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Review

Sleep disorders in the elderly

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Abstract

Sleep disorders and sleeping difficulty are among the most pervasive and poorly-addressed problems of aging. As the population ages, a burgeoning cadre of seniors will seek attention for sleeping difficulties and sleep disorders. Sleep changes with age, and sleeping problems and disorders generally increase with aging. At present, health care professionals are not receiving adequate preparation and training to help the elderly cope with age-related sleeping problems, and several specific areas are ripe for investigation.

Keywords: Geriatrics; Insomnia; Sleep-disordered breathing; Apnea; Restless legs syndrome; Hypnotics

1. Sleep changes with age

Several investigators have defined normal changes that occur with aging [1–4]. Sleep becomes more fragmented, and both arousals and awakenings increase. There are increased numbers of sleep stage shifts, indicating difficulty in maintaining states and stages. There are fewer REM/non-REM cycles, and ultimately reduced sleep efficiency (the ratio of time spent sleeping to time spent in bed). In a carefully-done study of 149 men aged 16–83, Cauter and colleagues found that total sleep time decreased on average by 27 min per decade from mid-life until the eighth decade, although sleep period time was not affected by age [4].

Slow wave sleep (SWS) decreases from young adulthood to middle age (from 18.9–3.4% of total sleep time), with a compensatory increase in stages 1 and 2 non-REM sleep [4]. In Cauter's study REM sleep was reduced by about 50% in late life vs young adulthood, but there were no further significant changes in slow wave sleep after age 50. Age-related decreases in growth hormone (which is secreted in association with SWS) followed a parallel course to that of SWS, with the majority of decrement of GH secretion occurring during young adulthood. On the other hand, age-related increases of cortisol secretion appear to follow a time course similar to that of REM sleep. Increases in evening cortisol did not occur until the fifth decade [4]. In further analysis, the authors suggested that age-related changes in the somatotropic (GH) and corticotropic axes may partially result from decreased sleep quality.

Traditionally, it has been believed that many older people 'phase advance,' i.e. experience a forward shift of the circadian rhythm. In fact, older adults do often report getting sleepy earlier in the evening and waking

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up earlier in the morning than they did when they were younger. One of the most common complaints in this age group is, in fact, early morning awakening [2]. Recent work which controlled for the confounding effects of sleep, changes in posture, and light exposure with aging has suggested that there is no age-related reduction of the intrinsic period of the human circadian pacemaker. However, the amplitude of the rhythm does decrease, which may result in the increased napping seen during the day and the increased frequency of awakenings during the night [5].

Significant reduction in sleep duration and consolidation do develop with aging, and sleep is particularly disrupted when attempted on the rising limb of the temperature curve, suggesting that elderly are more sensitive to arousal signals from the circadian pacemaker. Czeisler and colleagues suggest that both the internal circadian phase advance of wakening and the reduced sleep consolidation of aging are the result of age-related reduction in the promotion of sleep by the circadian pacemaker and reduced homeostatic pressure for sleep, perhaps reinforced by early morning light exposure [5].

Development of health problems also impacts on sleep in the elderly. In particular, nocturia, arthritis, headache, gastrointestinal illness, bronchitis, depression, cardiovascular symptoms, diabetes, menopause, osteoarthritis, and medication side effects have all been shown to disrupt sleep in the elderly [1].

There is much controversy about whether there is actually decreased sleep need with aging [1]. However, older adults who are healthy tend to both get and need about as much sleep as they did when younger, although they may have different sleep architectures and their sleep may be distributed differently during the 24 h period [4,6].

2. Sleep complaints in the aged

Sleep complaints are common in the geriatric age group [6], with more than half of the elderly endorsing a complaint about their sleep quality. The most common complaint is difficulty with maintenance of sleep. Although women are more likely to complain of sleep difficulty than are men, their sleep may actually be better preserved than that of their male counterparts [7]. Reports of poor sleep correlate strongly both with health complaints and with depressive symptoms [6].

The annual incidence rate of insomnia in those 65 years or older is approximately 5% [8]. Risk factors for sleeping difficulty in the elderly are depression, respiratory symptoms, disability, fair to poor perceived health, widowhood, and use of prescribed sedatives. Foley et al. [9] estimate that only 7% of the incident cases of insomnia in the elderly occur in the absence of one of these risk factors. The relationship between sleep disturbance and depression in the elderly is especially strong. It is difficult to determine whether depression causes insomnia or vice versa, but a study of 7954 respondents by Ford and Kamerow suggests that unremitting insomnia causes depression [10].

3. Effects of sleep loss and sleep disturbance on human function

Sleep restriction and insomnia lead to impaired mood, reduced vigilance, deterioration of memory and concentration, and an increased risk of automobile accidents [11–16]. Sleep deprivation has also been shown to increase the collapsibility of the upper airway [17] and to reduce respiratory drive [18]. Sleep loss also impairs performance on pulmonary function testing both in healthy older humans [19], and in older patients with chronic obstructive pulmonary disease. [20]. Further, severe insomnia may be a risk factor for mortality [21]. It is tempting to postulate therefore that the sleep loss which almost invariably accompanies aging might also contribute to the increased prevalence of sleep-disordered breathing in this group. Research studies will need to test this hypothesis.

