From Apnea of Infancy to Obstructive Sleep Apnea Syndrome in the Young Child

Christian Guillemault, M.D.; and Riccardo Stoohs, M.D.

Obstructive sleep apnea syndrome (OSAS) and heavy snoring during sleep, without sleep apnea, has been well described in children and adults. We report a case series of 25 full-term infants, prospectively obtained from a database of nearly 700 "apparent life-threatening event" (ALTE) cases, who presented between 3 weeks and 4½ months of age an ALTE and who progressively developed more florid symptomatology and polygraphic findings. All of them were classified as OSAS patients by five years of age. These index cases are compared with two other ALTE infant groups followed in parallel during the first year of life but whose symptoms were short-lived. The index cases presented more frequently a positive family history of OSAS and an early report of snoring or noisy breathing during sleep. Usage of an esophageal balloon to monitor esophageal pressure (Pes) and usage of nasal continuous positive airway pressure (CPAP) as a test may help in the early recognition of these infants, who appear to make more effort to breathe during sleep, based on the indirect evidence of Pes measurements. It is suggested that anatomic features, including a small posterior airway space leading to an abnormal degree of upper airway resistance, may be the cause of the symptoms presented by these infants. Considering the parental anxiety generated by persistence of symptoms after the first year of life in ALTE infants, recognition of this subgroup is important.

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ALTE = apparent life-threatening events; CPAP = continuous positive airway pressure; Pes = esophageal pressure; RDI = respiratory disturbance index; RR = respiratory rate; SIDS = sudden infant death syndrome; TST = total sleep time

In 1976 we engaged in a systematic study of infants referred for what was then called "near-miss sudden infant death syndrome (SIDS)" and is now called "apparent life-threatening events" (ALTE). Most of these infants presented in polygraphic evaluations some abnormal breathing patterns that today are called "apnea of infancy." A consensus conference held in 1978 recommended systematic workup for these infants, and we followed the outlined recommendations.

One of them was to perform systematic follow-up once an infant had been identified as a "near-miss SIDS" infant. We set up a system to follow prospectively all full-term infants referred as near-miss SIDS with polygraphic recordings at 4½, 6, 9, and 12 months. For those infants who were first seen very early in life, an earlier systematic recording was also scheduled at three months of age. (The age of the infants at the initial visit ranged from three weeks to four months.) The polygraphic recordings lasted 24 h until 6 months of age, after which they lasted all night.

This investigation was set up as a prospective study. We also decided that any infant who had to be kept on a home monitor past 12 months of age or who presented abnormal polygraphic monitoring at 12 months of age would continue to be followed polygraphically. To date, some of these children are still prospectively studied, and we hope one day to have information with follow-up on late teenage individuals with a history of ALTE and snoring. Some results of this systematic prospective study have been published previously.² ³ This report focuses on subjects followed up past 12 months of age during early childhood.

We used the definition of ALTE established at the 1978 consensus conference on near-miss-SIDS infants.¹ All infants had experienced an initial ALTE that occurred away from medical personnel, and in all infants an initial polygraphic evaluation revealed no clear cause for the reported event. Parents reported having found their infant not breathing and presenting a significant change in color. They performed different maneuvers (usually mouth-to-mouth resuscitation) to make the infant breathe again. All infants underwent a complete, in-hospital pediatric workup that included cardiac, respiratory, and neurologic investigation of respiratory problems and apnea. Infants with known problems, including facio-skeletal abnormalities, neuromuscular disorders, cardiac diseases, and CO₂ retention, and infants with reflux-induced apneas were excluded, per definition, from the study.

