Preface

Sleep Medicine—A Challenging Field With Many New Findings

Sleep disorders have finally reached a point where they are being acknowledged by the various disciplines of the medical community. The obesity epidemic, which has affected children and adults in the industrialized countries, has increased the frequency with which sleep-disordered breathing and its complications are seen. In obese individuals, in particular men, fat deposits have been found to infiltrate the abdomen, resulting in a restrictive chest bellows syndrome. In obese individuals, this restriction has a profound effect on oxygen saturation when they are awake and when they are asleep, especially in the supine position. This effect also becomes most pronounced during rapid eye movement (REM) sleep, when there is a loss of accessory muscle recruitment for breathing. Additionally, fat deposits have been noted to invade the neck, which, in combination with abdominal restriction, further increase the likelihood of upper airway collapse and obstruction during sleep.

The hyperactive adipocyte itself in these obese individuals adds its own degree of pathogenesis. The adipocyte has been found to secrete the leptin, ghrelin, adiponectin, obesin, and other peptides, which play key roles in metabolic regulation. The dysregulation of these peptides in obese individuals may worsen existing health problems and may establish feedback loops, aggravating negative outcomes. Although overweight subjects with snoring and upper airway obstruction during sleep have been increasingly labeled as obstructive sleep apneic patients, it is equally important to realize that these patients present with a more complicated syndrome, in which the roles of the obese abdomen and even more of the adipocyte have yet to be fully appreciated. The cardiac and cerebrovascular associations in this syndrome have been clearly demonstrated, and nasal positive airway pressure continues to be the most viable solution for most middle-aged and older subjects. In younger subjects, maxillomandibular surgery, performed by an experienced specialist, may be the most practical option given the high rate of noncompliance with treatment in this age group.

The role of familial predisposition for the development of upper airway obstruction during sleep has also been demonstrated in many studies in the 1990s. One of the predisposing risk factors has been the familial traits of facial anatomy and morphology. A better understanding of this risk factor has emerged in the past 10 years through the work of orthodontists and physiologists investigating the neuromuscular mechanisms of breathing. In addition to the static effects of...
anatomy on airway opening and collapse, the dynamic effects of dilator muscle contraction (and timing) have been found to play a key role in maintaining airway patency during breathing. In essence, upper airway constrictor muscles normally tense just before inspiration to prevent airway collapse from the negative pressures caused by inspiration. Prolonged turbulent airflow and snoring during sleep have been associated with an impairment of the sensory motor loop of the dilator response to negative intrathoracic inspiratory pressure. The possibility of such permanent neurologic sequelae\textsuperscript{5,6} serves to underscore the importance of early diagnosis and treatment of sleep-disordered breathing in children and young adults.

A consideration in adolescents is the influence of sex hormones, often resulting in enlargement of the tongue muscles and airway soft tissues. Enlarged tonsils and adenoids are commonly identified and easily treatable causes of sleep-disordered breathing in children and young adults. A young child with snoring who is treated with adenotonsillectomy and still has some residual symptoms, however, may show a resurgence of abnormal breathing and snoring after puberty or in early adulthood due to such hormonal changes. With respect to bony or dental anatomy, well-trained orthodontists should be able to identify children with narrow bone structures early and offer treatment to enlarge the airway in eligible subjects. On the other end of the spectrum, the prevention of lifelong health problems, specifically cognitive decline and cardiovascular risk, has not yet received similar attention from the medical community.

In the fight against pain syndromes, ranging from cancer to rheumatologic diseases, as well as in the implementation of methadone programs for drug rehabilitation, the past several years have witnessed a marked increase in opioid consumption. Among many other side effects, opioids have been found to have a profound effect on breathing during sleep. For this reason, special consideration must be given to the impact of opiate use on breathing during sleep and the overall well-being of sleepy patients. Patients with heart failure or opiate use may present with similar problems during sleep: a general decrease in diaphragmatic contraction leading to hypoventilation and abnormal upper airway constriction during inspiration. Although there are tools to address these issues and noninvasively assure normal breathing, positive airway pressure may be detrimental to some heart failure patients. Specifically, in some heart failure patients, positive airway pressure may change preload and afterload in a manner that worsens the condition. There is, however, the capability of identifying these at-risk individuals and tailoring treatment appropriately.