Ancoli-Israel and Roth showed that most people with insomnia don't seek help for the problem, but self-medicate with alcohol or over-the-counter aids [22]. Further, Meissner and colleagues documented that almost half of a group of mostly adult men admitted to a Veterans administration hospital had a significant sleep complaint when administered a questionnaire, but none of these patients records included mention of any patient symptom related to sleep [23]. Older patients, particularly those with dementia, may

have sleep disturbance with resultant interruption of the sleep of their caregiver(s). Since interrupted sleep of the spouse or caregiver is a risk factor for nursing home placement [24], it is imperative for clinicians caring for geriatric patients to recognize that sleep disturbances are common in this group but not normal, and that comprehensive care means addressing sleep issues, as well as medical issues.

4. Treatment of sleeping difficulty in the elderly

4.1. Non-pharmacologic treatment

Standard nonpharmacologic approaches to insomnia in the older person include exercise, a regular schedule (particularly rising time), reduced or no napping, exposure to bright outdoor sunlight (particularly in the late afternoon or early evening), and avoidance of caffeine, alcohol, and stimulant medications near bedtime [2,21,25,26].

Exercise has clearly been shown to be beneficial in promoting sleep in a group aged 50–76 years [27], and physical fitness benefits not only sleep quality, but also depressive symptoms, bone density, coordination, balance, arthritis, and muscle strength [28]. Even low intensity social and physical activity (such as gentle stretching and board games) improves subjective and objective sleep quality and daytime performance of elderly [29].

Although avoidance of napping is a standard part of sleep hygiene, there is actually very little solid data to support this approach [30]. One small study of daytime napping compared with television as a control found that the napping improved performance, decreased subjective sleepiness, attenuated EEG alpha band activity, and was associated with a significant decline in diastolic blood pressure [31]. Daytime napping was not associated with impaired nocturnal sleep in another small study (notably in Italians, where siestas are part of the culture for all age groups) [32]. Further, in patients genetically predisposed to Alzheimers disease, naps up to 60 min may have a protective effect, whereas habitual napping for more than an hour increased the risk of Alzheimers disease mortality [33]. The questions, therefore, may not be whether to nap, but rather how short or long the nap should be.

A more recent study suggested that daytime napping might be a risk factor for mortality, perhaps because it is a marker for significant nocturnal sleep disturbance, or because blood pressure declines as it does during sleep at night, therefore increasing the risk of cardiovascular and cerebrovascular events [34]. In a prospective population-based cohort of the elderly, the siesta seemed to be an independent predictor of mortality. The authors were careful to point out that it is unclear whether this association is causal. Critics of this study suggested that many cultures take siestas and many hospitals encourage napping behavior without the serious consequence of death. Proponents of napping suggest than an afternoon nap might represent a stress-coping mechanism that provides a protection against coronary artery disease [35,36]. It is important to note that in countries where siestas are common practice, people often go to bed much later and, in a 24-h period, sleep the same amount, albeit in two bouts, as those who do not take siestas. Additional research on napping behavior is needed to understand these relationships. In the meantime, in terms of good sleep hygiene, it is recommended that naps be limited to 30 min in the early afternoon for older people with sleep difficulties [37].

Behavioral therapy, including relaxation, stimulus control, sleep restriction, and combined cognitive-behavioral therapy (CBT), has recently been reviewed by Stepanski [37]. Among behavioral approaches to sleep disturbance in the elderly, CBT appears to have particular promise. In studies specifically addressing older adults, Morin found CBT with or without pharmacotherapy to reduce wake after sleep onset and sleep efficiency [38,39].

Bright light (1000 lux) exposure for one hour in the morning improved self-reported alertness, mood, motivation, and sleep quality in a small group of women whose average age was 67 years [40] 8000 lux morning bright light decreased the proportion of awakening time in the first one-third of the night, but increased awakening in the last one-third of the night [41]. In general, for older adults with advanced sleep phase, bright light exposure ($\geq$1000 lux) in the evening or late afternoon is recommended to delay the sleep phase [42].

The number of medications prescribed increases directly with age, and most drugs affect either nocturnal sleep or daytime alertness. Some attention to the

need for each drug and also to the timing of medication administration may be helpful. For example, diuretics should be given in the morning, as should the stimulating serotonin reuptake antagonist, fluoxetine. Sedating antihypertensives or antidepressants should be given in the evening.

Although there is little evidence that melatonin can improve sleep of insomniacs younger than 65 years of age, it may be effective for disrupted sleep in the elderly. Melatonin levels appear to decline with aging, and are lower in elderly insomniacs than in age-matched controls. Both insomnia symptoms and wrist actigraphy show improvement in geriatric insomniacs following treatment with varying doses of melatonin [43]. However, Youngstedt et al. [44] found that low melatonin production appears not to be an important factor in insomnia in the elderly. Some investigators have suggested that a combination of bright light and melatonin might be beneficial for treatment of sleeping disorders in the institutionalized demented elderly, a notoriously difficult group to treat [45]. However, because it may affect vascular tone and the effective dose is probably much smaller than what is currently being sold in health food stores, melatonin should be used cautiously if at all in the elderly, and always with the warning that it is not monitored by the FDA [2].

