

Diagnostic Techniques in Obstructive Sleep Apnea

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Only in the last 25 years has sleep apnea been recognized as a very common disorder and important cause of mortality. Overnight, attended polysomnography remains the reference diagnostic tool for sleep apnea, although the technology for diagnosis continues to evolve rapidly. In many instances, screening and ambulatory monitoring devices can provide similar, clinically relevant information, but larger validation studies including long-term clinical outcomes are necessary.

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Obstructive sleep apnea is now recognized to be a very common clinical condition that affects an estimated 4% to 5% of middle-aged men and 1% to 2% of middle-aged women.¹ This condition is associated with excessive daytime sleepiness and impaired daytime cognitive function, and is recognized as a cofactor in the etiology of road traffic accidents. Sleep apnea may also be associated with increased cardiovascular and increased cerebrovascular morbidity and mortality.²⁻⁴ Increased recognition of sleep apnea has inevitably resulted in a substantial increase in the number of specialist sleep centers and the number of referrals to such centers. This leads to lengthening waiting times for diagnostic studies, and increased health care resource use. There are increasing efforts to simply and accurately diagnose and treat sleep apnea, the overall strategy to be as efficient as possible in health care resource use. This article reviews currently available diagnostic techniques for sleep apnea.

Clinical Diagnosis of Sleep Apnea; Historical Perspective

The study of sleep and its disorders is less than 50 years old, and sleep apnea syndrome was virtually unknown in North America until the appearance

of Guilleminault and Dement's monograph in 1978,⁵ although the landmark studies were done more than 10 years earlier in Europe.⁶⁻⁸ However, there is little doubt that sleep apnea has been around since antiquity, and numerous, excellent descriptions of sleep apnea have appeared through the years, many of which have been nicely cataloged by Kryger.⁹ Such historical descriptions of sleep apnea are educational as well as entertaining. For example, in Shakespeare's *Henry the IV*, Part 1, Act II, Scene 4, we see the following exchange, which points out one of the relationships of sleep and breathing:

Peto: Falstaff is fast asleep behind the arras and snorting like a horse.

Prince: Hark! How hard he fetches breath.

The most detailed descriptions come from Charles Dickens' *The Posthumous Papers of the Pickwick Club*, first published in 1836. We learn of Joe, the fat boy who is excessively somnolent: "... and on the box sat a fat and red-faced boy in a state of somnolency. ... Joe—damn that boy, he's gone to sleep again." And of Joe who "snores as he waits at table ... the snoring of the fat boy penetrated in a low and monotonous sound from the distant kitchen." Other descriptions of sleep-disordered breathing and sleep patients can be found in a cohort with presumed familial narcolepsy¹⁰ "... At the onset of such an attack his head would fall forward and he would snore loudly, his face becoming cyanotic," and further,

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in describing a family member, "During his second stay in the hospital he had several minor attacks, during which the respiration increased in depth for 30 seconds. This was followed by apnea of 30 seconds, and then he became cyanotic, but he continued making slight inspiratory movements that did not go through, as if there were a mechanical obstruction to the respiration." Although these sleepy patients may have also had narcolepsy, they clearly had obstructive sleep apnea, although it was obviously not recognized as such.

These descriptions of sleep apnea went largely unnoticed until respiratory physiologists became interested in sleepy, obese patients. In 1956, Burwell et al¹¹ reported a case of excessive daytime somnolence associated with abnormal blood gases and polycythemia. This patient's history of excessive sleepiness is highlighted by ". . . playing poker once a week and on this crucial occasion he was dealt a hand of 3 aces and 2 kings . . . a full house. Because he dropped off to sleep, he failed to take advantage of this opportunity." Being very much like Joe, the term Pickwickian syndrome was coined. Obesity was thought to increase the mechanical load on the respiratory system, depressing respiratory centers and leading to hypercapnia and hypoxemia, which were thought to explain the sleepiness, cyanosis, polycythemia, and right ventricular failure. However, it was not until the mid-1960s that the sleepiness in such patients was related to sleep abnormalities and not abnormal blood gases.

Diagnosis of Sleep Apnea: Polysomnography, the Gold Standard

The landmark descriptions by Gastaut,^{6,7} Jung and Kuhlo,⁸ and others^{12,13} of obstructive apneas during sleep provided the much-needed physiological explanation of the clinical condition of sleep apnea. Sleepy, obese patients were found to obstruct their upper airways and have hundreds of awakenings each night. The obstructions were associated with severe hypoxemia, cardiac arrhythmias, and disturbed sleep. There finally seemed to be an explanation for polycythemia, pulmonary hypertension, and excessive daytime sleepiness, and it was clear that abnormal blood gases were not the cause of the sleepiness.

