Objective: To characterize the sleep pattern of children with atopic dermatitis in clinical remission.

Methods: Fourteen children with atopic dermatitis, with a mean ± SD age of 6 ± 2 years, were recruited consecutively from a pediatric dermatology clinic. No participant had any other medical or psychiatric illness. The control group (n = 9, mean age 7 ± 1.8 years) was composed of children with mild “benign” snoring and no evidence of respiratory disturbance during sleep. All participating children were evaluated by formal all-night polysomnography, scratch electrodes, and self-reported questionnaires filled in by their parents.

Results: The patients were studied when their skin condition was in remission. Sleep latency, total sleep time, and sleep efficiency were similar to the control group. The atopic dermatitis group had an average of 24.1 ± 8.1 events per hour of arousals and awakenings, compared with 15.4 ± 6.2 events per hour in the control group (P < .001). Direct observation, video monitoring, and scratch electrodes provided evidence of between 1 to 19 bouts of scratching per night, accounting for only 15% of the arousals and awakenings. The rest of the arousals and awakenings were not associated with any specific, identifiable polysomnographic event, such as apnea or jerks.

Conclusion: Children with atopic dermatitis in clinical remission have sleep disturbances that are not related to scratching per se.


Editor’s Note: Well, we can scratch that long-held theory.

Catherine D. DeAngelis, MD
STUDY POPULATION

Fourteen children (8 girls and 6 boys) with a mean ± SD age of 6.7 ± 1.8 years, who met the diagnostic criteria of AD and had no other medical or psychiatric illness, were recruited consecutively from a pediatric dermatology clinic. Sleep-related symptoms were neither an inclusion nor an exclusion criterion. At the time of recruitment, disease was active in these subjects, but an effort was made to schedule patients for sleep assessment when their skin condition was in remission. Systemic and local medication (except emollients) were discontinued 7 days prior to the sleep study. At the time of the sleep study, 2 to 4 weeks following the recruitment visit, most patients were experiencing clinical remission.

The mean ± SD age of the 9 control children (5 girls and 4 boys) was 7 ± 1.8 years, which was not significantly different from that of the patient group. The controls were recruited among children diagnosed at our sleep disorders unit as “benign” snorers without respiratory disturbances during sleep.

This study was approved by the institutional ethics committee and all the children’s parents gave written informed consent to the study. All subjects were accompanied by 1 or both parents, who stayed in the sleep laboratory with the child throughout the night. No sedation was used to induce sleep.

QUESTIONNAIRES

With the assistance of the laboratory staff, parents answered questionnaires about their children’s sleep on the morning following the study. The questionnaire was composed of 4 parts: (1) personal details, including age, sex, weight, and height; (2) historical details, including previous disease, previous surgery, current disease, and current medication; (3) sleep hygiene, including usual sleeping hours and usual sleeping habits; and (4) sleep quality, e.g., “How did your child sleep in the laboratory compared with normal sleep at home?” The answers were assessed using a 5-point scale.

DERMATOLOGICAL EVALUATION

Patients were enrolled in the study if they had a history of a chronic relapsing pruritic skin condition for at least 1 year that was consistent with the diagnostic criteria of AD. A dermatological evaluation was conducted 2 to 4 weeks prior to the sleep study.

POLYSOMNOGRAPHIC EVALUATION

Participants reported to the sleep laboratory at 8:30 PM and were discharged at 7:30 AM the following morning. They were encouraged to maintain their usual daily routine. To compare reproducibility of sleep characteristics, 8 of 14 patients with AD agreed to participate in a second-night polysomnographic evaluation. In 6 of 8 patients, the second polysomnographic evaluation was conducted the following night. None of the controls agreed to participate in a second polysomnographic study.