4.2. Hypnotics

Although conventional wisdom advises against the use of pharmacologic agents in the elderly and for those with disorders of respiratory control, the use of hypnotics among institutionalized patients is 34% [46,47]. Among independently living individuals over the age of 65, benzodiazepine use is 12% for women and 9% for men [48]. In a group of 222 veterans queried about sleep complaints at the time of admission to a general medical ward, 34% had a complaint of insomnia, and a third of these were taking hypnotic medication [23]. Thus, we actually have accumulated a fair amount of experience with hypnotic use in the sick and elderly without ever condoning it.

The Cardiovascular Health Study is an ongoing, prospective study of 5201 adults, aged 65 and older that was specifically designed to identify factors related to the onset and course of coronary heart disease and stroke. As part of the Cardiovascular Health Study, Newman and colleagues [48] reported that benzodiazepine use was associated with daytime sleepiness in men, and warned, 'not surprisingly…the use of benzodiazepines in our cohort was associated highly with trouble falling asleep and, perhaps, with residual daytime sleepiness. Clinicians must consider these risk when prescribing benzodiazepines for older patients,' (p. 6) The following year the same investigators, this time led by Whitney [47] reported more detail about sleepiness in this group of subjects. Using the Epworth Sleepiness Scale [49], they more closely evaluated sleepiness in these subjects. In this study, they found no association between benzodiazepine use and sleepiness in men; in fact, the women who took benzodiazepines reported less daytime sleepiness. They then conservatively concluded, 'However, it is generally accepted that EDS is commonly observed in the elderly after hypnotic use because of a 'hangover' effect from the long half-life of many of these medications….A clinical trial will be necessary to determine whether or not occasional use of hypnotics for insomnia results in more or less daytime sleepiness in the elderly,' (p. 35). In fact, such clinical trials have been done with the newer, short-acting non-benzodiazepine hypnotics such as zolpidem and zaleplon; they rarely cause daytime sleepiness or hangover.

Much controversy and not a little confusion surrounds the issue of hypnotic treatment of insomnia. In this brief discussion, we will address pharmacologic therapies for insomnia as 'non-hypnotics,' (e.g. antidepressants, antihistamines, and antipsychotics), long-acting benzodiazepines (e.g. flurazepam, diazepam), short and intermediate-acting benzodiazepines (e.g. triazolam, temazepam), and nonbenzodiazepine type-1 selective gamma-aminobutyric acid (GABA) receptor agents (e.g. zolpidem and zaleplon).

Physicians cite concern about adverse reactions to hypnotics as justification for use of antipsychotics, antidepressants, and antihistamines for the complaint of insomnia. As a result, treatment of sleeping difficulties in the sick and old often is not addressed, or is addressed ineffectively. Walsh and Schweitzer recently reported 10-year trends in the treatment of insomnia [50]. They noted that: (1) Pharmacologic treatment of insomnia fell dramatically between 1987–1996; (2) The use of antidepressants, notably trazodone, has grown substantially. The authors

present evidence that the use of antidepressants in insomnia has grown because of concern about dependence rather than because of recognition and treatment of depression in those reporting insomnia. Trazodone is associated with significant side effects, including daytime somnolence, orthostatic dizziness/hypotension and priapism [51–53]. Further trazodone appears to improve sleep in the non-depressed patient only in the short term and is less effective than zolpidem [54]. In the standard text of sleep medicine, Roehrs and Roth say, 'Although studies have shown that H1 antihistamines do increase sleepiness in healthy normal individuals, no studies have clearly established the dose range over which hypnotic effects in people with insomnia might be found. Low-dose antidepressants have also been used as hypnotics. It is the sedating side effect of the drug that is being sought. However, the antidepressants have cardiotoxic side effects and anticholinergic side effects that make this class of drugs a poor choice as a hypnotic in the absence of clinical depression' [55].

Adverse reactions to benzodiazepines has been addressed by several studies. Primary side effects of the benzodiazepines are residual effects, amnestic effects, discontinuation effects, and dependence [55,56]. In the elderly, the risk of falls, cognitive impairment, and respiratory depression are of particular concern. In an analysis of sedative/hypnotic use and adverse reactions carried out in a 1000-bed teaching hospital over a 3 year period, Mendelson et al. [55] documented an adverse reaction frequency ranging from 0.05% of lorazepam doses to 0% of chlorazepate doses. Most of these 'adverse reactions' could be viewed as an extension of the therapeutic effect. In a related paper, these authors correlated the use of sedative/hypnotic medication with falling down in the hospital, and found that the rates of falls with antidepressants were comparable to those of benzodiazepines, and that temazepam and alprazolam had the highest rates of falls, while diazepam, triazolam, chlordiazepoxide and chlorazepate had very low rates of falls [56]. In a large and careful study of nursing home residents, Ray et al. [57] concluded that elimination half-life of the benzodiazepine is an important determinant of fall risk; those drugs with a half life of less than 12 h had a reduced rate compared with that of longer-acting benzodiazepines.