The usual laboratory tests (such as complete blood cell count [CBC], electrolytes, blood tests, electrocardiogram [ECG], chest roentgenograms, electroencephalogram [EEG]) were performed on all infants. No significant findings were noted, and the diagnosis of sepsis was ruled out. However, in some of them (group D infants), cultures (including syncitial and other respiratory viruses), fluorescent antibody tests, or both were found positive. Culture results came back once the infant had been discharged from the hospital; thus, positive results were merely a laboratory finding. All infants considered to have had an ALTE were placed on the prospective follow-up program and had an initial polygraphic recording. Twenty-

²From the Stanford University Sleep Research Center, Stanford, Calif.
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six infants (one unavailable for long-term follow-up) had continuous problems past one year of age.

**Methods**

**Population Selection Criteria**

All the infants who were kept on home monitors past 12 months of age and who were followed up prospectively past 18 months of age were identified.

For purpose of comparison, we selected two groups of full-term infants who had had an ALTE event and who had been studied prospectively until 12 months of age but had discontinued home monitoring before that time. One (group C) was composed of infants who presented an ALTE at a date as close as possible (and within at least four weeks) of each index case. These infants must have had completely negative findings in the pediatric examination at the time of the initial hospitalization, including a negative culture or a negative fluorescent antibody test or both, following systematic investigation of an infectious illness that might have been responsible for the ALTE.

The second control group (group D) consisted also of full-term infants referred for an ALTE; however, these infants had had a positive culture, a positive fluorescent antibody test, or both at the time of the initial examination. The infant to be selected as a control must have had his or her initial examination during the same general period as an index case. As these infants were less common than group C infants, a longer time interval from 4 weeks to the date of the index case ALTE had to be allowed (5 to 14 weeks). Group A consisted of normal full-term infants monitored at similar ages during the first year of life but collected at a time different from most of the ALTE (population characteristics and population data previously published).3,4

Following are the remaining requirements for all cases in groups B, C, and D: (1) full-term infants; (2) an ALTE before 4½ months of age; (3) full polygraphic monitoring at the time of the ALTE; (4) followed up clinically and polygraphically until at least the age of 12 months; and (5) charts and polygraphic recording results at the time of transcription on the entry system sufficiently documented to provide long-term follow-up information. This last requirement eliminated one index case: one infant with persistent problems at 12 months of age was unavailable for follow-up before 18 months of age. Also, three group C infants whose charts were insufficiently documented at the time of data entry were replaced by three infants who had had an ALTE at a date slightly farther away from the date of the ALTE of the index cases. The ALTE population involved in the study is presented in Table 1.

**Polygraphic Monitoring**

All subjects had the same standardized initial polygraphic monitoring protocol. Polygraphic monitoring was performed on a polygraph (Grass) and included EEG (C/A, C/Ah and O/Ah), chin electromyogram (EMG), electro-oculogram (EOG), ECG (modified V1 lead), and respiration monitoring. Airflow (nasal and buccal) was monitored by thermistors, and chest and abdominal efforts were monitored by strain gauges or infant inductive plethysmography (Vitalog, Inc.). Oxygen and CO2 tensions were monitored with transcannulae electrodes (Kentron) (tcPO2 and tcPCO2). Esophageal pH was monitored in 68 of the 75 infants with a nasally placed esophageal electrode. Placement of the electrode was verified by fluoroscopy. Esophageal pressure monitoring was combined with esophageal pH monitoring in 46 of the 75 infants.

All ALTE infants were placed under a cardiorespiratory home monitor. Infants were prospectively followed up clinically during the first 6 months on a monthly basis. Parents were requested to keep written track of monitor alarms and their type. Systematic polygraphic recordings were prospectively scheduled at 4½, 6, 9, and 12 months of age. The 4½- and 6-month polygraphic monitorings were of 24-hour duration. Nocturnal polygraphic recordings only were obtained thereafter. After nine months of age, oxygen saturation was monitored, in most instances, by pulse oximetry. Polygraphic monitoring was performed at approximately eight weeks, four months, and between two and four years of age, with further follow-up until the decision to have surgery.

Esophageal pressure monitorings were irregularly performed at follow-up recordings in the total ALTE group, except for the index cases. Index cases seen after 1984 who were untreated and who were between two and four years of age underwent two systematic testings: esophageal pressure monitoring at long-term follow-up, with and without nasal continuous positive airway pressure (CPAP), and cephalometric roentgenograms.

