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SPECIAL ARTICLES

History of the Development of Sleep Medicine in the United States

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Sleep Medicine has only recently been recognized as a specialty of medicine. Its development is based on an increasing amount of knowledge concerning the physiology of sleep, circadian biology and the pathophysiology of sleep disorders. This review chronicles the major advances in sleep science over the past 70 years and the development of the primary organizations responsible for the emergence of Sleep Medicine as a specialty, sleep disorders as a public health concern and sleep science as an important area of research.

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With this inaugural issue of the *Journal of Clinical Sleep Medicine* it seemed appropriate that the history of the development of Sleep Medicine and sleep science in the United States be reviewed. Major advances in sleep science have occurred over the past half-century since the discovery of rapid eye movement (REM) sleep in 1953. Scientific progress combined with an increasing recognition that disorders of sleep are highly prevalent in our society has led physicians to acquire knowledge necessary for the diagnosis and treatment of disorders of sleep. Centers focused on the evaluation and management of sleep disorders have developed only within the past quarter-century. Consequently, the history of the development of Sleep Medicine in the United States is relatively short and most of the individuals involved with its development are still living. This review has been organized to briefly recount the major developments in sleep science and then to summarize the development of the major organizations active in promoting the practice of sleep medicine or sleep research. The authors have been selected on the basis of their first hand knowledge of how these organizations evolved and the roles they have played in establishing Sleep Medicine as an independent area of medical practice.

The development of any new medical specialty must be based on major new concepts in medical science. Historically, medical and surgical specialties have been organized on an anatomic or organ-based model. The development of organ-based specialties appeared congruent with advances in organ-system physiology. Developmentally based specialties ranging from neonatology to geriatrics have also evolved as medical knowledge specific to the aging process has accumulated. More recently, specialties have

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emerged that are related to basic areas of biology, such as the regulation of cell growth (oncology), that cut across the traditional, anatomically based medical specialties. In this context, sleep is viewed as a basic biologic process that affects all individuals and has significant impact on the function of all organ systems. Over the past 50 years, technologic advances leading to substantial modifications in lifestyle have combined with an explosion of scientific information and medical knowledge to generate a need for physicians trained in the diagnosis and management of disorders of sleep.

DEVELOPMENTS IN SLEEP SCIENCE

Sleep is biologically necessary for life

Sleep Medicine has evolved over the past 25 years based on the convergence of major developments in the science of sleep and circadian rhythms (chronobiology). The critical importance of sleep to good health and life was dramatically illuminated by the classic experiments conducted in rats by Rechtschaffen et al.[1] In these experiments, total sleep deprivation resulted in the death of all rats within 2 to 3 weeks. Selective deprivation of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep also resulted in the death of the animals over a slightly longer period of time. With progressive sleep deprivation, the rats became hypermetabolic and lost weight despite increasing food intake. They developed skin lesions and erosions of the gastrointestinal tract, with hypothermia developing just prior to death. Subsequent investigation documented that these rats died of sepsis thereby suggesting that sleep deprivation may impair the ability of the body's immune system to deal with infection.[2] The finding of bacterial invasion in association with sleep deprivation in rats may have major clinical importance in humans. For instance, sleep-deprived critically ill patients in intensive care units often succumb to sepsis.

Although studies of prolonged sleep deprivation have not been performed in humans for ethical reasons, there is little doubt that the prolonged deprivation of sleep unfortunately has been used as a form of torture with detrimental consequences to the individual. A large body of knowledge has accumulated over the past quarter century documenting the adverse consequences of short-term, total or partial sleep deprivation on human learning, mood, behavior, performance, and organ-system function.[3] In contrast, there is a paucity of information on the long-term effects of insufficient sleep. An early study conducted by Kripke et al[4] used epidemiologic data collected by the American Cancer Society on more than 1 million subjects. Mortality rates after 6 years of follow-up were significantly increased for subjects reporting less than 4 hours or more than 10 hours of sleep per night at baseline. These results were essentially reconfirmed in a second survey of 1.1 million subjects conducted between 1982 and 1988.[5] The consistency of these reports suggests that deviations in sleep duration from the norm (insufficient or excessive) may adversely influence human longevity.