With regard to respiratory depression, older studies suggested that a long-acting benzodiazepine (flurazepam) might increase the risk or severity of sleep-disordered breathing [58–60], but more recent studies suggest that they do not [61]. Concerns about dependence and blunted respiratory drive have probably been significant factors in limiting hypnotic use in chronic obstructive pulmonary disease (COPD) patients. In truth, there is very little data documenting adverse complications in this situation, despite a wealth of clinical experience.

Development of newer selective short-acting type-1 GABA benzodiazepine receptor agonists has rendered the argument about benzodiazepine sleeping aids and their risk/benefit ratio in the elderly somewhat academic. Zaleplon and zolpidem have inactive metabolites, short half-lives, and absence of respiratory depressive side effects [62]. In carefully-controlled trials and in post-marketing surveillance, these drugs appear not to result in increased risk of falls, daytime sedation, driving impairment, tolerance, rebound, respiratory depression, or exacerbation of sleep-disordered breathing [62–68]. Therefore a more germane issue is whether or not it is ethical to withhold such agents from sleepless individuals in whom efforts should be focused on improving quality of life.

Sleeping difficulty, like pain, is probably inadequately evaluated and treated in the elderly. New hypnotic agents have minimal side effects and excellent efficacy. We may be missing opportunities to improve the quality of life in aging individuals by failing to anticipate, ask about, evaluate, and treat sleeping difficulty.

5. Sleep apnea/sleep-disordered breathing

Against the backdrop of deteriorating sleep in the aging human is the high prevalence of sleep-disordered breathing (SDB), or obstructive sleep apnea hypopnea syndrome (OSAHS).

5.1. Clinical presentation

The clinical history of OSAHS almost always includes snoring, which is the most common symptom in patients with SDB. However, the majority of people who snore do not have sleep apnea. Snoring accompanied by apnea, snorting, gasping, and choking

during sleep is predictive of OSAHS. Witnessed apneas are more predictive of SDB than are self-reported episodes of waking up gasping for breath, which may be symptoms of other diseases such as congestive heart failure, gastro-esophageal reflux disease, nocturnal asthma or panic disorder.

Excessive daytime sleepiness should increase the suspicion for OSA. Subjective sleepiness may be assessed by use of the Epworth Sleepiness Scale, which has been validated in clinical studies and correlates roughly with objective measures of sleepiness [49]. Patients both under and over report their own sleepiness, so querying their significant 'others' may also be useful. An Epworth score greater than 10 suggests significant daytime sleepiness, and although it is not specific for OSAHS. Patients who report falling asleep while driving should be evaluated for sleep disorders including SDB. Many sleep problems may result in falling asleep while driving, including sleep deprivation. However, because of the threat that this symptom poses to the patient and to others, clinicians should have a low threshold to refer sleepy drivers to a sleep center for thorough evaluation. A history of hypertension should also increase the clinicians suspicion for OSAHS. Four very recent studies have strongly linked sleep apnea to hypertension [69–72]. These studies strongly suggest that SDB may be a risk factor for hypertension and consequently for cardiovascular morbidity.

The physical finding that is most predictive of OSAHS is central obesity. A Body Mass Index (BMI) of 28 kg/m^2 in both men and women should increase the suspicion for OSAHS. Roughly 40% of those with a BMI over 40 and 50% of those with a BMI over 50 have significant sleep-disordered breathing [73]. Measures of central obesity such as neck size are very useful in predicting the presence of OSAHS. Men with a neck size of 17″ (43 cm) or greater and women with a neck size of 16″ (41 cm) or greater are very likely to have OSAHS confirmed by overnight polysomnography. In the elderly though high BMI is often less of an issue, it is still the best predictor of the presence of SDB [74].

Sleep apnea is about twice as common in men as in women [73–75]. This is probably due at least in part to hormonal influences. Androgens stimulate truncal deposition of body fat including the neck area. In addition, sex hormones modulate upper airway muscular activity during sleep. Whereas progesterone appears to have a salutary effect on SDB [76–80], testosterone may worsen it [81,82]. In clinical studies, medroxyprogesterone has resulted in modest improvements in some indices of sleep-disordered breathing in studies of menopausal or post-menopausal women [76,77], but appears not to be beneficial in non-hypercapneic men [78,79]. Endogenous testosterone-producing tumors have been associated with the reversible development of obstructive sleep apnea in women [81]. Exogenous testosterone administration causes the development of OSAHS in some hypogonadal men [82]. Consistent with these findings is the age distribution of the increased prevalence. The male predominance for sleep-disordered breathing is most pronounced during middle age. Before puberty, the male to female ratio for SDB is roughly 1:1. After menopause, the incidence of SDB rises rapidly in women, and the prevalence difference between the sexes is small with a slight male predominance. In one prevalence study of SDB in the elderly, 28% of men and 19% of women had SDB [74].