**The Long-term Follow-up Esophageal Pressure Monitoring**

Esophageal Pressure Monitoring and CPAP Test: Eleven index cases with clinical symptoms, including two children with respiratory disturbance index (RDI) of 2 and 3 at the noninvasive polygraphic recording, were brought back for a new polygraphic investigation at a mean age of 29.2±7 months. During the second monitoring, esophageal pressure was also monitored by means of an esophageal balloon calibrated following the recommendations of Baydur et al.4 Once a complete sleep cycle (ie, NREM and REM sleep) had been obtained, the child was equipped with an "Pediatric Petite" (or a small custom-made) nasal CPAP mask (Respironics, Monroeville, Pa). During the successive sleep cycles, nasal CPAP was administered and positive end-expiratory pressure (PEEP) was progressively increased, following the well-documented procedure for determination of appropriate PEEP in the treatment of obstructive sleep apnea in children and adults.5 The impact of each increase of 1 cm H2O PEEP (from +3 cm H2O on) on esophageal pressure (PES), respiratory rate, snoring, continuously monitored SaO2, and presence or disappearance of complete or partial upper airway obstruction served as a guide for the decision to increase PEEP to the next +1 cm H2O step. Each child was his own control.

**Cephalometric Roentgenograms:** Twelve of the children followed up after two years of age underwent cephalometric roentgenograms awake, seated, at end inspiration, as classically performed.7 Ten healthy children who had no history of ALTE and who had cephalometric roentgenograms performed at a mean age of three years (usually for orthodontic problems) in the same laboratory and under the same conditions were used as age-matched controls in addition to the literature data.8

**Results**

**Initial Evaluation**

None of the three ALTE infant groups could be differentiated by age. The information obtained at entry is summarized in Table 1 and Figure 1.

**Polygraphic Results:** All results were compared with those obtained on normal controls. Respiratory events were scored following published criteria in infants. "Respiratory pauses" of 3 to 10 s duration and "apnea" lasting 10 s or longer were scored as reported in previous polygraphic monitoring reports of controls and near-miss SIDS infants. Obstructive and mixed events were scored together and differentiated from "central" (or, more accurately, diaphragmatic) events, as previously defined. No sleep apneic event could last longer than 30 s, because infants with apneas of this duration were systematically awakened. "Signifi-
Table 1—ALTE Infant Population Involved in the Study*

<table>
<thead>
<tr>
<th></th>
<th>Group B (Index Cases)</th>
<th>Group C (Matched ALTE Infants)</th>
<th>Group D (Matched ALTEs with Positive Cultures)</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home monitor alarms at 9 mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequent</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stopped</td>
<td>10</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>15</td>
<td>14</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>11</td>
<td>11</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>X birth weight, g</td>
<td>2.839 ± 187</td>
<td>2.762 ± 179</td>
<td>2.678 ± 201</td>
<td>NS</td>
</tr>
<tr>
<td>Vaginal delivery</td>
<td>24</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Cesarean delivery†</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>X mother’s hospital stay, h</td>
<td>56</td>
<td>52</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>X age of mother, yrs</td>
<td>22.1 ± 3</td>
<td>22.8 ± 4</td>
<td>23.4 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>23</td>
<td>14</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Mexican-American</td>
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<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Birth order</td>
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<td></td>
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</tr>
<tr>
<td>First</td>
<td>18</td>
<td>14</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Second</td>
<td>7</td>
<td>8</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Third</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Any mothers chronic drug or alcohol users?</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Snoring/noisy breathing</td>
<td>7</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Positive culture/antibody test</td>
<td>0</td>
<td>0</td>
<td>25‡</td>
<td></td>
</tr>
<tr>
<td>Family history of snoring</td>
<td>14</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Family history of OSAS</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*ALTE = apparent life-threatening events; ANOVA = analysis of variance; OSAS = obstructive sleep apnea syndrome.
†Infant was delivered by cesarean section because of fetal distress during descent.
‡Syncytial virus, 14; echovirus, 8; pertussis, 2.

