMS) According to Tanner Stage. Data Without Normal Distribution. Values are Displayed as Median (Range).

	Tanner Stage					P value
	1	2	3	4	5	
Number of patients	15	10	7	19	17	
Sleep efficiency (%)	85.0 (71–94)	86.0 (74–95)	87.0 (66–92)	89.0 (43–97)	89.0 (56–98)	0.719
Sleep latency (minutes)	19.0 (0–42)	22.5 (3.5–76)	14.0 (5.0–33.5)	14.5 (1.0–83.5)	16.5 (2.5–72.0)	0.862
REM latency (minutes)	154.5 (60.5–267.0)	102.0 (53–325)	194.5 (133.5–329)	136.5 (69.0–392.0)	116.5 (44.5–287.0)	0.106
PLM index (N/hour)	0.0 (0.0–7.2)	0.0 (0.0–0.9)	0.6 (0.0–2.4)	0.2 (0.0–13.1)	0.0 (0.0–4.1)	0.025

REM, rapid eye movement; PLM, periodic limb movements. No significant differences were observed between the different Tanner stages in regards to sleep efficiency, sleep latency, and REM latency. There was a statistically significant difference between the groups in regards to the PLM index. However, after adjusting the P value to account for the multiple pairwise comparisons none of the pairwise tests were statistically significant.

**Table 3**—Respiratory Rate During Sleep Stage N1, N2, N3, and REM, According to Tanner Stage.

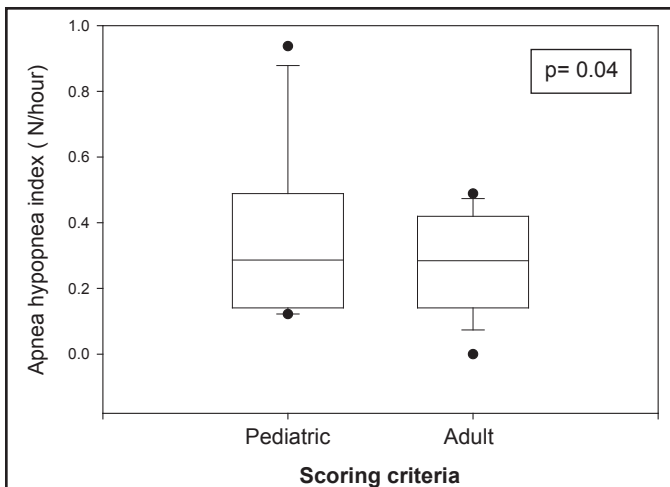
Respiratory Rate (breaths/min)	Tanner Stage					P value
	1	2	3	4	5	
Stage N1	17.7 $\pm$ 2.3	17.2 $\pm$ 1.9	16.7 $\pm$ 2.1	18.0 $\pm$ 3.1	16.5 $\pm$ 2	0.38
Stage N2	16.0 $\pm$ 1.9	17.1 $\pm$ 1.8	16.1 $\pm$ 1.8	16.3 $\pm$ 2.8	15.5 $\pm$ 1.9	0.43
Stage N3	16.6 $\pm$ 1.9	17.7 $\pm$ 1.8	16.7 $\pm$ 2.3	17.1 $\pm$ 2.7	16.6 $\pm$ 2.3	0.75
Stage R	16.3 $\pm$ 1.4	17.9 $\pm$ 1.7	15.9 $\pm$ 2.3	17.5 $\pm$ 3.1	16.6 $\pm$ 2.1	0.24

Values are displayed as mean  $\pm$  SD. There were no significant differences in respiratory rate between the different Tanner stages.