Sleep deprivation and disorders of sleep are highly prevalent

Coinciding with the availability of electric lighting, sleep patterns have been substantially altered for both social and economic reasons. Overall, the Report of the National Commission on Sleep Disorders Research estimated that total sleep time for the US population has decreased by 20% over the past century.[6] The consequences of sleep deprivation can be disastrous. Sleep deprivation with operator fatigue has been implicated in numerous public disasters, such as the grounding of the Exxon Valdez and the nuclear meltdown at Three Mile Island. The US National Highway Traffic Safety Administration estimates that 100,000 motor vehicle accidents annually are the consequence of driver drowsiness or fatigue.[7] Shift work is estimated to affect 20% of the US workforce, with sleep deprivation of varying severity a resulting consequence.

In addition to the major problem of sleep deprivation related to social or occupational activities, the International Classification of Sleep Disorders (ICSD)[8] lists 88 sleep-related disorders, and Partinen[9] has published a detailed summary of their prevalence. Although insomnia affects everyone occasionally, about one out of every three adults indicates it is a significant problem, and 50% of these persons consider it to be severe. Snoring is another highly prevalent condition that has been reported to disrupt the sleep of bed partners.[10] Obstructive sleep apnea (OSA) and restless legs syndrome (RLS) (discussed below) are also highly prevalent conditions. The prevalence of sleep disorders within the population, combined with scientific progress in our ability to diagnose and treat these disorders, has created a tremendous demand for knowledgeable physicians trained in the area of Sleep Medicine.

Sleep: Scientific Progress

First steps: Discovery of the electroencephalogram and stages of sleep

The development of modern Sleep Medicine is closely linked to the discovery of the electrical activity of the brain. Caton was the first to record brain electrical activity of animals in England in 1875,[11] but it was Berger who discovered and reported the "electroencephalogram of man" in Germany in 1929.[12] In 1937 Loomis in the US first documented the characteristic electroencephalogram (EEG) patterns of what is now called NREM sleep: vertex waves, sleep spindles, K complexes, and delta slowing.[13] He divided sleep into 5 stages of increasing depth from A through E, which form the basis for the current classification of NREM sleep.

In 1951 Kleitman, a professor of physiology at the University of Chicago, studied eye movements during sleep with the assistance of his graduate student, Aserinsky. This work culminated in a seminal paper in 1953 in which a new sleep state, REM sleep, was described and a correlation with dreaming hypothesized.[14] In 1957, Dement and Kleitman described the human sleep cycle of NREM sleep stages of increasing depth followed by periods of REM sleep, with the cycles repeating through the night.[15] They proposed a new classification of sleep stages, using four stages of NREM sleep[1-4] and REM sleep, a schema still used today with very few alterations. This understanding of the electrophysiologic substrate of human sleep has been the basis for the vast literature on sleep that has accumulated over the ensuing half century.

Narcolepsy: From bedside to bench

The story of narcolepsy is an example of the major advances that Sleep Medicine has made in the last 50 years. It clearly indicates how scientific progress in the neurobiology of sleep has

resulted in novel understanding of a strange and disabling disease known clinically for over a century. Narcolepsy was first described in 1880 by Gelineau,[16] a neuropsychiatrist in France, who recognized a group of patients with irresistible sleep. The disorder consists clinically of excessive daytime sleepiness in combination with cataplexy, a loss of muscle tone in response to laughter and other emotional stimuli. Some patients also experience paralysis or hallucinations at sleep onset and on awakening.