Following the lead of these early investigators,

many more studies of patients during sleep appeared, and soon overnight polygraphic recordings, "polysomnography," became the de facto reference or gold standard for sleep apnea. Full polysomnography usually includes measurements of: electroencephalogram (EEG), eye movements (electrooculogram, EOG), postural muscle tone (electromyogram, EMG), typically using the submental EMG), peripheral limb movements (upper- and/or lower-limb EMG), oxygen saturation (Sao₂), air flow, respiratory effort, and heart rate. Various devices can be used to assess and measure airflow (thermistors, pressure transducers, expired CO₂) and respiratory effort (inductance plethysmography, piezoelectric crystals). Unfortunately, the differences in technologies result in different detection capabilities for disordered breathing events (see definitions below). It has been argued¹⁴ that the majority of patients with significant sleep apnea do not require a measurement of sleep EEG and that oxygen saturation alone may be all that is necessary to diagnose sleep apnea (see ambulatory monitoring below). This view is not shared by all, and full overnight polysomnography continues to be performed in most centers. However, this testing was (and still is) very costly to perform, and before computerization was very expensive. In addition, recognition of the problem was limited, and in the early days of polysomnography, only the most severe cases came to attention and were referred to one of the few "sleep labs" around at the time. Given its cost, complexity, and lack of availability, and without knowing the prevalence of the sleep apnea, it is not surprising that polysomnography evolved as the reference standard without rigorous validation or agreement on what level of polygraphical abnormality is required to produce the clinical syndrome.

Sleep Apnea Syndrome: Definitions

The definitions of apnea, hypopnea, sleep-disordered breathing, and/or sleep apnea syndrome, along with the clinical presentations, are discussed in detail elsewhere in this issue (see article by Kryger). However, a brief review of the differences in definitions will be important in understanding the reported differences in sensitivity, specificity, and predictive value of various diagnostic techniques in sleep apnea.

Guilleminault et al first defined apnea as a cessation of air flow at the nose and mouth for at least 10 seconds, and noted that a sleep apnea syndrome is diagnosed if during 7 hours of nocturnal sleep, at least 30 apneic events are observed in both rapid eye movement (REM) and non-rapid eye movement (non-REM) sleep some of which must appear repetitively in non-REM sleep.⁵ The recent International Classification of Sleep Disorders (ICSD)¹⁵ relies more on clinical criteria for the diagnosis of sleep apnea syndrome: a history of excessive sleepiness, frequent episodes of obstructed breathing occurring during sleep, and associated features including loud snoring, morning headache, a dry mouth on awakening or chest retraction during sleep in young children. Although not part of the minimal criteria for sleep apnea, the ICSD includes polysomnographic monitoring that shows more than five obstructive apneas more than 10 seconds in duration per hour of sleep, along with other associated findings including arterial oxygen desaturation (degree not specified), arousal from sleep, and bradycardia and/or tachycardia. These definitions do not include any mention of hypopneas or partial upper airway obstructions during sleep, and yet these are clearly important. Gould et al¹⁶ were among the first to report a number of patients with the full clinical picture of obstructive sleep apnea syndrome in whom no apneas were detected, but instead in whom recurrent episodes of nocturnal hypoventilation were detected. Strictly speaking, these patients did not have complete upper airway obstruction (apnea) but rather partial upper airway obstruction (obstructive hypopnea) during sleep. Regardless, these subjects with recurrent hypopneas were clinically indistinguishable from and had a similar frequency of oxygen desaturation and arousals from sleep as patients with frequent apneas. In an attempt to better define hypopnea, these investigators expanded the spectrum of disease that could be included under sleep apnea syndrome and led the way for a more inclusive term of sleep-disordered breathing. Depending on the degree of increase in upper airway resistance, there are patients who snore loud enough and/or whose work of breathing during sleep is high enough to disrupt sleep without meeting the criteria for sleep apnea or sleep hypopnea. By quantifying respiratory effort by means of changes

in esophageal pressure, Guilleminault et al¹⁷ clearly showed that such changes (caused by increases in upper airway resistance) produced recurrent arousal from sleep. Such loudly snoring patients, but without obvious apnea, hypopnea, or oxygen desaturation, nonetheless were clinically very much like sleepy patients with polysomnographically defined apnea. Thus there exists a spectrum of increased upper airway resistance ranging from simple snoring to complete upper airway obstruction, ie, apnea. Intermediate values of increased resistance may produce sleep disruption or hypopnea and/or oxygen desaturation (of variable degree) en route to apnea. The variation in clinical expression of such patients has prompted much debate. In November 1997, the American Sleep Disorders Association (ASDA) and the American Thoracic Society (ATS) jointly sponsored a conference held in Chicago that was designed to refine, by consensus, the definition of hypopnea and its relevance to the sleep apnea syndrome. The proceedings of this Chicago conference are now before the board of the ASDA and should be published. Even with this consensus there will still exist much debate regarding the level of apneas and hypopneas necessary for increased daytime morbidity. However, without consensus definitions for one of the important variables used to characterize the sleep apnea syndrome, results of published literature will continue to be subject to different interpretations and conflicting viewpoints.