SDB is seen more commonly in patients with a family history of SDB. In a study by Pillar et al. [83] 41% of the offspring of 45 randomly selected patients with OSAHS had a AHI $>$ 5 and 13.3% had a AHI $>$ 20. Other large family studies have shown a much higher prevalence of OSAHS among offspring of family members with OSAHS when compared to the general population. It is likely that the inheritance of OSAHS is multigenic, and its development depends on environmental as well as genetic factors. The clinical relevance of this finding may be that older patients with signs and symptoms of sleep-disordered breathing need to be queried about a diagnosis of sleep apnea in their middle-aged offspring, who may be more likely to have been diagnosed.

SDB may be more prevalent in certain races. Redline et al. showed an increased prevalence of SDB in young ($<$25 years old) African Americans [84]. Ancoli-Israel et al. [85] demonstrated that the prevalence of SDB was no different in older African-Americans than in older Caucasians, but that SDB was significantly more severe with a twofold relative risk in elderly African Americans. The cause of these racial differences is still not well defined, but it could not be accounted for by differences in BMI, alcohol, or tobacco use. It is hypothe-

sized that some of the differences may be secondary to the high prevalence of hypertension seen in African-Americans.

Alcohol and sedative medications decrease upper airway neuromuscular drive, predisposing to recurrent upper airway collapse. Tobacco smoke causes an increase in nasal and pharyngeal irritation, resulting in narrowing of the upper airway. OSA has been shown to be more prevalent in current smokers than in non- or ex-smokers [86]. Removing the influence of these agents is the simplest intervention to decrease the risk for SDB.

5.2. Diagnostic definitions and techniques for OSAHS

The gold standard for the diagnosis of OSAHS remains overnight polysomnography (PSG). A nocturnal PSG includes recordings of airflow, ventilatory effort, oxygen saturation, electrocardiogram, body position, electromyography (EMG), and electroencephalography (EEG). In standard, laboratory-based polysomnography, a technician is present for the entire study to monitor the patient. A single overnight study is generally sufficient to diagnose OSAHS. In many instances, the level of SDB is severe enough that the diagnosis of OSAHS can be established early in the study. In this event, a 'split-night' study may be performed, where the second half of the study is used to titrate treatment (positive airway pressure) for OSAHS.

A normal overnight study makes significant SDB very unlikely, but it does not completely exclude it. Factors which may contribute to a false negative sleep study include: (1) poor quality sleep during the study (particularly absence of Rapid-Eye Movement sleep), (2) sleeping on one's side during the study instead of one's usual supine sleeping position (sleep apnea tends to be most severe in the supine position), (3) omitting one's usual alcohol or sedative agent on the night of the study, which may precipitate SDB in many patients, (4) insensitive monitors of airflow and/or respiratory effort, which allow subtle decrements in airflow and/or marked increases in respiratory effort to go undetected.

The apnea-hypopnea index (AHI) is the most commonly used criterion to quantify the severity of and to establish the diagnosis of OSAHS. The AHI is defined as the sum of episodes of apnea and hypopneas divided by the hours of sleep. Many clinicians and investigators use the term, 'respiratory disturbance index,' or RDI, interchangeably with the AHI. In adults, apnea is defined as a cessation or near cessation of airflow for 10 s or longer. In obstructive sleep apnea, this cessation of airflow occurs despite continued ventilatory efforts. Hypopnea is less well defined. An hypopnea is a disturbance in airflow that results in a physiologic consequence such as an oxygen desaturation and/or an arousal. This term has had widely varying definitions in the literature and in clinical practice [87]. The amount of airflow reduction required (from any to $>50\%$), the requirement for or the degree of oxygen desaturation (from 0 to at least 4%), and whether or not an arousal is required have been among the discrepancies in working definitions of hypopneas reported in published literature. In addition, there has been considerable variation in recording techniques for measures of airflow and respiratory effort. This has almost certainly resulted in varying sensitivity for detection of sleep-disordered breathing events.

Like most conditions in medicine and in nature, sleep-disordered breathing is a spectrum with no clear boundaries between pathological and normal. Measurement tools and definitions of indices of SDB have been neither precise nor standardized. This lack of standardization and precision has resulted in confusion both in clinical practice and in research about how to measure and to quantify sleep disordered breathing, what the consequences of SDB are, and what benefits intervention confers.

To address these issues of definition and technology, the American Sleep Disorders Association (now American Academy of Sleep Medicine) developed a task force in conjunction with the European Respiratory Society, the Australian Sleep Association, and the American Thoracic Society. After wide circulation, including a presentation at both the Associated Professional Sleep Societies and at the American Thoracic Society Meetings in 1998, the document was published in Sleep in 1999 as 'Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research' [88]. Despite the fact that this report was accompanied by an editorial declaring it to be applicable primarily to clinical research, it is bound to be unifying and widely accepted in clinical prac-

tice. Among the findings in the report are: (1) Thermocouples do not truly measure airflow; respiratory inductive plethysmography and pneumotachography (which currently are rarely used in clinical practice) are more reliable and better-validated. Nasal pressure also has been recently validated as a more quantitative measure of airflow than are thermocouples [89]. (2) Hypopnea is defined as 50% reduction in airflow (measured with a validated technique) or a reduction in airflow associated with a 3% fall in SaO_2 and/or an arousal. (3) 'respiratory effort-related arousal (RERA)' event is defined as 'a sequence of breaths characterized by increasing respiratory effort leading to an arousal from sleep, but which does not meet criteria for an apnea or hypopnea'.