The first breakthrough in understanding the disease came in 1960, when Vogel recognized that REM sleep commenced near sleep onset in narcoleptics, rather than 1 to 2 hours later.[17] This insight led to the concept that cataplexy and sleep paralysis represent the muscle atonia of REM sleep intruding into wakefulness, while hypnagogic hallucinations are dissociated dreams occurring without loss of consciousness. The next phase in unraveling narcolepsy was triggered by the observation that Japanese narcoleptics were highly likely to carry the HLA haplotype DR2,[18] a finding that was later confirmed in American Caucasians. A lower frequency of HLA DR2 in African-Americans led to the conclusion that the actual predisposing antigen was DQ1 rather than DR2.[19] Finally, the responsible subtype was identified as HLA DQB1*0602,[20] present in 85% to 90% of narcoleptics who have cataplexy.[21]

The major breakthrough, however, occurred in the last 6 years and is a fascinating story of scientific discovery. In 1998, two peptides were identified in the hypothalamus and named hypocretin (Hcrt)-1 and Hcrt-2,[22] names reflecting their hypothalamic origin and homology to secretin. Almost simultaneously, another group of investigators independently identified the same peptides, which they named orexin-A and orexin-B, based on their appetite-stimulating effect.[23] These molecules arise from a precursor, prepro-hypocretin, synthesized by a small number of cells in the posterior and lateral hypothalamus, especially the perifornical area. They project to a diverse set of targets in the brain and spinal cord, especially the monoaminergic and cholinergic fields of the brainstem tegmentum comprising the ascending reticular activating system.[24,25] Two membrane receptors have been identified, Hcrt receptor-1 with a high affinity for Hcrt-1, and Hcrt receptor-2, with a high affinity for Hcrt-1 and Hcrt-2.

Narcolepsy in dogs is transmitted as an autosomal recessive trait. Painstaking research by the Stanford Center for Narcolepsy under the direction of Mignot reached fruition in 1999 with the discovery that the disorder was caused by a deletion in the Hcrt receptor-2 gene.[26] Another group of investigators, working with a Hcrt knockout mouse model, serendipitously recognized that the mutant mice developed episodes of either REM sleep or cataplexy while awake.[27] Following these seminal observations, studies of narcoleptic patients revealed low or undetectable Hcrt-1 in the cerebrospinal fluid (CSF) of most (87%) patients with cataplexy and in some patients without cataplexy (14%). In contrast, low levels were not found in control subjects (0%) and observed rarely in patients with other neurological conditions (<2%).[28] Autopsy studies of the brains of human narcoleptics have revealed that Hcrt is absent in the hypothalamus, cortex, and pons, and Hcrt neurons are reduced by 90% compared to controls.[29,30] Clinical manifestations of the disease, such as cataplexy, appear to reflect a lack of Hcrt-mediated synaptic excitation of serotonergic and noradrenergic pathways normally responsible for REM-sleep inhibition. The sleepiness of narcolepsy more likely reflects lack of Hcrt's excitatory influences upon histaminergic, dopaminergic, and cholinergic components of the ascending reticular activating system (ARAS), which normally function to promote thalamocortical arousal.

The next step in understanding the disorder will involve probing the mechanism of reduced Hcrt production by the hypothalamus. Despite the animal data, the search for human mutations has been disappointing and only a single point mutation in the Hcrt signal peptide has been described in one patient.[30] The strong association with HLA DQB1*0602 has led to the hypothesis that narcolepsy may be due to a localized autoimmune attack on the hypothalamus, but there is as yet no direct proof of this. Further advances are expected to lead to novel therapies and, thus, complete the loop from bedside to bench and back to bedside.

Restless legs syndrome: The dopamine-iron connection

Restless legs syndrome (RLS) was first described by Ekbom in Sweden more than 50 years ago, but for many years was thought to be a rare curiosity. However, current epidemiologic studies suggest it may be one of the most common sleep-related disorders, with a prevalence as high as 10%.[31] Patients complain of severe discomfort in their legs while sitting or lying in bed, associated with an uncontrollable desire to move to obtain relief. Almost 90% of patients experience regular jerks of their legs while asleep, known as periodic limb movements (PLM) of sleep.