History and Physical Diagnosis of Sleep Apnea

In the past 10 to 15 years, there have been numerous attempts to accurately diagnose (or exclude a diagnosis of) obstructive sleep apnea using history and physical findings. The reference standard in all of these has been the overnight polysomnogram, although the definitions of apnea and hypopnea have varied. Moreover, there are clear differences in diagnostic equipment that alters the apnea-hypopnea index (AHI). Kapuniai et al¹⁸ showed that the combination of loud snoring and stopping breathing during sleep predicted an apnea index >10 and an AHI >10 with a sensitivity of 83% and 78% respectively, and a specificity of 63% and 67% respectively. The limitations of this approach are that each clinical

variable is assumed to be of equal importance and that an arbitrarily determined score must be achieved before determining disordered breathing from no disordered breathing categories. Moreover, a sensitivity of only 80% means that a substantial number of patients with disturbed breathing during sleep will be missed with this simple approach. Crocker et al¹⁹ used an alternative approach by developing a statistical model to predict disturbance of breathing during sleep using clinical data. One hundred consecutive patients referred to their center were used to develop the model, and this was subsequently tested in an additional 114 consecutive patients. The four terms found to contribute significantly to the model were witnessed apneas, hypertension, body mass index, and age, with witnessed apneas being by far the most predictive term (adjusted odds ratio, 19.7). This study showed an increased sensitivity of 92% but a specificity of only 51% for an AHI greater than 15. These and other variables such as neck circumference, waist circumference, and alcohol intake have been used to formulate clinical prediction rules for sleep apnea using multiple regression techniques.^{20,21} Hoffstein's group employed logistic regression analysis to use clinical criteria to predict AHI in patients with a high (clinical) pretest probability of sleep apnea.²² They showed that subjective impression alone or in combination with clinical features is not a reliable screening test for sleep apnea. However, the logistic regression model treats the AHI as a dichotomous variable that divides all patients into apneics and nonapneics based on an AHI of 10. This cutoff is arbitrary (different from the ICSD), and the results of logistic regression analysis for one particular AHI cutoff (10) cannot be applied to a different cutoff (eg, 5, 15, 20). They repeated their study using AHI as a continuous rather than dichotomous variable (multiple linear regression) and a larger data set ($n = 594$).²³ Although clinical features such as age, sex, BMI, witnessed apneas, and pharyngeal appearance explained 36% of the variance in AHI, subjective clinical impression alone is not sufficient to reliably identify patients with and without sleep apnea. Even if these and other such multiple regression techniques could explain more of the variance in AHI,^{24,25} the problem faced by most clinicians attempting to use these rules is that they involve complicated

mathematical formulas. Flemons et al²⁶ generated a four-item clinical prediction rule that included neck circumference, hypertension, habitual snoring, and partner reports of choking or gasping during sleep, and simplified this into a table that could be used to determine a patient's sleep apnea clinical score. The higher the score, the more likely it is that a patient has sleep apnea and the calculated likelihood ratio to generate estimates of the probability the patient has sleep apnea. Recognizing that previous models did not account for craniofacial dysmorphism or disproportionate craniofacial anatomy (risk factors for obstructive sleep apnea independent of obesity²⁷⁻³¹) Kushida et al³² incorporated oral cavity measurements into a morphometric model of obstructive sleep apnea using measures of palatal height, maxillary and mandibular intermolar distance, and degree of maxillary overjet (a measure of mandibular retroposition) in combination with neck circumference and BMI. Their model had a sensitivity of 98%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 89% for an AHI >5 . These investigators suggest that the model could be used by primary care physicians as a screening tool to help decide which patients should be considered for further investigation, because the model does not suggest the severity of obstructive sleep apnea. In a complimentary but slightly different approach, we have used a neural network approach to determining which patients not need be considered for further evaluation.³³ Artificial neural networks are computer programs modelled after the biological nervous system that are capable of recognizing complex patterns in data based on experience. Artificial neural networks are "trained" by presenting a set of data together with the outcomes that the trainer wishes the network to learn. The trained artificial neural network can then be evaluated by inputting similar but previously unseen data. This artificial intelligence approach for outcome prediction has been used successfully in multiple medical applications, including the prediction of acute myocardial infarction in patients presenting to an emergency room physician,³⁴ the diagnosis of pulmonary embolism^{35,36} and the predicted length of stay of patients in an intensive care unit.³⁷ Using a backward error propagation artificial neural network using 23 clinical variables and a

leave-k-out strategy, we have found the positive predictive value that a patient would not have sleep apnea was 98%, and a negative predictive value the patient would have sleep apnea ($AHI > 10$) to be 89%. In this study the use of the artificial neural network could have reduced polysomnograms performed by 22%. We are in the process of replicating these findings in a larger prospective analysis.