After rescored the events with the new adult rules,<sup>3</sup> there was no significant difference in the median central apnea index with pediatric (0.05, range: 0–0.6/h) and adult (0, range: 0–0.4/h) criteria ( $P = 0.13$ ). However, the difference between AHI index values as scored by pediatric and adult respiratory rules did attain statistical significance ( $P = 0.04$ , Figure 3), which was caused by a decrease in the distribution range from 0.1–0.9/h with pediatric rules to 0–0.5/h with adult rules, since short hypopneas did not meet the adult criteria. The median AHI however, did not change (pediatric criteria = 0, adult criteria = 0). This observed difference (mean difference = 0.048, SD = 0.14, 95% confidence interval = –0.001 to 0.098) is so

small that it would not be of clinical relevance. We did not find differences between the 2 adult hypopnea rules. Specifically, 15 subjects had 36 hypopneas with pediatric rules, but only 23 hypopneas lasted  $\geq 10$  sec. Those 23 hypopneas were characterized by drops in nasal pressure  $\geq 50\%$  and  $\geq 4\%$  desaturation from pre-event baseline. Therefore, the described events met the 2 adult hypopnea rules. In addition, 15 hypopneas were associated with arousal.

Twenty-nine of 32 subjects had accurate end-tidal CO<sub>2</sub> measurements. The 3 outliers with high CO<sub>2</sub> levels from this subset were described in the previous section. Gas exchange data are shown in Table 3. Since the percentages of total sleep time



**Figure 3**—Apnea hypopnea index in subset of subjects aged 13–18 years scored by pediatric and adult criteria. Apnea hypopnea index results using pediatric and adult respiratory scoring criteria. The boundaries of the boxes represent the 25th and 75th percentiles. The line within the boxes marks the medians. The whiskers indicate the 10th and 90th percentiles, and the points represent the range. The apnea hypopnea index obtained with adult respiratory rules was significantly lower than with pediatric respiratory rules. However, the observed difference (mean difference = 0.048, SD = 0.14, 95% confidence interval = –0.001 to 0.098) is so small, that it would not be of clinical relevance.

with end-tidal  $\text{CO}_2 > 50$  torr and  $\text{SpO}_2 < 92\%$  failed the normality test, the cut-off values were calculated at the 95th percentile (Table 4).

## DISCUSSION

The American Academy of Sleep Medicine published *The AASM Manual for the Scoring of Sleep and Associated Events*<sup>3</sup> in 2007 to encourage standardized polysomnogram scoring based on the medical literature. Since there was no study comparing adult and pediatric criteria in adolescents,<sup>3</sup> the recent rules allow children aged 13–18 years to be scored with either pediatric or adult criteria, based on empiric observations.

This is the first study analyzing the polysomnographic respiratory parameters of healthy non-obese asymptomatic adolescents between 13 and 18 years old, comparing the new pediatric and adult scoring criteria. We have shown no clinically significant apnea hypopnea index differences using either set of criteria in normal, asymptomatic subjects. We have also confirmed that healthy, asymptomatic, non-obese children and adolescents between 8 and 18 years rarely have obstructive events (including respiratory effort related arousals) during sleep. This result is independent of the Tanner stage. Additionally, this study has also corroborated that slow wave sleep (stage N3) decreases during puberty.<sup>18,19</sup>

Adolescents have been underrepresented in the sleep literature.<sup>3</sup> They have been analyzed either with younger children<sup>20,21</sup> or with young adults,<sup>22</sup> but rarely as a solo group. Acebo et al. described sleep architecture, respiratory variables and cephalometrics in healthy boys and girls aged 9.7–16.8 years along with young adults.<sup>22</sup> The subjects were characterized by Tanner stage, but the results were analyzed according to age. Uliel et al.

reported 70 healthy children and adolescents between 1 and 15 years,<sup>21</sup> and Verhulst reported 60 subjects between 6–16 years.<sup>20</sup> However, Tanner staging was not included in their methods. Therefore, the main difference between our study and previous publications describing normal populations<sup>20–23</sup> is that we focused our analysis on the changes in respiratory parameters with Tanner stage to clarify whether there was a rationale for the use of pediatric or adult scoring criteria in children approaching adulthood. In addition, we included data on respiratory rate during sleep, respiratory effort related arousals, and periodic limb movements, and used the recommended nasal pressure signal rather than thermistor flow as the primary signal for determining respiratory events.