**Figure 1.** Results of first recording during infancy. 1A (left): Indices of mixed and obstructive events. 1B (right): Indices of central events. Groups are as follows: A = normal controls; B = ALTE index cases; C = ALTE control group, negative culture; and D = ALTE control group, positive culture. ALTE = apparent life-threatening events. Asterisk: Mean age (± SD) at time of ALTE (in postnatal weeks) is indicated, with each letter indicating the group. The ordinate axis presents the number of respiratory events per sleep hour (ie, number of events divided by total sleep time multiplied by 60). The standard deviation for each group is presented above each mean index.
cant bradycardia” was scored when heart rate was equal to or below 70 beats/min for two successive heart beats from a preceding mean heart rate of 138 ± 14 beats/min. Abnormal cardiac rhythms and ventricular events were systematically scored, and their relationship to any abnormal respiratory event was noted.

None of the infants presented abnormal tcPCO2 monitoring or abnormal wakeful arterial blood gas values; these results ruled out central alveolar hypventilation. None of the infants presented “significant bradycardia” as defined as abnormal cardiac rhythms. (Drops in heart rate were seen in association with respiratory events during sleep, but the lowest heart rate drop ever noted in the 75 ALTE infants was to 78 beats/min, calculated as defined above.)

All of the 75 ALTE infants had more short respiratory pauses and apneas than were seen in the control group (A), but there were no significant statistical differences (analysis of variance) among the three ALTE infant groups (see Fig 1).

Analysis of Pes monitoring: During obstructive events, Pes had a more negative nadir. During nonobstructive events, the mean peak Pes in the total population was −4 ± 1 cm H2O. The calculation of this mean was obtained by analysis of one 30-s epoch of the sleep monitoring without abnormal respiratory events every 15 min. Visual analysis indicated that certain polygraphic epochs presented a significant increase in peak Pes nadir. For ease of visual determination, epochs with at least four successive Pes nadirs equal to or above −10 cm H2O (which were easily recognized due to a calibration standard of 1 cm H2O = 2 mm on recording paper) were identified. Eleven index cases, one infant in group C, and three infants in group D presented epochs with Pes nadir above or equal to −10 cm H2O without apnea. These epochs were seen in clusters and were all noted during quiet sleep while the infant was supine. The clusters of epochs with increased Pes nadir took up a mean of 72 ± 20 min in index cases, 22 ± 11 minutes in group C infants, and 63 ± 34 min in group D infants. No interpretation of the finding was given at the time of the monitoring.

Summary: Initial Evaluation: Seventy-five full-term infants were seen just after an ALTE that occurred during the first two months of life. Twenty-four-hour polygraphic monitoring with a noninvasive technique was unable to find any difference among the 75 ALTE children. Clinical symptoms and family history evaluations indicated that history of “snoring” or “noisy breathing” in infants and a family history of snoring were more prominent in the index cases. Index cases also demonstrated a more prominent increase in inspiratory Pes nadir during sleep. This increase is an indicator of increased inspiratory effort requirement.

Results at 6 and 9 Months (Groups B, C, and D)

At the 6-month polygraphic recording, 50 ALTE infants (groups C and D) had had no reported alarms from the cardiorespiratory monitor for at least the prior 3 weeks. There was indication of normal infant development. At 9 months of age in these 50 ALTE infants, no growth retardation, allergies, snoring, or noisy breathing during sleep was noted. Sleep behavior was normal and polygraphic findings were no different from those of the control group A (Fig 2).