Overall the probability estimates of sleep apnea generated by clinical prediction rules are usually not low enough or high enough to exceed the thresholds for diagnostic decision making. However these estimates can be used as a priori probabilities for subsequent diagnostic testing with either polysomnography or portable monitoring.

Laboratory Diagnosis of Sleep Apnea

Laboratory-based polysomnography has been used as the gold standard for sleep-disordered breathing. However, the utility of a single overnight recording for diagnosis of or exclusion of clinically significant sleep apnea has never been rigorously assessed. It is clear that there may be considerable night-to-night variability in AHI, particularly when the AHI is low.³⁸⁻⁴² Although there are many factors that may produce a false negative test result, available literature suggests that this will be a very unlikely event in general. If, despite a negative overnight polysomnogram, patients are still symptomatic or the clinical

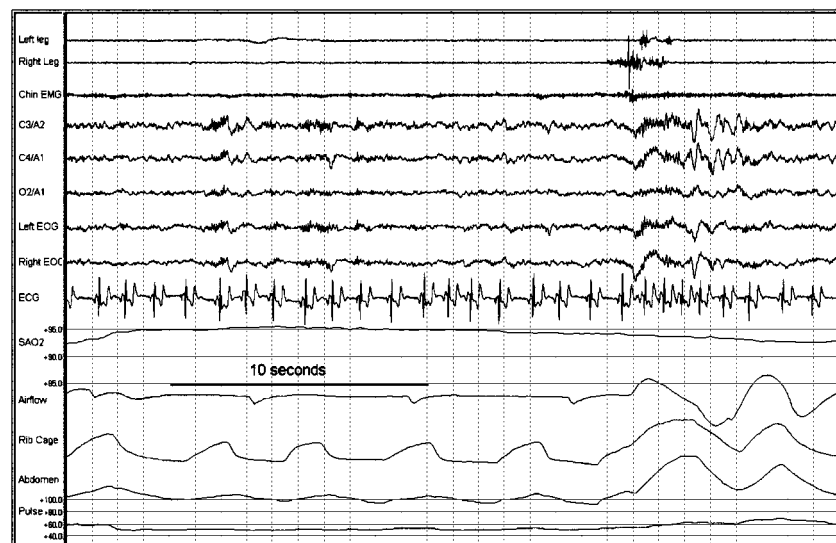
suspicion remains high, a repeat study should take place.

Figure 1 shows a typical polysomnogram of a patient with significant sleep apnea. Upper airway obstruction (absence of air flow with continued respiratory effort) is accompanied by oxygen desaturation and arousal from sleep. There is movement associated with the arousal and a brief period of cardioacceleration. Altering the time scale (Fig 2) shows the repetitive nature of the events. Figure 3 shows the same events but without the sleep related measures—EMG, EEG, EOG—whereas Figure 4 shows only the SaO_2 . Because sleep-disordered breathing is easily detectable using these later two figures, there have been many efforts to simplify the diagnostic equipment required and to move the diagnosis from the laboratory to the ambulatory setting.

Oximetry

Changes in oxygen saturation invariably occur in association with sleep apnea (Figs 1 to 4), however, the degree of desaturation is variable. The magnitude of the change in saturation depends on many factors, including end expiratory lung volume at the time of the event, baseline saturation, degree of respiratory effort during the event, degree of upper airway obstruction (partial versus complete). Many investigators have tried to evaluate the utility of oximetry in the diagnosis of sleep apnea. Using computerized algorithms to independently assess the oxygen saturation profile and

Fig 1. Typical overnight polysomnogram showing obstructive apnea. Channels recorded: electromyogram (EMG) of chin, both legs; electroencephalogram (EEG) from standard locations C3/A2, C4/A1, Oz/A1; electrooculogram (EOG) from both eyes; electrocardiogram (ECG); oxygen saturation (SaO_2); air flow, respiratory effort (Respirtrace) of rib cage; abdomen; and pulse rate.