Overnight polysomnographic evaluation was performed as follows. Four gold cup electroencephalogram (EEG) electrodes filled with electrolyte were applied to the C3, C4, O1, and O2 locations, and reference electrodes were attached behind the ears in the left (A1) and right (A2) mastoid areas. Two electromyographic (EMG) electrodes were applied over the submental muscles. Two electro-oculographic (EOG) electrodes were applied 1 cm above the outer canthus of one eye and 1 cm below the outer canthus of the other eye. The montage arrangement for polysomnographic reading consisted of C3A2 and O1A2 or C4A1 and O2A1, 2 EEG electrodes, and an electrocardiogram electrode (modified V1 lead). Nasal air flow was monitored by a pressure transducer (Synectics Sleep Inc, Stockholm, Sweden); thoracic and abdominal movements were monitored by strain gauge electrodes; and hemoglobin oxygen saturation was monitored by pulse oximetry (Ohmeda 4700; OxiCap, Louisville, Colo). Leg movements were measured using a mechanical strain gauge sensor (SLP Inc, Tel Aviv, Israel) that was recently validated in our laboratory.

STUDY POPULATION

Fourteen children meeting the inclusion criteria were enrolled in the study by the pediatric dermatologist (H.R.). All of the children with AD had mild to moderate disease. During the 2- to 4-week waiting period prior to sleep evaluation, treatment was restricted to emollients, local corticosteroid creams, and oral antihistamines. During the last week prior to the polysomnographic study, patients were treated with emollients only. Control subjects were children with benign snoring who underwent complete polysomnographic evaluation and were found to be in the normal physiological range. None of the children in the control group complained of pruritus. The mean ± SD ages of the AD and control groups was 6.0 ± 2 years and 7.0 ± 2 years, respectively.

QUESTIONNAIRES

There was no significant difference between the groups in self-reported nocturnal sleep or sleep habits. The self-report estimate of sleep latency was similar in the 2 groups (range, 15-40 minutes), and was not significantly different from the polysomnographic measurements of sleep latency. Both groups reported similar normal sleeping times of 8 to 9 hours. Total sleep time, remembered number of awakenings, sleep quality, and sleep quantity were not significantly different in the groups.
Scratching movements were evaluated by a mechanical strain gauge placed on both index fingers and by an EMG measurement of the extensor digitorum muscle of the dominant hand. The act of scratching was monitored by these gauges and the activity was verified, in the first 3 patients only, with a closed-circuit videotape system.

Nocturnal sleep/wake cycles were scored in accordance with the Rechtschaffen and Kales criteria. Data were collected using a commercially available sleep monitoring system (SensorMedics Inc, Yorba Linda, Calif) and streamed through to an optical disk for later analysis. Signals were analyzed with computer software and the results were edited by a trained technician and by 2 of the investigators (G.C. and Dr Tara-sky). Sleep latency was defined as time from lights out to the first occurrence of 3 consecutive epochs (90 seconds) of stage 1 sleep, or the first epoch (30 seconds) of any other stage of sleep. Rapid eye movement sleep latency was defined as the time from sleep onset to the first epoch of REM sleep. Sleep efficiency was calculated as the ratio of total sleep time to time in bed. The time spent in each sleep stage was expressed as the percent of total sleep time.

Arousals and awakenings were scored according to the American Sleep Disorders Association Task Force recommendation, modified for children. We recently used this approach to investigate sleep characteristics in children with juvenile rheumatoid arthritis. arousals were defined by the presence of any of the following: (1) a more than 1.5-second period of alpha frequency EEG activity with augmentation of the submental EMG; (2) the presence of an EEG K-complex or desynchronization of EEG, if clearly associated with leg movement or apnea; or (3) a sleep stage shift, if clearly associated with leg movement or apnea. Awakenings were defined as the presence of a more than 15-second waking EEG following sleep onset with augmentation of the submental EMG. The arousal index and awakening index were calculated as the number of arousals or awakenings per hour of sleep. In addition, all arousals and awakenings were designated as (1) associated with leg movement (jerks), if a jerk signal preceded the EEG or submental EMG signal; (2) associated with apnea or hypopnea (see below); (3) associated with the act of scratching; and (4) spontaneous, if not associated with any of the above. In children, most arousals and awakenings are associated with nonspecific movements, so we did not score movements separately. The mean duration of the arousals was calculated for the control and AD groups.