Index cases (group B) had a different evolution, and parental reports indicated persistence of home monitor alarms not related to lead disconnection. The parents noted “color change” and “absence of breathing” (no information on pulse was reliably obtained). When touching and/or gently shaking the infant did not convince them of the normalcy of breathing, they initiated mouth-to-mouth resuscitation. Usually one or two breaths were sufficient, and, commonly, adults heard a “pop” or a “click” that came from the back of the infant’s throat with the return of breathing. (The term “click” was used by many of the parents of this subgroup of infants.) The infant then regained color and cried.

Specific Points on Index Cases: (1) Parental reports indicated “noisy breathing” or snoring during sleep in 23 of 25 index cases. Mouth breathing during wakefulness was also noted in 11 cases. (2) Growth: Three infants were below the fifth percentile at 9 months. (They were the only 3 out of the 75 ALTE infants.) Three infants were reported to have allergic reactions to certain food formulas (also the only 3 of the 75 ALTE infants). (3) Twelve infants had nightly head-neck perspiration of a sufficient amount to be reported spontaneously by parents. (4) Nocturnal polygraphic monitoring (see Table 1) indicated that all index cases had noisy breathing during sleep, compared with one infant in group D. Respiratory events during sleep were statistically more frequently seen in index cases compared with the other ALTE groups. There were no statistically significant (analysis of variance) polygraphic differences between normal controls and ALTE groups C and D. In association with sleep-related respiratory events, recording indicated at least one event during the night with tcPO2 reading below 60 mm Hg or an SaO2 drop to 93 percent or below. None of the other groups showed SaO2 drops to below 95 percent.

By 9 months of age, the 50 ALTE infants of groups C and D had normal development and normal polygraphic monitoring during sleep, regardless of their initial clinical picture. The 25 index cases were different with respect to parental complaints and reports and with respect to polygraphic monitoring. These were the only infants still kept on home
monitoring. Because of their different results, these children were again followed up prospectively. The other children had one more systematic follow-up with polygraphic monitoring at 12 months and were not followed up systematically thereafter because of the normalcy of the findings.

**Index Cases during the Second Year of Life**

**Clinical Symptoms:** All subjects were noted to be "snoring" or to be "noisy mouth breathers" during sleep by relatives, and 21 cases were reported to have "restless" or "agitated" nightly sleep. Night sweats, which sometimes led to change of clothes during the night, were reported in 22 cases. Unusual sleeping position, with the head hyperextended, often associated with prone position and knees under the stomach, was seen in 12 cases. Twelve children were considered small for their age, and five were labeled "failure to thrive" by 24 months of age.9

**Clinical Evaluations and Nocturnal Polygraphic Recordings:** Systematic otolaryngologic examination performed at 2 years of age in 21 cases indicated that there was in 14 children a "smaller than expected" oropharynx with an elongated uvula and/or some palatal soft-tissue redundancy. Only one child had severe tonsillar hypertrophy (quoted 4 + from a subjective scale from 0 to + 4), and three were scored 3 + (moderately severe hypertrophy). Polygraphic monitorings obtained at 17 and 22 months of age indicated presence of obstructive and mixed sleep apnea. As indicated in Table 2, although certain children had clearly intermittent obstructive and mixed sleep apnea during sleep, oxygen saturation drops were always moderate, and certain children had very few apneic events, despite laborious, noisy breathing.10 No significant cardiac arrhythmias were noted in the recordings, with the exception of bradycardia with obstructive sleep apnea. Bradycardia was defined as a drop in heart rate for at least two successive heart beats to 10 beats/min below the heart rate measured just after onset of sleep with quiet breathing. By two years of age, six children underwent tonsillectomy or tonsillectomy and adenoidectomy, based on clinical symptoms and polygraphic recordings.

**Index Cases between 2 and 4 Years of Age**

The 19 untreated children were followed up further.

### Table 2—Results of Polygraphic Recordings Performed at 22 Months of Age in Group B Children*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result (n = 23†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexes of M and O pauses</td>
<td></td>
</tr>
<tr>
<td>≥10s (X ± SD)</td>
<td>16 ± 10</td>
</tr>
<tr>
<td>Indexes of C pauses</td>
<td></td>
</tr>
<tr>
<td>≥10s (X ± SD)</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>Lowest So2</td>
<td>88</td>
</tr>
</tbody>
</table>

*M = mixed; O = obstructive; C = central. All infants were tachy- neic. Indexes = apnea + H × 60/Total sleep time.