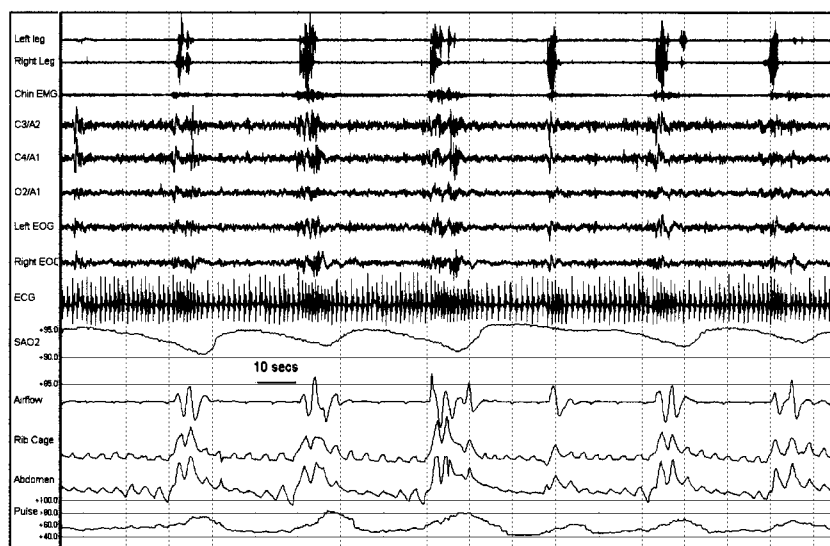


Fig 2. In this example, there are six obstructive apneas. Note that SaO_2 changes are not striking (particularly during the third apnea) and that SaO_2 stays above 90%.

then compare with the full polysomnogram, several investigators^{14,43-45} have shown that changes in saturation track nicely with the apnea/hypopnea index. Although changes in saturation can result from obstructive apnea, obstructive hypopnea, or central apnea, oximetry alone cannot provide details of the type of sleep-disordered breathing. Nonetheless it does give some indication of the frequency and severity of the sleep-disordered breathing. Although laboratory comparisons of oximetry to full polysomnography are useful, they do not provide any information on the utility of such simple measurements in the ambulatory setting. The study of Sériès et al⁴⁶ is

one of the few to assess the utility of home oximetry in the diagnosis of sleep apnea.⁴⁶ In that study, 240 patients underwent home oximetry compared with subsequent polysomnography. Although home oximetry detected only 108 of 176 patients with sleep apnea syndrome (positive predictive value, 61.4%), it correctly excluded 62 of 64 patients (negative predictive value, 96.9%). The Calgary group has added a measurement of snoring to saturation detection in an attempt to improve the ambulatory diagnosis of sleep apnea. They compared the SNORESAT (recording snoring and oxygen saturation) with standard overnight polysomnography.⁴⁷ Depending on the sever-

Fig 3. Only the ECG and respiratory channels of Fig 1 are displayed. The sum of the ribcage and abdomen has been included.

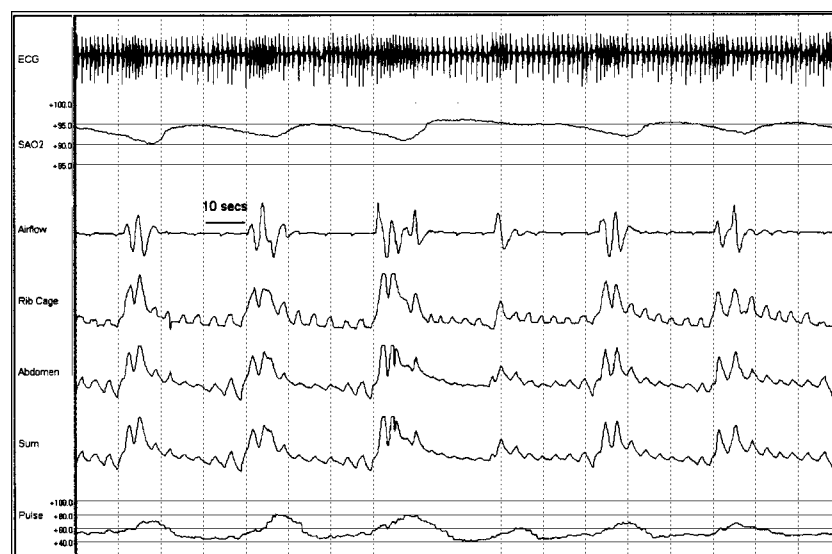
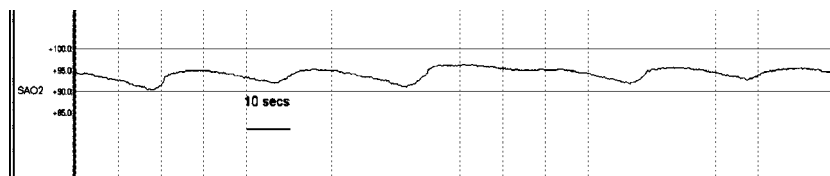