A range of studies using different methodologies has produced striking insights into the pathogenesis of the disorder. Pharmacologic studies have indicated that levodopa and dopamine-receptor agonists are effective therapies for RLS, indicating that the disorder is associated with a decrease in dopaminergic function in the brain. However, contradictory results have been obtained with 18-fluorodopa positron emission tomographic (PET) scans, with two studies finding reduced dopaminergic activity in the basal ganglia,[32,33] and one finding no differences from controls.[34]

Functional magnetic resonance imaging (MRI) of patients with RLS suggests involvement of the cerebellum and the thalamus with additional activation of the red nucleus, pons, and midbrain when PLMs are also present.[35] Physiologic studies have suggested that a disturbance of inhibitory subcortical pathways, such as the reticulospinal tract, may allow expression of a normally suppressed neural generator at the level of the spinal cord.[36] About 50% of patients with RLS have a family history of the condition,[37] and a recent report has described a family with linkage to chromosome 12q.[38]

However, one of the most interesting developments in understanding the pathogenesis of RLS is related to iron metabolism. It has been known since Ekbom's time that RLS may be associated with iron deficiency anemia. Studies have revealed that RLS severity correlates with serum ferritin concentrations below 45 to 50 mg/L, values usually considered in the normal range.[39,40] Low ferritin concentration in the CSF has been demonstrated in RLS patients with normal serum ferritin concentrations compared to controls, suggesting that low iron stores in the brain may be associated with RLS.[41] An MRI study has shown reduced brain iron in the substantia nigra in RLS patients compared to controls, with the reduction proportional to RLS severity.[42] The most recent preliminary data involves autopsy studies, with reduced iron content being demonstrated in the substantia nigra in three brains of

RLS patients (Earley, unpublished data). A possible explanation linking the role of dopamine and iron in the pathogenesis of RLS is that iron is a necessary cofactor for the function of tyrosine hydroxylase, a rate-limiting step in dopamine synthesis.

REM sleep behavior disorder: Early marker of neurodegenerative diseases

Skeletal muscle tone is greatly reduced during REM sleep, preventing the acting out of dreams. One of the most striking parasomnias (disorders of abnormal behavior during sleep) is REM sleep behavior disorder (RBD), in which skeletal muscle remains active during dreaming, resulting in vocalization and sometimes violent activity of the arms and legs. A high percentage of patients injure themselves or their bed partners, usually dreaming that they are defending themselves against attack. Since the disorder was first formally described 15 years ago by Schenck, Mahowald and colleagues,[43] basic science and clinical research have provided increased understanding of its pathogenesis and significance.

The physiology underlying normal REM sleep atonia has been meticulously elucidated. Axons from cells of the pedunculopontine nuclei in close proximity to the primary REM-sleep generator in the dorsal pons inhibit ventral medullary neurons that in turn suppress anterior horn cells in the spinal cord. Lesions to this descending inhibitory pathway in cats produce varying degrees of motor activity during REM sleep depending on the size of the lesions, culminating in stalking and attack behaviors.[44]

In humans, RBD occurs overwhelmingly in men, commencing in middle or older age. A range of epidemiologic, psychometric, radiologic, and pathologic data has shown that the disease is linked with certain specific neurodegenerative disorders. At least 50% of patients in large studies carry diagnoses of Parkinson's disease, multiple system atrophy, or dementia.[45] Clinical and psychometric data have suggested that dementia associated with RBD indicates the presence of Lewy body pathology (with or without associated Alzheimer changes) rather than that of Alzheimer's disease alone.[46,47] This is confirmed by the available autopsy data on 14 patients with RBD: 13 have shown Lewy bodies (including 1 case with no neurologic signs clinically) and 1, the pathology of multiple system atrophy.[48] Thus RBD appears to be associated with those neurodegenerative disorders with alpha-synuclein positive inclusion bodies. There is also retrospective and prospective evidence that RBD may sometimes be the first manifestation of one of these neurologic disorders,[49] and thus at least some patients with apparently idiopathic RBD may with time evolve to develop a neurodegenerative disease. Further evidence to support this contention comes from two radionuclide studies showing that neurologically normal RBD patients have reduced striatal dopamine activity, suggesting they may be in the presymptomatic stages of Parkinson's disease.[50,51] These insights may provide a way of identifying patients at high risk of developing serious neurologic disease, perhaps allowing preventive therapies to be administered in the future.