†Two infants who had previous tonsillectomy or tonsillectomy and adenoidectomy not included.
The absence of a significant number of apneas during sleep and the belief at that time that a large number of apneas during sleep should be documented before any surgical treatment led to regular follow-up of these children.

Clinical Symptoms: In the 19 children, loud snoring was reported on a nightly basis, associated with abnormally restless sleep and nightly sweats. Sweating was of variable intensity and occurred mainly behind the neck but was reported in some cases on the neck and chest. Also reported was a tendency to drool during sleep. Twelve of the 19 children presented one or more of the following symptoms: behavioral problems, such as easily becoming “cranky,” “aggressive,” or “hyperactive,” attentional problems, frequent upper airway infections (reported at least once a month), a tendency to vomit or to have difficulty swallowing large pieces of food, excessive drooling during the day, and complaints of intermittent morning headaches. Responses concerning daytime somnolence were impossible to interpret. Five children were reported to have no daytime symptoms.

Clinical Evaluation and Polygraphic Monitoring: Seven children were below the fifth growth percentile (including one without daytime symptoms). Ten children were below the 30th growth percentile.

Polygraphically, the mean total sleep time (TST) was 565 ± 22 min. Delta sleep was always present and took up a mean of 21 ± 4 percent of TST: The mean apnea-hypopnea index (also called the RDI) was 20 ± 9 (median, 18; range, 2 to 39). All children snored significantly. Three of the children still had a low RDI (2, 3, and 5). The mean lowest SaO2 during sleep was 84 ± 6 percent.

The 11 children monitored with Pes recording and nasal CPAP trial had the following results.

During quiet supine wakefulness, Pes oscillated during one respiratory cycle between 0.2 ± 0.05 cm H2O and −4 ± 1.5 cm H2O. During the first NREM-REM cycle, respiration was irregular: during NREM sleep, mean respiratory rate (RR) was 22 ± 3 breaths/min; during REM sleep, mean RR was 27 ± 6 breaths/min (mean RR was calculated from epochs without apnea or hypopnea). Intermittently, an obstructive apnea was seen associated with SaO2 drop, and also an obstructive hypopnea, classically defined as reduction in airflow associated with a drop in SaO2, was noted. The mean RDI (apnea + hypopnea) was 26 ± 15 (range, 2 to 39). The mean peak Pes nadir was −25 ± 9 cm H2O. The mean lowest SaO2 was 86 ± 5 percent.

With nasal CPAP, the mean PEEP was 6 ± 1.5 cm H2O. The mean NREM sleep RR was 16 ± 1 breaths/min during REM sleep. The mean lowest SaO2 was 96.1 percent, and the mean peak Pes nadir was −5 ± 2 cm H2O. The two children with RDI of 2 and 3 presented an increase in Pes nadir, with peak inspiratory Pes reaching respectively −23 and −27 cm H2O before nasal CPAP. Pes nadirs more negative than −10 cm H2O were seen without any evidence of SaO2 drops, hypopnea, or apnea. Snoring, abnormal sweat, and laborious breathing were completely eliminated with nasal CPAP in all children.

Cephalometric Roentgenographic Results: The 12 children investigated presented a mean posterior airway space of 6 ± 1.6 mm. The ten nonsnoring control children studied in the same laboratory had a mean posterior airway space of 11.4 ± 1.2 mm (p<0.0001, paired t test). The literature data from Gunn and Tonkin indicate a mean posterior airway width of 11 mm on lateral roentgenograms of the neck in normal six-month-old infants.

Follow-up Report End-Point: All children presented persistence of clinical signs and symptoms between the ages of two and four years. Further, some additional clinical symptoms were reported.