Fig 4. Only the SaO₂ is displayed, as would be derived from pulse oximetry.



ity of apnea and the referral population, the sensitivity and specificity of the monitor in detecting sleep apnea syndrome ranged between 84% and 90% (sensitivity) and 95% and 98% (specificity). In a follow-up study,⁴⁸ comparing both at-home with simultaneous in-laboratory measurements, they found that the at-home SNORESAT monitorings were highly correlated ($r = .92$) and that the correlation between home SNORESAT and polysomnography AHI was similarly high ($r = .83$). Although the SNORESAT AHI tended to underestimate that determined in the laboratory, SNORESAT misclassified patients 1% of the time or less. Although these data suggest that oximetry, or oximetry combined with snoring measurement, may be used in identifying patients with obstructive sleep apnea, it is important to remember that not all oximeters are made equally and that the detection of some events may be missed by some devices in some situations.⁴⁹⁻⁵² Using different devices with different algorithms may show different results. Clinicians need to be aware of these limitations when interpreting the literature.

Portable Monitoring

There have been a number of portable monitors developed over the years. These attempt to simplify the ambulatory diagnosis of sleep apnea while retaining the essential recording features of polysomnography. Articles by Emsellem et al⁵³ and Redline et al⁵⁴ were the first to report the feasibility and reliability of recording sleep disordered breathing in the ambulatory setting. They used an EdenTrace portable monitor, which measured nasal and oral air flow using thermistors, chest wall impedance, oxygen saturation with finger pulse oximetry, heart rate, and movement detected by electrical comparison of the signals from the ECG and the pulse oximetry. Discrepancies between these channels is indicated as "motion" on the saturation channel. Two other studies, by Parra et al⁵⁵ and Whittle et al,⁵⁶ also evaluated the EdenTrace. Of these four studies,

two compared the ambulatory device only in the laboratory with simultaneously recorded polysomnography, and two others had both home and laboratory recordings. In all studies there is good agreement between the AHI measured in the laboratory and with the EdenTrace device in the ambulatory setting. Ten percent or more of studies require repetition because of difficulty with recordings; the most recent study by Whittle et al suggested that home sleep studies have benefits in terms of time and cost, but for diagnostic reliability, an in-laboratory sleep study may be required in more than half of the cases.

The MESAM IV system, widely used in Europe, evaluates sleep-disordered breathing based on an analysis of snoring, heart rate, and saturation change. Cyclical variation of heart rate in association with decreases in saturation and snoring are taken into account at the same time to determine sleep apnea.⁵⁷ Several previous studies evaluating the diagnostic validity of MESAM IV have had conflicting results.⁵⁸⁻⁶¹ This is because not all studies have the same design, patient populations varied and diagnostic criteria were different. Even accepting the utility of MESAM IV to diagnose sleep apnea, a recent study by Krieger et al⁶² suggested that patients diagnosed with sleep apnea using the MESAM IV had poorer compliance with continuous positive airway pressure (CPAP) therapy compared with a matched group of sleep apnea patients who were diagnosed in the laboratory. The investigators concluded that there is a risk that ambulatory diagnostic procedures may alter the relationship of patients to their disease and/or the medical staff so that subsequent compliance with treatment may be decreased.

Nasal CPAP devices have become one of the most common treatments for obstructive sleep apnea (see article by Strollo, this issue). Recent modifications to the self-adjusting CPAP system, Autoset (ResMed), allow for an additional means of portable, diagnostic monitoring. The Autoset has two functional modes, diagnostic and treat-

ment. In the diagnostic mode, the Autoset measures pressure generated in the anterior nares through standard nasal cannulae. The internal pressure transducer in the system software allows estimation of the nasal air flow and the flow-time relationship. The snoring is qualitatively assessed by analyzing the flow signal after band pass filtering. Using an external digital oximeter, nocturnal arterial oxygen saturation is measured and recorded simultaneously by the Autoset although oximetry data are not used in defining a respiratory event. The Autoset uses two independent detectors; one detects apneas, and the other detects apneas and hypopneas combined. The device does not separately record hypopneas. These variables are calculated per hour of total study time because the system does not record sleep stages. Apneas are determined if there is a decrease in the ventilation signal by more than 75% averaged over each 2-second interval for at least 10 consecutive seconds. The apnea and hypopnea detectors triggered if the decrease in ventilation is 50% or more averaged over any 10-second interval.