The number of sleep stage shifts (downward shifts) was recorded as the number of shifts from deeper to lighter non-REM sleep or to wakefulness, or from REM sleep to any other stage or wakefulness, in accordance with previously described methods. Frequency analysis of consecutive epochs was performed to improve the definition of sleep continuity. This technique involves the determination of each occurrence of every sleep stage and its duration, in epochs. An occurrence is defined as the uninterrupted consecutive number of epochs at that stage. A frequency distribution is then created for each stage, composed of the length in epochs of each occurrence of that stage. The median duration of the occurrences of each sleep stage is reported. Fragmented sleep, with a shorter occurrence of each stage, is represented in this analysis by a smaller median duration of any sleep stage. Obstructive apnea was scored when air flow ceased for more than 4 seconds but abdominal or thoracic movements continued in a paradoxical manner (out of phase, indicating upper airway obstruction). Obstructive hypopnea was scored as obstructive apnea. In addition, the percent of time spent in paradoxical breathing, indicative of upper airway obstruction (increased upper airway resistance), was measured. Paradoxical breathing was measured with the subjects on their backs or sides.

Data for control and AD groups were compiled and tested for normal distribution (Kolmogorov-Smirnov test) and presented as mean ± SD. Data were compared using 2-tailed t tests for nonpaired groups. The frequency analysis of consecutive epochs was presented as the median and analyzed using the Mann-Whitney U test. The null hypothesis was rejected at the 5% level.

The frequency analysis of consecutive sleep and the number of shifts to lighter sleep stages are summarized in Table 2. The median length of occurrences of all sleep stages was similar in the 2 groups, indicating that the median duration of these sleep stages was not significantly different. The total number of stage shifts from deeper to lighter stages of non-REM sleep was similar in both groups.

Scratching frequently occurred as an isolated event. Bouts of scratching appeared mainly during stages 1 and 2 and sporadically at the onset of sleep. The number of bouts ranged from 1 to 19 per night (mean ± SD, 1.8 ± 0.6 bouts per hour), accounting for 15% of the arousals and awakenings. There was no significant difference in the amount of scratching between the first and second polysomnographic studies.

SLEEP CHARACTERISTICS

The results of the polysomnographic tests revealed no significant differences in the groups for sleep latency, total sleep time, sleep efficiency, or percentage of time spent in any of the sleep stages (Table 1). The most striking sleep abnormality noted in the AD group was sleep fragmentation. The AD group had a mean of 24.1 ± 8.1 arousals and awakenings per hour (range, 12.3–40.2) compared with 15.4 ± 6.2 in the controls (P < .001). Furthermore, in 6 patients the arousals and awakening index was more than 20 events per hour, while in the control group none had an index of more than 20. The mean duration of the arousals in the AD group was 4.6 ± 0.6 seconds and in the control group it was 4.5 ± 0.9 seconds. In both groups 85% to 90% of the arousals and awakenings were unassociated with a specific, definable polysomnographic event, such as apnea, jerks, and/or scratching.

Table 2: The median length of occurrences of all sleep stages was similar in the 2 groups, indicating that the median duration of these sleep stages was not significantly different. The total number of stage shifts from deeper to lighter stages of non-REM sleep was similar in both groups.

SCRATCHING
SECOND POLYSOMNOGRAPHIC STUDY

Itching, the hallmark of AD, is considered to be the main factor leading to chronic sleep problems in children with AD. Previous studies have found a scratching index of about 20 bouts per hour in AD patients during clinical flare-ups, compared with 1.8 bouts per hour in their patients experiencing remission. Itching can interfere with the process of falling asleep. However, in the present study, sleep abnormalities were not associated with scratching per se. Only 15% of the overall arousals and awakenings were associated with the act of scratching. The rest were not associated with specific, definable polysomnographic events, such as apnea, jerks, movements, and so on.