At 5 years of age, all 25 index cases had had tonsillectomy with or without adenoidectomy. All index cases at a follow-up three months after surgery had a disappearance of the clinical complaints and improved polygraphic monitoring findings with the disappearance of laborious breathing during sleep.

DISCUSSION

Limitations of the Study

This is a case series study, not a general population prospective investigation. Although all the ALTE children were prospectively followed up until the end of the first year of life and all index cases were systematically prospectively followed up past 12 months of age because of their persistent abnormal findings, one index case was unavailable for long-term follow-up. The 25 index cases were collected over a period of years, and different tests were systematically applied depending on the clinical wisdom at the time of the follow-up. In the children seen more recently, the decision to perform tonsillectomy and adenoidectomy occurred earlier, based on past experience.

Positive Findings of the Study

This is, however, the first report on a very long-term prospective follow-up of a subgroup of infants who were poorly understood when first seen. There was some self-selection: infants were still presenting problems at home, and pediatricians could not attribute the reported history to any well-defined syndrome. By nine months of age, polygraphic recordings indicated differences compared with age-matched peers. The developmental history of these index infants when reviewed, however, is very similar.

Undoubtedly, these index infants are uncommon. The 25-case series was self-selected from a total population of nearly 700 full-term infants referred for...
ALTE between 3 weeks and 5 months of age. However, considering the difficult questions that they raise for the practitioner, they must be recognized early.

In order to have comparison groups for our index infants, we took (1) one infant referred for a similar episode at the same time as an index case (group C) to ensure that each index case would have one control infant who had had the same workup, and (2) infants in whom a viral infection was probably involved in the ALTE, based on the initial tests (group D). This approach allowed comparative analyses. These tabulations indicated that the polygraphic recordings, as initially performed, did not aid in the distinction between the different subgroups of ALTE infants. In fact, the clinical interview gave more clues: not only the positive family histories of obstructive sleep apnea, but also a very early appearance of noisy mouth breathing or snoring, but none of these is pathognomonic. Although they were clearly seen more frequently in our index cases, they were occasionally seen in some other ALTE infants.

However, different monitoring techniques may help in their evaluation. The cluster of increase in Pes nadir during polygraphic recordings may be an informative finding, as it was predominantly but not exclusively noted in the index cases. The increase in Pes nadir is an indication of increased inspiratory effort and may suggest an increase in upper airway resistance during sleep. Measurements of Pes with and without nasal CPAP were also helpful in suggesting the role of abnormal upper airway resistance during sleep in the reported symptomatology, particularly when clinical symptoms are not associated with a high number of apneas or hypopneas as classically defined. Cephalometric roentgenograms or lateral roentgenograms of the neck, timed with inspiration and expiration as described by Gunn and Tonkin \(^{a}\) may also be advantageous to obtain, particularly with the normative information obtained at six months of age."\(^{a}\)

It is interesting to note that our index cases more frequently had a positive family history of obstructive sleep apnea syndrome or parents who snored during sleep than any of the control ALTE infants. The fact that obstructive sleep apnea and obstructive sleep apnea syndrome can cluster in some families from a very young age has already been indicated.\(^{11-13}\) Greater attention should be paid to a positive family history of abnormal breathing during sleep, particularly if abnormal reports persist for months in an infant after an ALTE, and if "apnea of infancy" is seen.

Considering the familial clustering of obstructive sleep apnea in many of these cases and also the abnormal cephalometric roentgenographic findings, the existence of some anatomic features leading to a more narrow upper airway may be postulated as a factor in the appearance of abnormal breathing during sleep in very early infancy.

Finally, in view of the parental anxiety created by the persistence of abnormal symptoms in ALTE infants with apnea of infancy, it is important to be aware of the existence of this infant group. As these infants were some of the youngest subjects identified with obstructive sleep apnea, we hope to pursue the ongoing prospective study until the late teenage years on as many subjects as possible.

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REFERENCES

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