Further, the report redefines the syndrome of sleep disordered breathing. Previous nosology included only apneas in the definition. Thus, insurers typically (and with some justification) did not pay for treatment for sleep-disordered breathing in patients who did not meet the published criteria of 30 or more apneas in a night of sleep. As defined in the new recommendations, the obstructive sleep apnea-hypopnea syndrome exists when clinical features are present and overnight monitoring demonstrates five or more obstructed breathing events per hour of sleep, including any combination of apneas, hypopneas, or respiratory event related arousals (Table 1). While imperfect and subject to revision as our knowledge grows, these recommendations go a long way toward unifying the field and standardizing our approach to diagnosis of SDB. All clinicians working in the field of sleep disorders are encouraged to read this report, and to share it with medical insurance companies!

Table 1
Diagnostic criteria for the obstructive sleep apnea-hypopnea syndrome (OSAHS)[a]

The individual must fulfill criterion A or B, plus criterion C

A. Excessive daytime sleepiness that is not better explained by other factors
B. Two or more of the following that are not better explained by other factors:
  Choking or gasping during sleep
  Recurrent awakenings from sleep
  Unrefreshing sleep
  Daytime fatigue
  Impaired concentration; and/or
C. Overnight monitoring demonstrates five or more obstructed breathing events/h during sleep. These events may include any combination of obstructive apneas/hypopneas or respiratory effort related arousals

[a] Adapted from Reference [88].

5.3. Sleep-disordered breathing and aging

Several studies have investigated the prevalence and natural history of sleep-disordered breathing in the elderly. Breathing disturbances during sleep increase with increasing age. Early studies of the frequency of sleep apnea in the elderly found prevalence rates of 24–73% [90]. In the largest series on the elderly, Ancoli-Israel, Kripke and colleagues have demonstrated the following prevalence rates for minimal diagnostic criteria ($AI > 5$) for independently-living adults over age 65: 24%; acute-care inpatients: 33%; elderly nursing home patients: 42% [91–93]. Both longitudinal [94–97] and cross-sectional [98,99] studies have shown that sleep apnea prevalence increases or is stable with increasing age. While clinical populations have tended to find a peak prevalence of clinically-significant sleep-disordered breathing in middle age [99], population-based studies have found increasing levels of sleep-disordered breathing with aging [1,100]. This occurs even though obesity is less prevalent with aging [101,102]. There may be differences in the effect of obesity as a risk factor for SDB by age and gender; Redline [100] found that a clinical population with sleep apnea included women that were younger and heavier than men, but in the population-based sample, women with sleep apnea were older but weighed the same as apneic men. Young and Bliwise [1,103] suggest that obesity may be a more important risk factor for SDB in middle-aged women than it is in men, whereas age may be a more important risk factor for men.

There are complex and multiple reasons for the increase in sleep-disordered breathing with age. Central sleep apnea increases, probably because of increasing cardiovascular and neurologic disease with aging [104–106]. Bixler found a peak prevalence of clinically significant obstructive sleep apnea in middle age with increasing levels of central apneas and decreasing severity with aging [99]. However, most investigators have found that the apneic events in older individuals are predominantly obstructive

[1,90]. Sleep apnea also appears to be increased in dementia [98,106–108] which increases with aging, but it is unclear if the apnea causes the dementia or vice versa [110]. Levy et al. and Bliwise summarize the changes in airway structure, sleep, and respiratory drive which might contribute to increasing sleep-disordered breathing with aging [1,90]. It might also be that the varying and imprecise diagnostic criteria for sleep-disordered breathing do not adequately distinguish between true pathology and normal changes with aging, and that we have branded normal changes of aging as pathologic based on inappropriate criteria [87,88,110–112].

Studies of the natural history of sleep-disordered breathing lend some insight into this last issue. Results from clinical populations suggest that SDB in the elderly has minimal effect on mortality or morbidity, but population based studies suggest otherwise. In a study of SDB and mortality in older adults, Ancoli-Israel et al. [113] found that those with more severe SDB (defined as an RDI >30) had significantly shorter survival than those with mild-moderate or no SDB. However, RDI was not a predictor of death while age, pulmonary, and cardiovascular disease were. This group also found that RDI was highly predictive of survivorship in very old (mean age 84) women in a nursing home [114]. Bliwise et al. found a mortality ratio of 2.7 (CI 0.95, 7.47) for those with an RDI of over ten events/h in a cohort of 198 non-institutionalized individuals (mean age 66) who were followed for 12 years [115]. Hoch et al. reported that SDB was associated with an excess mortality rate of 450% in elderly patients with depression and cognitive impairment [116]. However, Mant et al. [117] found that RDI over 15 did not predict death in 163 non-demented retirement village residents, and Phillips et al. found no excess mortality in healthy seniors with AHI > 5 followed for 5 years [118]. Further, He et al. [119] showed that an AHI >20 predicted increased mortality in those under 50, but not those over 50.