In this study we scored arousals and awakenings of short duration according to criteria set for children. For adults these might be called “micro-arousals.” This may explain why there were no differences in sleep efficiency despite increased arousals and awakenings in the AD group. However, this does not change the basic finding that frequent brief arousals have daytime sequelae, even though sleep efficiency and total sleep were comparable. Experimentally induced arousals at a rate of 20 events per hour causes impaired daytime alertness in adults. It is difficult to evaluate daytime sleepiness in these children, since they are often mistakenly diagnosed with learning disabilities or behavioral disorders. The clinical signs of sleepiness, such as yawning, impaired concentration, deficits in the performance of vigilance tasks, or irritability, are similar to those of learning disabilities or behavior disorders. Dahl et al used questionnaires to demonstrate that school-aged children with AD have daytime symptoms indicating poor sleep, including difficulty waking up for school, difficulty staying awake in the afternoon, and major discipline problems. Recently we showed that children with juvenile rheumatoid arthritis have similar amounts of awakenings and arousals, associated with longer afternoon naps and abnormal multiple sleep latency test results. Thus, we tested for daytime sleepiness in AD patients we would have expected to find evidence of it. However, this aspect was not included in the study design.

Several explanations may by provided for the sleep fragmentation observed in AD patients. First, during the active phase of the disease, scratching is intense and may mask other polysomnographic findings. Thus, it is difficult to determine whether the fragmented sleep observed by several investigators is related to scratching only. Second, during clinically active AD, the itching sensation may lead to active scratching. The itching sensation during clinical remission may be sufficient to induce arousals and awakenings, but may not be enough to induce active scratching. Third, the

### Table 1. Sleep Characteristics*

<table>
<thead>
<tr>
<th>Group</th>
<th>TST, min</th>
<th>Sleep Efficiency, %</th>
<th>Sleep Latency, min</th>
<th>REM Latency, min</th>
<th>TAT During Sleep, min</th>
<th>AR/AW, No.</th>
<th>Sleep Stage, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>380.6 ± 38.3</td>
<td>86.1 ± 7.4</td>
<td>15.8 ± 11.6</td>
<td>161.2 ± 61.1</td>
<td>24.9 ± 25.5</td>
<td>150.2 ± 44.9</td>
<td>0.81 ± 0.72</td>
</tr>
<tr>
<td>Controls</td>
<td>367.8 ± 39.4</td>
<td>89.8 ± 6.3</td>
<td>9.1 ± 8.0</td>
<td>154.0 ± 82.8</td>
<td>19.6 ± 15.7</td>
<td>80.6 ± 46.1</td>
<td>0.46 ± 0.34</td>
</tr>
</tbody>
</table>

* Data are presented as mean ± SD. TST indicates total sleep time; REM, rapid eye movement; TAT, total awake time; AR/AW, arousals/awakenings; and SWS, slow-wave sleep.

### Table 2. Frequency Analysis of Consecutive Epochs*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2</td>
<td>23.6 ± 10.4</td>
<td>26.8 ± 10.3</td>
</tr>
<tr>
<td>SWS</td>
<td>35.8 ± 24.0</td>
<td>36.3 ± 23.1</td>
</tr>
<tr>
<td>REM</td>
<td>30.7 ± 16.6</td>
<td>35.8 ± 10.9</td>
</tr>
<tr>
<td>Downward shifts</td>
<td>15.9 ± 6.5</td>
<td>12.7 ± 2.9</td>
</tr>
</tbody>
</table>

* Data are presented as median ± SD number of consecutive epochs encompassing each occurrence of each sleep stage. An epoch is defined as 30 seconds of polysomnographic recording. A downward shift indicates the number of stage shifts from deeper to lighter non-rapid eye movement (REM) sleep stages or to REM sleep. SWS indicates slow-wave sleep. None of the differences were statistically significant.