## Sleep Architecture

We found that slow wave sleep stage decreased significantly with Tanner stage, with a concomitant increase in stage N2. Since our older subjects were at a more advanced puberty stage, the result is concordant with previous studies<sup>18,24</sup> showing that stage N2 increases and stage N3 (slow wave sleep) decreases with age. Feinberg et al.<sup>25</sup> have demonstrated in a longitudinal study that slow wave sleep decline starts at age 12 years, and is independent of Tanner stage.

Our results on sleep latency and sleep efficiency are similar to other publications.<sup>22,24,26</sup> We did not find stage R (REM sleep) differences with Tanner stage, which is also concordant with other publications.<sup>19,27</sup>

## Arousal Index

The arousal index increases linearly from childhood to old age<sup>28</sup> but remains unchanged during adolescence.<sup>29</sup> Similarly, we did not find differences in the arousal index across the different puberty stages.

## Respiratory Parameters According to Tanner Stage

We add to the field further data that normal adolescents have infrequent respiratory events, and no gas exchange abnormality. Our results are concordant with the published data in younger children<sup>30–32</sup> and provide evidence that biological maturation expressed by Tanner staging is not associated with respiratory events. As previously reported,<sup>20</sup> hypopneas were the most frequent obstructive event observed.

In addition, this is the first study, to our knowledge, reporting respiratory rates during sleep in association with Tanner stage. Carskadon et al. previously studied 22 children aged 9–13 years, but without Tanner staging, and found similar mean respiratory rate values.<sup>33</sup> The respiratory rate during sleep is the cause of the main difference in scoring criteria between children and adults.<sup>3</sup> Since children have faster respiratory rates than adults and a lower functional residual capacity that could lead to rapid desaturation with short respiratory events, the AASM pediatric committee considered that the 10-second rule would overlook many respiratory events in children. We expected older and more biologically mature children to have a respiratory rate during sleep close to 12 breaths/minute, since with that rate the 10-second adult apnea scoring rule would be appropriate (2

**Table 4**—Respiratory Events According to Tanner Stage. Values are Displayed as Median (Range)

	Tanner Stage				
	1	2	3	4	5
Apnea hypopnea index (N/h)	0.1 (0.0–0.9)	0.0 (0.0–0.5)	0.1 (0.0–0.5)	0.1 (0.0–1.2)	0.0 (0.0–0.7)
Obstructive apnea index (N/h)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.3)	0.0 (0.0–0.3)	0.0 (0.0–0.5)
Hypopnea index (N/h)	0.1 (0.0–0.9)	0.0 (0.0–0.5)	0.0 (0.0–0.4)	0.1 (0.0–1.0)	0.0 (0.0–0.3)
Central apnea index (N/h)	0.1 (0.0–1.3)	0.0 (0.0–1.5)	0.1 (0.0–1.3)	0.0 (0.0–0.4)	0.1 (0.0–0.6)
% TST with end-tidal CO <sub>2</sub> >50 torr	0.1 (0.0–88.6)	0.5 (0.0–79.0)	0.0 (0.0–0.2)	0.4 (0.0–59.4)	0.0 (0.0–64.6)
Peak end-tidal CO <sub>2</sub> (torr)	50.0 (47–59)	51.5 (43–59)	47.0 (45–55)	50.0 (51–59)	48.5 (45–53)
% TST with SpO <sub>2</sub> <92%	0.4 (0.0–2.3)	0.4 (0.0–4.2)	0.0 (0.0–1.0)	0.0 (0.0–1.5)	0.0 (0.0–1.0)
Nadir SpO <sub>2</sub>	93.0 (90–97)	93.5 (88–98)	93.0 (89–96)	94.0 (88–96)	93.0 (89–97)

TST, total sleep time; SpO<sub>2</sub>, oxyhemoglobin saturation. No significant differences in respiratory events between the different Tanner stages were observed.