In sum, two types of sleep apnea may exist. The first type is the type primarily seen in clinical sleep centers, and is age-related. It peaks in prevalence at about age 55, and is associated with increased morbidity and mortality. The second type is an age-dependent type and it is unclear if it is associated with the same increase in morbidity and mortality.

5.4. When to treat OSAHS in the aged?

While SDB in the elderly might not be the same thing as SDB in clinic patients, those who have symptoms or findings suggestive of sleep-disordered breathing should be treated. Patients with higher levels of sleep disordered breathing (AHI >20 or 30) deserve a trial of treatment. In patients with milder levels of SDB, treatment should be considered if morbidity associated with SDB is present such as daytime sleepiness, cognitive dysfunction, nocturia or hypertension. There is some level of pathologic SDB above which treatment will be both beneficial and generally acceptable. This level is not clearly established. For now, we use our best clinical judgment to decide when it is appropriate to look for the diagnosis and initiate treatment in the geriatric population.

Despite the confusion about what constitutes a 'pathological' level of sleep-disordered breathing in the elderly, clinically significant OSAHS certainly does exist in this age group [109]. Given the debate about the clinical significance and putative benefits of treatment of OSAHS in general [120], it is difficult to base diagnostic criteria or treatment decisions on a single level of AHI in this age group.

Certain conditions should raise concern about the possibility of OSAHS and need for treatment in older patients. Although sleepiness per se is a worthless symptom in any age group, having an automobile accident or near-accident due to sleepiness should raise a red flag. Middle-aged drivers demonstrate the lower rates of fatal motor vehicle accidents than elderly or young drivers [121]. Drivers over 60 years of age who are involved in road crashes are more likely to be 'at fault,' more likely to have medical conditions, but much less likely to be intoxicated than their younger counterparts [121,122]. Thus, as with any age patient, the older patient who is suspected of sleep apnea or excessive daytime sleepiness ought to be queried about car wrecks and near-miss accidents.

Hypertension is a common medical problem in the elderly, and whether to ascribe it to OSAHS and to treat SDB on that basis has been controversial [120]. However, four very recent large epidemiologic studies that have been controlled for important confounders including obesity have clearly demon-

strated that obstructive sleep apnea hypopnea syndrome is a risk factor for hypertension [69–72]. Lavie et al. [69] clearly demonstrated a 'dose-response' relationship for apnea severity and blood pressure elevation: each additional apneic event per hour of sleep increases the odds of hypertension by about 1%, and each 10% decrease in nocturnal oxygen saturation increases the odds by 13%. In a report of 6132 subjects from the Sleep Heart Health Study, 46.7% of whom were 65 years or older, Nieto et al. [70] found an odds ratio for hypertension of 1.37 (CI 1.03–1.83), comparing the highest category of AHI (>30/h) with the lowest (<1.5/h). Grote et al. [71] reported an increasing risk of hypertension with increasing AHI, and noted that there was an increased likelihood of SDB-associated hypertension in younger subjects. In a prospective four year study of 709 subjects, Peppard and colleagues found that even low levels of SDB (AHI 0.1–4.9) increased the risk of subsequent development of hypertension compared to an AHI of 0 [72]. Berry et al. [123] found an association between mild levels of SDB and hypertension in healthy seniors. Thus, hypertension, particularly hypertension that is difficult to control should tip the balance in favor of sleep apnea investigation and treatment.

The issue of sleep apnea and cognitive dysfunction is more clear-cut. Severe sleep-disordered breathing (AHI > 40) is associated with neuropsychological deficits, some of which may be reversible with treatment [124–126]. However, milder levels of sleep-disordered breathing (RDI 10–20) do not appear to cause cognitive dysfunction in the absence of sleepiness [124]. Both Cheshire [125] and Kim [126] found a correlation between AHI and neuropsychological test results. Psychomotor efficiency and visual vigilance appear to be most sensitive to SDB [126]. Deterioration in cognitive performance correlates both with degree of hypoxemia and with degree of sleep fragmentation [125]. The association of SDB with dementia, then, depends on degree of SDB. Kim et al. estimate than an AHI of 15 is equivalent to the decrement of psychomotor efficiency associated with 5 additional years of age, or 50% of the decrement associated with hypnosedative use [126]. In institutionalized demented elderly, 70% had SDB. Sleep apnea was significantly correlated with all subscales of the dementia rating scale. In addition, those with severe dementia had significantly more severe SDB than those with mild or no dementia. Conversely, those with severe SDB had significantly more severe dementia [108]. Bliwise speculates that the dementia is of vascular origin [1] because of the association between OSAHS and hypertension, arrythmias, and decreased cerebral perfusion. Although depression is frequently cited as a result of OSAHS, research diagnostic criteria-defined depression was no more common in elderly subjects with an AHI > 5 than in controls (although dementia was) [127]. These data suggest that evaluation and treatment of the older patient who has cognitive dysfunction and suspected sleep apnea would seem prudent. (Logistically, however, application of either polysomnography or nasal CPAP treatment is not easy in the demented patient).

Nocturia, defined as urination at night associated with the interruption of sleep [128], increases with age, affecting 80% of those 80 years of age and older, and results from many causes. Nocturia is well-associated with OSAHS and may improve with CPAP treatment.