### Table 3. Reproducibility of the Polysomnographic Evaluation in 8 Patients*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>First Night</th>
<th>Second Night</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time, min</td>
<td>382.6 ± 54.2</td>
<td>413.0 ± 20.5</td>
<td>.1</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>86.5 ± 8.4</td>
<td>92.6 ± 4.0</td>
<td>.06</td>
</tr>
<tr>
<td>Latency to sleep, min</td>
<td>17.6 ± 7.6</td>
<td>8.0 ± 8.6</td>
<td>.01</td>
</tr>
<tr>
<td>REM latency, min</td>
<td>234.8 ± 76.5</td>
<td>131.4 ± 14.5</td>
<td>.02</td>
</tr>
<tr>
<td>Stage 1, %</td>
<td>8.1 ± 5.6</td>
<td>5.5 ± 3.8</td>
<td>.2</td>
</tr>
<tr>
<td>Stage 2, %</td>
<td>58.0 ± 7.1</td>
<td>49.4 ± 24.6</td>
<td>.2</td>
</tr>
<tr>
<td>SWS, %</td>
<td>20.4 ± 9.4</td>
<td>13.7 ± 7.2</td>
<td>.1</td>
</tr>
<tr>
<td>REM, %</td>
<td>11.6 ± 5.3</td>
<td>19.1 ± 3.3</td>
<td>.02</td>
</tr>
<tr>
<td>AWAR index, events per h</td>
<td>22.1 ± 13.1</td>
<td>18.0 ± 5.9</td>
<td>.2</td>
</tr>
</tbody>
</table>

* Data are presented as mean ± SD. SWS indicates slow-wave sleep, REM, rapid eye movement; and AWAR, arousals/awakenings.
development of sleep patterns is influenced by associated conditions, habits, and learned self-comforting behavior. Thus, some of the sleep problems may be related to the severity and chronicity of AD during early childhood, which might impair the development of normal sleeping patterns.\textsuperscript{10,15} Fourth, sleep may be disturbed in children with asthma,\textsuperscript{29} partly because of nocturnal asthma. It is also well documented that more than 50% of children with AD have or will develop asthma.\textsuperscript{30} Therefore, the sleep fragmentation may result from lower nocturnal lung function. Our results do not support any of these possible explanations. However, in treating children with AD, the clinician should aim to treat the skin condition and associated impairments in quality of life and daily function. Medications to improve sleep onset and sleep continuity have not shown long-term efficacy in children. Tolerance effects, withdrawal effects, and occasional paradoxical effects in the arousal system are potential difficulties resulting from the use of hypnotics and sedatives to treat chronic sleep problems.\textsuperscript{31} Further studies are needed to clarify the exact relationship among the AD skin condition, sleep patterns, and daytime functioning.

A “first-night effect” on sleep architecture has been described, in which sleep disturbances are observed on the first night in the polysomnographic evaluation. We do not think that this affects the interpretation of our data, since they were compared with a control group tested under similar circumstances. Furthermore, the distribution of the sleep study results was essentially normal in both groups. According to Mathur and Douglas,\textsuperscript{16} the arousal index in healthy individuals aged 15 to 30 years is in the range of 11 to 15 events per hour.\textsuperscript{16} The arousal index of the control group in our study was within this range and similar to our previously reported findings.\textsuperscript{14} Finally, the reproducibility of our findings was established in a second-night polysomnographic evaluation in which sleep efficiency, sleep latency, and REM latency improved as expected in the second night. No significant change was seen in the total number and index of awakenings, arousals, movements, or scratching.

We conclude that there is objective polysomnographic evidence for abnormal sleep fragmentation in patients with well-controlled AD. This sleep abnormality is not associated with the act of scratching, respiratory-related arousals and awakenings, or leg movements. The excess amount of arousals and sleep fragmentation in AD children at a time in which their skin disease is in remission may cause clinical evidence of chronic sleep disturbances and daytime sleepiness. These may be manifested by an increased duration of afternoon napping and a decreased sleep latency test, an objective measure of daytime sleepiness.\textsuperscript{14} In addition, children with excessive daytime sleepiness may develop learning disabilities or daytime behavioral problems such as irritability, difficulty with concentration, and emotional liability.\textsuperscript{10,15-19}

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Reprints not available from the authors.

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