There have been several studies comparing polysomnography with simultaneous Autoset detection of sleep apnea.⁶³⁻⁶⁷ These papers show reasonable sensitivity and specificity when compared with the polysomnographic AHI; however, there were only 20, 27, 31, and 36 subjects in four of the studies, with the largest study being only 95 subjects. Moreover all of these are done within the laboratory, and the utility of such an approach requires home and laboratory comparisons. Autoset will likely facilitate screening for sleep apnea but only with a high pretest probability and when a negative Autoset results, full polysomnography will still need to be performed.

The ambulatory monitoring systems previously described do not actually monitor sleep itself, making it difficult to determine the frequencies of apneas and hypopneas. Given that the AHI is a standard measure of sleep-disordered breathing, its absence from most home sleep reports makes interpretation of the results potentially difficult. Notwithstanding one study that suggests sleep staging even in the laboratory does not substantially improve diagnostic accuracy,¹⁴ recording of sleep is preferred by many. In addition signal quality during home evaluation is only assessed during subsequent analysis, and as a result poor

signal quality or lost signal caused the studies to be a failure. Up to one third of studies may have data loss. To obviate this, the Nightwatch system includes some measures of behavior allowing an AHI to be calculated. Secondly, near-real-time data can be intermittently transmitted from the home to the laboratory by modem so that signal quality can be verified and corrected throughout the night if necessary. On a compact solid-state recorder, the Nightwatch system records eye movement (1 channel, piezo electrode), leg movement (1 channel, piezo electrode), arterial oxygen saturation (finger pulse oximeter), nasal oral air flow (thermistor), chest and abdominal movements (piezo electrodes), body position and movement (mercury gauge placed on the chest), and heart rate. The Nightwatch system has the ability to send to the laboratory data for analysis by modem 2-minute portions of the complete recording so that signal quality can be assessed and transducer function corrected if needed. There are three published reports using the Nightwatch system.⁶⁸⁻⁷⁰ The most extensive is that by White et al.⁶⁸ In this study 30 patients in the laboratory were monitored simultaneously with the Nightwatch system and polysomnography. An additional 79 subjects were recorded in the home and subsequently in the laboratory, and comparisons were made. During in-laboratory comparisons, there was a modest correlation between Nightwatch and polysomnogram for total sleep time ($r = .72$), with the Nightwatch tending to score some awake time as non-REM sleep. The correlation for AHI was higher ($r = .94$), with a sensitivity of 100% and a specificity of 64% at an AHI threshold of 10. For the home laboratory comparison, the correlation for AHI was similarly high ($r = .92$), with a sensitivity of 91% and a specificity of 70% at an AHI threshold of 10. The investigators also expressed their comparisons in a slightly different way, reasoning that standard measures of sensitivity and specificity do not always apply when assessing the validity of a new diagnostic approach to sleep apnea. In particular, because there is no well-defined cut off above which sleep apnea is diagnosed and below which it is excluded, small differences in AHI between the two systems (one to two events per hour) that are clinically unimportant may be interpreted as total diagnostic errors using the standard measures of sensitivity and specificity. Their defini-

tions were: diagnostic agreement, $AHI \geq 40$ on both systems, or if $AHI < 40$ on polysomnography, the AHI was within 10 events/hour on both systems; overestimate of AHI, AHI was 10 events per hour greater on Nightwatch than polysomnography (both < 40 /hour); underestimate of AHI, AHI was 10 events/hour less on Nightwatch than polysomnography (both < 40 /hour). For their home-laboratory study, the results were: overall agreement, 78.6%; overestimation, 17.1%; and underestimation, 4.3%. The investigators thought that these results were quite acceptable given the night-to-night variability in sleep apnea.

Whereas the Nightwatch simplifies recordings, home sleep systems that can acquire, store, and analyze full polysomnographic data in the ambulatory setting have been recently developed such as Digitrace Home Sleep Systems (DHSS). The recent article by Fry et al⁷¹ using 77 subjects suggests that all parameters are scoreable for more than 95% of all epochs. It suggests that full polysomnography in this way can be extended to a large patient population because it no longer limits the number of sleep laboratory beds, and there is an overall reduction in costs attributable to elimination of overnight staff and facility costs. In addition, this technology can be used for more than sleep apnea. However, further studies are necessary before this technology can be put into widespread use.