Finally, there is the issue of whether or not to search for and to treat OSAHS in the elderly to prevent excess mortality. As outlined above, population-based studies of 'healthy elderly' have tended not to find excess mortality associated with OSAHS that is found in non-institutionalized, non-demented seniors. [119–121,129,130].

In sum, the findings of sleepiness leading to accidents, cognitive dysfunction, nocturia and perhaps hypertension in the elderly patient with mild levels (AHI < 20) of sleep-disordered breathing might be reasonable indicators to attempt treatment. Patients who have higher levels of SDB (AHI > 20 or 30) probably deserve a trial of treatment. It is important, however, not to focus on the AHI alone. The degree of oxygen desaturation and sleep disturbance are important determinants of the damage. Treatment decisions ought to take these variables into account.

5.5. How to treat OSAHS in the aged

Standard treatment of OSAHS is nasal continuous positive airway pressure (CPAP), which has a compliance rate of approximately 50% in all age groups [131]. Although most studies have not compared

CPAP compliance among age groups, one recent study of over 100 patients found that the non-compliant group was older than the compliant group (58 vs. 53 years) [132] Several factors, including milder levels of SDB (which is associated with poorer compliance), cognitive dysfunction, impaired sleep, restless legs syndrome, and nocturia might be expected to adversely affect compliance in this group. Nevertheless, CPAP is safe, reasonably inexpensive, and effective in reducing many of the sequelae of OSAHS.

Oral devices are indicated for mild sleep apnea, snoring, and sleep apnea in which no other form of treatment is available or tolerated. They are a particularly useful option for geriatric patients, and some of them can be made to fit over dentures [133].

Surgical treatment, most commonly uvulopalatopharyngoplasty (UPPP), is widely employed in patients who are CPAP intolerant. It has a success rate of approximately 50%, however, and age > 50 is associated with poorer surgical outcome [134]. Further, the underlying medical condition of many older patients puts them at higher risk for general anesthesia. 'non-invasive' surgical procedures, e.g. laser-assisted uvulopalatopharyngoplasty (LAUP) have not yet been well-evaluated, but appear to have a success rate comparable to that of scalpel UPPP [135]. Radio-frequency volumetric reduction (RFVTR) of the palate has recently been reported as a treatment for sleep-disordered breathing by Powell [136,137] and others [138,139]. RFVTR appears to be safe and less painful than LAUP, but has been used primarily for snoring, rather than for significant obstructive sleep apnea. Because it is a new technique, there are no data available for individuals over 65 years of age. However, in the study that did report RDI's post-operatively, there was actually an increase in SDB [138] after the procedure.

Patients of all ages with SDB need to be advised to quit smoking and to lose weight, if applicable. Many will sleep better in the lateral decubitus position or mostly upright in a recliner.

6. Restless legs syndrome and aging

Restless legs syndrome (RLS) and periodic limb movements of sleep (PLMS) deserve mention here because of their association with OSAHS and their extremely high prevalence in the geriatric population [140,141]. Restless legs syndrome is a collection of symptoms, and can be diagnosed by history. PLMS is defined by electromyographic criteria in the sleep laboratory. Although PLMS is present in about 80% of patients with RLS, it is neither necessary nor sufficient to make the diagnosis [142]. Periodic leg movements occur with a variety of sleep disorders and in asymptomatic individuals. Montplaisir et al. recently reported that 55% of controls, 40% of insomniacs, 30% of hypersomniacs, 80% of narcoleptics, and 85% of RLS patients have a PLMS index (events/h) of over 5 [143]. Recently, clinical criteria for diagnosing RLS have been developed. They are: a desire to move the extremities, often associated with paresthesias/dysesthesias; motor restlessness; worsening of symptoms at rest with at least temporary relief by activity; worsening of symptoms in the evening or night [144]. This disorder probably affects 10–15% of the population, and is strongly associated with increasing age [145–147]. Phillips et al. [148] found an increasing prevalence of endorsement of RLS symptoms by age, with 19% of those aged 80 years or more having restless legs symptoms at least 5 nights per month. Ancoli-Israel, in a population based study of the elderly, found PLMS in 44% [140]. OSAHS, renal failure, anemia, many medications, diabetes, cigarette smoking, and obesity all predispose to this condition [145–147]. Its presence should be considered in geriatric patients presenting with sleeping difficulty.

In a study of 222 consecutive adults (mean age 60 ± 14 years) admitted to a general medical ward in a veterans affairs tertiary care hospital, Meissner [23] documented that 21% had either restless legs or a combination of leg jerks and leg kicking or twitching during sleep, associated with a sleep complaint. In no instance was the presence of this symptom documented in the patients medical record! This study points out that symptoms of RLS are common in sick patients, this diagnosis ought to be considered in geriatric patients presenting with sleeping difficulty.

6.1. RLS treatment

Treatment of RLS/PLMD is by eliminating contri-

buting factors, if possible. Four classes of medications have been successfully used to treat the symptoms of RLS. They are the dopaminergic agents, anticonvulsants, benzodiazepines, and narcotics [148]. The association of RLS with OSAHS is complex, and treatment of OSAHS may relieve PLMS [149].

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