**Table 5**—Respiratory Events with Pediatric Criteria in the Subset of Subjects Aged 13–18 Years (32 Patients)

	Median	Range	Limit of normality
Age (years)	15.8	13.3–18.7	
Apnea hypopnea index (N/h)	0.0	0.0–0.9	0.8
Obstructive apnea index (N/h)	0.0	0.0–0.5	0.1
Hypopnea index (N/h)	0.0	0.0–0.9	0.8
Central apnea index (N/h)	0.06	0.0–0.6	0.4
% TST with end-tidal CO <sub>2</sub> >50 torr	0.2	0.0–64.6	24.0
Peak end-tidal CO <sub>2</sub> (torr)	50.0	45.0–54.0	53.0
% TST with SpO <sub>2</sub> <92%	0.0	0.0–1.5	1.0
SpO <sub>2</sub> Nadir (mm Hg)	93.0	88.0–97.0	89.0

TST, total sleep time; SpO<sub>2</sub>, oxyhemoglobin saturation. The limit of normality was calculated as the 95th percentile for all the parameters, except for SpO<sub>2</sub> nadir that was calculated as the 5th percentile.

missed breaths = 10 seconds). However, we found that the respiratory rate did not change significantly with biological maturation during adolescence. Few studies have analyzed age-related changes in respiratory rate during sleep in adults.<sup>34–36</sup> Shore et al studied 12 healthy young adult subjects (19–29 years) and 12 elderly (> 65 years) subjects during sleep, and found that the elderly had a significantly lower respiratory rate during wakefulness (13.1 breaths/min) and sleep stages N1 and N2 (12.4 breaths/min) compared to the younger group (16.4 and 14.9 breaths/min respectively).<sup>35</sup> However, the results from the younger adults were similar to the adolescents reported in the current study. Data from middle-aged adults reported in the literature<sup>34,36</sup> and summarized by Krieger,<sup>37</sup> also suggest that adults have a respiratory rate during sleep (mean respiratory rate of 15 breaths/min) that is similar to that of the adolescents

in the current study. Thus, in these adults, an apnea that is 2 missed breaths in duration would last for 8 seconds.

Our SpO<sub>2</sub> results are in agreement with Gries and Brooks,<sup>38</sup> Verhulst,<sup>20</sup> Poets,<sup>30</sup> and Marcus.<sup>23</sup> Virtually all our subjects had SpO<sub>2</sub> > 92% throughout the night.

Similar to Uliel,<sup>21</sup> the majority of the subjects did not have any period of total sleep time with end-tidal CO<sub>2</sub> > 50 torr. This result is also in agreement with previous data in younger children,<sup>31,32</sup> and our previous data measuring end-tidal CO<sub>2</sub> with mass spectrometry.<sup>23</sup> This observation did not change with Tanner stage. However, the 95th percentile for total sleep time with end-tidal CO<sub>2</sub> > 50 torr was 24%. Therefore, we recommend that patients with values above this cut-off point should be assessed to rule out clinical hypoventilation. The outliers in this study spent most of the night with end-tidal CO<sub>2</sub> in the low 50s.

### Respiratory Parameters in Subjects 13–18 Years Old

We did not find significant differences in the central apnea index after rescoring the respiratory events with pediatric and adult respiratory rules. The statistically significant difference observed in the AHI after scoring with adult respiratory rules was due to a decrease in the number of hypopneas since short hypopneas did not meet adult criteria. Despite attaining statistical significance, this difference is so small that it would not be of clinical relevance. However, the results in adolescents with the obstructive sleep apnea syndrome may be very different. Further studies are warranted.

### Limitations

Study limitations include a relatively small number of subjects per Tanner stage, but larger than most other normative studies.<sup>20,22,23</sup> Our research was based on normal children, who we know rarely have respiratory events.<sup>21–23,39</sup> The subjects were mostly African American or Caucasian, with only a few Asians

and Hispanics. Thus, these data may not be applicable to other racial ethnic groups. The results are also limited by our cross-sectional study design. Future longitudinal studies are desirable.

## CONCLUSIONS

This study has confirmed that apneas and hypopneas in normal adolescents are rare. We add to the field evidence that respiratory effort related arousals are virtually non-existent in normal subjects, that the respiratory rate and the frequency of respiratory events does not change with Tanner stage, which is a marker of biological maturation, in normal subjects.