Undoubtedly, insomnia remains one of the most common complaints for most practitioners, and prescription sleep aids place a substantial burden on health care spending. Novel hypnotic agents are continuously being developed, some of which are in entirely different drug classes from existing medications. Although the arrival of novel sleep aids is awaited, there are some closely related compounds that are already becoming available or in the final stages of investigation. Despite the promise of novel sleep agents, the past several years have shown the limited impact of these medications, especially on the complaint of poor sleep. This may be related to underlying problems that emerge during sleep but also may be related to conditioning or other factors these drugs cannot address in the long term. For this reason, behavioral treatments for insomnia have had great success and substantial results have been well documented recently.

Beyond organic illness, motor vehicle accidents continue to be a major cause of fatality in young individuals. Alcohol is a well-known cause of accidents, but
increasingly, sleepiness at the wheel has emerged as an even greater contributor. Sleep deprivation, increasingly common, has been associated with an alarming frequency of “lapses of attention” and “near misses.” Sleep fragmentation related to shift work, regular employment, or an unrecognized organic problem may also be responsible for these accidents; the quality and quantity of sleep should always be considered. Syndromes of sleepiness, which may present with tiredness and fatigue from the time of waking, must be recognized and treated aggressively, with a constant consideration for abnormal breathing during sleep (not solely obstructive sleep apnea) as well as narcolepsy.

Since the discovery that narcolepsy was related to the destruction of a small group of cells in the lateral hypothalamus, many questions have been raised. There is much ongoing research to investigate why this cell loss occurs and what results from the loss of the hypocretin/orexin peptides. The hypothesis that narcolepsy is an autoimmune disorder has recently received increasing support, with the identification of a specific T-cell receptor involved in pathogenesis. In the search for treatment of daytime sleepiness and fatigue, the significant limitations of current treatments have become apparent. Commonly used amphetamine compounds, in addition to elevating blood pressure and exerting many psychiatric effects, have also been known to produce insomnia during use and rebound hypersomnia on daily end of action. Hypersomnia can also be seen periodically in Kleine-Levin syndrome (KLS), which affects adolescents and adults. Less is known about KLS than narcolepsy, but there is an understanding that the symptomatic period results from a hypoperfusion of the thalami. A prolonged period of these recurrent episodes has also been shown to result in permanent neurocognitive impairment and deficit. As with narcolepsy, there is evidence that there may be some autoimmune etiology underlying KLS, although more research is needed in this field.

Attention-deficit/hyperactivity disorder (ADHD) is a syndrome that affects children, teenagers, and adults, although there is no current objective test to confirm its diagnosis. It has also been discovered that certain sleep disorders may induce symptoms of ADHD, such as hyperactivity and inattention. The diagnostic problem is complicated by the fact that several primary psychiatric disorders may present with symptoms similar to ADHD. Before making the diagnosis of ADHD, it is of paramount importance to eliminate the possibility of sleep disorders that may present with similar behavioral elements. At this time, ADHD is probably greatly overdiagnosed and overtreated, often with potent stimulant medications. The concern is when this is done without consideration of alternative causes of hyperactivity, impulsivity, and inattention resulting from disturbed sleep.

Finally, through a better understanding of narcolepsy, with its prominent phenotype, and possibly KLS, sleep research may lead to a better understanding of autoimmune disorders in general. Research in the field of REM sleep behavior disorder (RBD) has opened a new window on neurodegenerative disorders. Significant progress has been made in understanding this condition, in which there is a loss of normal motor inhibition during REM sleep, commonly associated with dreaming. The loss of REM atonia results in dramatic presentations, in which an otherwise calm and composed individual may become a raging, aggressive, and possibly dangerous dreamer. This disappearance of physiologic muscle atonia that normally prevents acting out dreams has been associated with other neurodegenerative diseases and with delirium. Long described as an idiopathic process, RBD may actually herald the onset of several neurodegenerative disorders affecting the brainstem in a gradually ascending fashion. Schenck and colleagues have demonstrated how RBD may precede the onset of Parkinson
disease or dementia, specifically dementia with Lewy bodies, diseases again affecting lower brainstem structures. Can the diagnosis of RBD in middle-aged patients lead to preemptive treatment of an evolving subclinical neurodegenerative process? This will be the challenge over years to come.

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REFERENCES