Other Diagnostic Approaches

Actigraphy refers to portable motion detectors that use accelerometers and digital technology to assess motion. Actigraphs are usually worn on the nondominant wrist, and depending on the degree of movement, one can infer sleep and wake. Such actigraphs have been very useful in determining disorders of the sleep-wake rhythm.⁷² Because patients with sleep apnea invariably have increased motor activity during sleep, activity monitoring could offer a useful approach in the assessment of obstructive sleep apnea. Only two studies have addressed the use of activity monitoring in obstructive sleep apnea.^{73,74} In an early study, Aubert-Tulkens et al⁷³ included only patients with severe sleep apnea, whereas Middelkoop et al⁷⁴ combined the use of wrist actigraphy and self-assessment of sleep in the screening of obstructive sleep apnea patients in a community-based

sample. The earlier study suggested the actigraph could reliably detect obstructive sleep apnea in patients with a high pretest probability of obstructive sleep apnea. One hundred and sixteen subjects suspected of having sleep apnea were evaluated by portable four-channel mini-log recorder (recording of respiration and oral and nasal airflow by thermistors) and actigraphy. Both high sensitivity and specificity were found when comparing the actigraph with a portable monitor. Different results may have been found had this been compared with polysomnography in-house. Moreover, the time resolution of the actigraph may influence its diagnostic effects.

Other surrogate measures have been used in an attempt to assess sleep apnea. Guilleminault et al⁷⁵ reported on cyclical changes in heart rate on 24-hour ECG (Holter) monitoring. They showed quite impressive periods of alternating bradycardia/tachycardia, and suggested this as a screening device for obstructive sleep apnea. However, these subjects had quite severe disease, and the sensitivity and specificity of Holter monitoring has not been established, particularly in patients with mild disease. Davies and colleagues⁷⁶ proposed changes in blood pressure profile as a means for identifying sleep-disordered breathing because arousal from sleep causes a transient blood pressure increase and each inspiration causes a transient blood pressure decrease. They developed two computer algorithms to identify blood pressure decreases caused by inspiration and increases related to arousal from a large sample of blood pressure readings from a wide variety of patients, including those with sleep apnea. From these samples, normal ranges for the number of arousal-related systolic increases and average size of inspiratory decreases were established. This was then prospectively applied to all-night unedited blood pressure recordings from a further 20 subjects. They could identify all 6 of 20 patients studied prospectively with sleep-related breathing disorders. Again, such measurements are made in the laboratory and have not yet been validated in the ambulatory setting.

In 1994 the American Sleep Disorders Association (ASDA) published standards and a review of the available literature at that time on nonpolysomnography methods for diagnosing sleep apnea.⁷⁷ That report pointed out that there were more than 25 portable systems marketed, but

validation studies were few. Most studies had very few subjects, and at that time, fewer than 50 were studied unattended at home. Since that report, more diagnostic devices have appeared (and some are no longer made), but still the number of ambulatory-based studies remain small. As pointed out by Flemons and Remmers,⁴⁸ standards for the conduct of studies that investigate diagnostic systems have been previously published.⁷⁸ These standards include (1) an independent blind comparison with a reference standard; (2) an appropriate spectrum of patients; (3) avoidance of work-up bias; (4) methods for performing the test described in detail, allowing for duplication of the study; (5) adequate description of study population; (6) adequate sample size (conservative estimate is that there should be greater than or equal to 200 patients in the study, approximately equally divided between those with and without the condition. This allows for competence intervals of approximately $\pm 10\%$ for estimates of sensitivity and specificity); (7) avoidance of a selection bias—in the case of patients with sleep apnea, this means a consecutive sample of patients referred to a sleep clinic rather than those referred to a sleep laboratory, avoiding filtering of patients; and (8) adequate description of study setting and appropriate setting—for instance, basic descriptors of the study should include whether it is a tertiary referral sleep clinic or a community sleep clinic, types of physicians referring to the sleep clinic, population base, type of patients, etc. Because most portable monitors are intended for use outside of the sleep laboratory, this is the setting in which they should be studied. Still, there are very few studies that meet these criteria.

Summary

Polysomnography remains the gold standard for diagnosis of sleep apnea and other disorders of sleep. However, depending on the prevalence of sleep apnea in the population in question and the diagnostic device used, an ambulatory strategy can be adopted. All patients, whether symptomatic or asymptomatic, can be stratified according to history, physical examination, and clinical prediction strategies. The probability of sleep apnea could be estimated, and where there is a moderate to high probability, portable monitoring may confirm the suspicion and subjects can

immediately go on to treatment. If there is no sleep apnea and patients are asymptomatic, it can be argued that no further testing is necessary and only follow-up is required. Symptomatic patients would go on to polysomnography. If the pretest probability for sleep apnea is low, polysomnography would be used only for symptomatic patients.

There have been no long-term outcome studies of such an approach. Individual clinicians will have to apply this algorithm within the confines of the local resources, patient expectations, and clinical practice.

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