Since we did not find a rationale for the scoring of respiratory events with pediatric or adult criteria in children, we recommend using either rule for scoring respiratory events in polysomnograms of normal adolescents between 13 and 18 years old recruited for research purposes. However, further studies are needed in patients with respiratory conditions, such as the obstructive sleep apnea syndrome, within this age group.

In addition, we suggest that adult apnea duration criteria should be reconsidered, based on the fact that the respiratory rate during sleep in adults is similar to that of adolescents. We suggest that 2 missed breaths, regardless of the duration in seconds, may be a more accurate criterion to score respiratory events at any age.

## ABBREVIATIONS

AHI	Apnea hypopnea index
SpO <sub>2</sub>	Oxyhemoglobin saturation
TST	Total sleep time
REM	Rapid eye movement

## ACKNOWLEDGMENTS

The authors thank the children participating in this study and their families, the sleep laboratory technicians, and Mary Tate, the sleep laboratory scheduler, for their valuable help. This research was supported by the National Institutes of Health R01 HL 58585, MO1-RR-000240 and UL1 RR 024134.

## DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Marcus has received research support and the use of equipment from Respiromics. The other authors have indicated no financial conflicts of interest.

## REFERENCES

1. Marcus CL. Sleep-disordered breathing in children. *Am J Respir Crit Care Med* 2001;164:16-30.
2. Redline S, Budhiraja R, Kapur V, et al. The scoring of respiratory events in sleep: reliability and validity. *J Clin Sleep Med* 2007;3:169-200.
3. Iber C, Ancoli-Israel S, Chesson Jr AL, Quan SF. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester, IL: American Academy of Sleep Medicine, 2007.
4. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associa-

- tions with obesity, race, and respiratory problems. *Am J Respir Crit Care Med* 1999;159(5 Pt 1):1527-32.
5. Arens R, Marcus CL. Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* 2004;27:997-1019.
6. Carroll JL. Obstructive sleep-disordered breathing in children: new controversies, new directions. *Clin Chest Med* 2003;24:261-82.
7. Marcus CL. Obstructive sleep apnea syndrome: differences between children and adults. *Sleep* 2000;23 Suppl 4:S140-1.
8. Marcus CL. Pathophysiology of childhood obstructive sleep apnea: current concepts. *Respir Physiol* 2000;119:143-54.
9. Bandla P, Brooks LJ, Trimarchi T, Helfaer M. Obstructive sleep apnea syndrome in children. *Anesthesiol Clin North America* 2005;23:535-49.
10. Rosen CL, D'Andrea L, Haddad GG. Adult criteria for obstructive sleep apnea do not identify children with serious obstruction. [see comment]. *Am Rev Respir Dis* 1992;146(5 Pt 1):1231-4.
11. Herman-Giddens ME, Kaplowitz PB, Wasserman R. Navigating the recent articles on girls' puberty in Pediatrics: what do we know and where do we go from here?[see comment]. *Pediatrics* 2004;113:911-7.
12. Herman-Giddens ME, Slora EJ, Wasserman RC, et al. Secondary sexual characteristics and menses in young girls seen in office practice: a study from the Pediatric Research in Office Settings network.[see comment]. *Pediatrics* 1997;99:505-12.
13. Herman-Giddens ME, Wang L, Koch G. Secondary sexual characteristics in boys: estimates from the national health and nutrition examination survey III, 1988-1994.[see comment]. *Arch Pediatr Adolesc Med* 2001;155:1022-8.
14. Coleman L, Coleman J. The measurement of puberty: a review. *J Adolesc* 2002;25:535-50.
15. Rosen DS. Physiologic growth and development during adolescence. *Pediatr Rev* 2004;25:194-200.
16. Bandla P, Huang J, Karamessinis L, et al. Puberty and upper airway dynamics during sleep. *Sleep* 2008;31:534 - 41.
17. Karamessinis L, Galster P, Schultz B, et al. Relationship between REM density, duty cycle, and obstructive sleep apnea in children. *Sleep* 2007;30:837-43.
18. Campbell IG, Darchia N, Khaw WY, Higgins LM, Feinberg I. Sleep EEG evidence of sex differences in adolescent brain maturation. *Sleep* 2005;28:637-43.
19. Jenni OG, Carskadon MA. Spectral analysis of the sleep electroencephalogram during adolescence. *Sleep* 2004;27:774-83.
20. Verhulst SL, Schrauwen N, Haentjens D, Van Gaal L, De Backer WA, Desager KN. Reference values for sleep-related respiratory variables in asymptomatic European children and adolescents. *Pediatr Pulmonol* 2007;42:159-67.
21. Uliel S, Tauman R, Greenfeld M, Sivan Y. Normal polysomnographic respiratory values in children and adolescents.[see comment]. *Chest* 2004;125:872-8.
22. Acebo C, Millman RP, Rosenberg C, Cavallo A, Carskadon MA. Sleep, breathing, and cephalometrics in older children and young adults. Part I -- Normative values. *Chest* 1996;109:664-72.
23. Marcus CL, Omlin KJ, Basinki DJ, et al. Normal polysomnographic values for children and adolescents.[see comment]. *Am Rev Respir Dis* 1992;146(5 Pt 1):1235-9.
24. Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan.[see comment]. *Sleep* 2004;27:1255-73.
25. Feinberg I, Higgins LM, Khaw WY, Campbell IG. The adolescent decline of NREM delta, an indicator of brain maturation, is linked to age and sex but not to pubertal stage. *Am J Physiol Regul Integr Comp Physiol* 2006;291:R1724-9.
26. Palm L, Persson E, Elmquist D, Blennow G. Sleep and wakefulness in normal preadolescent children. *Sleep* 1989;12:299-308.

27. Jenni OG, van Reen E, Carskadon MA. Regional differences of the sleep electroencephalogram in adolescents. *J Sleep Res* 2005;14:141-7.
28. Boselli M, Parrino L, Smerieri A, Terzano MG. Effect of age on EEG arousals in normal sleep. *Sleep* 1998;21:351-7.
29. Carskadon MA. The second decade. In: Guilleminault C, ed. *Sleep and waking disorders: indications and techniques*. Menlo Park, CA: Addison Wesley, 1982:99-125.
30. Moss D, Urschitz MS, von Bodman A, et al. Reference values for nocturnal home polysomnography in primary schoolchildren. *Pediatr Res* 2005;58:958-65.
31. Montgomery-Downs HE, O'Brien LM, Gulliver TE, Gozal D. Polysomnographic characteristics in normal preschool and early school-aged children. *Pediatrics* 2006;117:741-53.
32. Traeger N, Schultz B, Pollock AN, Mason T, Marcus CL, Arens R. Polysomnographic values in children 2-9 years old: additional data and review of the literature.[see comment]. *Pediatr Pulmonol* 2005;40:22-30.
33. Carskadon MA, Harvey K, Dement WC, Guilleminault C, Simmons FB, Anders TF. Respiration during sleep in children. *West J Med* 1978;128:477-81.
34. Krieger J, Maglasiu N, Sforza E, Kurtz D. Breathing during sleep in normal middle-aged subjects. *Sleep* 1990;13:143-54.
35. Shore ET, Millman RP, Silage DA, Chung DC, Pack AI. Ventilatory and arousal patterns during sleep in normal young and elderly subjects. *J Appl Physiol* 1985;59(5):1607-15.
36. Stradling JR, Chadwick GA, Frew AJ. Changes in ventilation and its components in normal subjects during sleep. *Thorax* 1985;40:364-70.
37. Krieger J. Respiratory physiology: breathing in normal subjects. In: Kryger M, Roth T, Dement WC, eds. *Principles and practice of sleep medicine*. 4th ed. Philadelphia: Elsevier Saunders, 2005:232-44.
38. Gries RE, Brooks LJ. Normal oxyhemoglobin saturation during sleep. How low does it go? *Chest* 1996;110:1489-92.
39. Witmans MB, Keens TG, Davidson Ward SL, Marcus CL. Obstructive hypopneas in children and adolescents: normal values. [comment]. *Am J Respir Crit Care Med* 2003;168:1540.