Obstructive sleep apnea: Discovery to epidemic

In 1956, Burwell et al published their classic description of the obesity hypoventilation (Pickwickian) syndrome.[52] Following publication of this article, pulmonologists believed that alveolar hypoventilation (respiratory failure) was responsible for the excessive daytime somnolence observed in these patients. This misconception was not corrected until 1966 when Gastaut et al polysomnographically monitored the sleep of these patients.[53] They documented repetitive episodes of upper-airway obstruction terminated by brief arousals that in turn fragmented nocturnal sleep. Obstructive sleep apnea (OSA) was discovered, and it was correctly postulated that sleep fragmentation was responsible for the excessive daytime somnolence observed in these patients. Subsequently, it has been determined that reductions in tidal volume (hypopneas) as well as increases in upper airways resistance also produce sleep fragmentation and daytime sleepiness.

This major new concept in medical science stimulated considerable research in the area of sleep and breathing. By 1978, Remmers et al had documented the relationship between intralumial airway pressure and EMG activity of the genioglossus muscle in the pathophysiology of upper-airway collapse in the pharyngeal segment of the airway,[54] and tracheostomy was recognized as an effective treatment. Three years later, Sullivan et al demonstrated that the application of continuous positive airway pressure (CPAP) via the nose would prevent upper-airway collapse, normalize nocturnal sleep, and alleviate daytime hypersomnolence.[55] This latter discovery revolutionized the treatment of OSA and has resulted in the use of nasal CPAP as the most commonly used treatment of this condition. Initially, OSA was felt to be a rather uncommon condition affecting only severely overweight men. However, the small number of sleep specialists and pulmonologists interested in this condition in the early 1980s soon realized that OSA was a common condition affecting women as well as men. The first major epidemiologic study of the prevalence of OSA was published in 1993 by Young et al.[56] They found OSA to be present in 2% and 4% of middle-aged women and men respectively. Subsequent epidemiologic studies have confirmed that obesity remains one of the major risk factors for OSA, but also have shown familial aggregation and differences among different age and ethnic groups, and between genders.

This high prevalence in the population combined with evidence suggesting adverse cardiovascular consequences led the National Institutes of Health (NIH) to fund studies investigating these important relationships. Resulting publications have established a clear association between sleep-disordered breathing and the development of hypertension,[57,58] along with an increased prevalence of coronary heart disease, heart failure, and stroke at levels of an apnea-hypopnea index equal to or greater than 5 per hour.[59] Based on these recent findings, the Centers for Medicare and Medicaid Services (CMS) have recently published guidelines for the reimbursement of nasal CPAP therapy in symptomatic patients with an apnea-hypopnea index equal to or greater than 5 per hour or asymptomatic patients with an apnea-hypopnea index equal to or greater than 15 per hour.

Insomnia: Progress toward relief for many

Insomnia is the most prevalent of all sleep problems. Although its etiology and pathogenesis remain elusive, significant strides have been made in terms of its epidemiology, phenomenology, and treatment. Insomnia is the subjective complaint of difficulty falling asleep, difficulty staying asleep, poor quality sleep, or inadequate sleep duration despite having an adequate opportunity for sleep. Two points in this definition deserve specific attention. First, insomnia is a subjective complaint and is not defined

by laboratory test results or by a specific duration of sleep or wakefulness. Second, the insomnia symptom occurs despite the individual having adequate opportunity to sleep. This factor distinguishes insomnia from sleep deprivation, which has different causes, consequences, and clinical presentations.

Recent epidemiologic studies indicate a prevalence of 30% to 45% for insomnia symptoms in the prior year.[60-62] The prevalence of insomnia disorders is lower but still in the range of 10% to 15%.[63-64] Consistent risk factors for insomnia include a previous history of insomnia, increasing age, female gender, psychiatric symptoms and disorders, medical symptoms and disorders, impaired activities of daily living, anxiolytic and hypnotic medication use, and low socioeconomic status. Between 50% and 80% of individuals with insomnia at baseline have a persistent complaint after follow-up intervals of 1 to 3.5 years.[60,65-67]

Studies in populations of working adults show that individuals complaining of insomnia have more mood symptoms, gastrointestinal symptoms, headache, and pain.[68] In addition, individuals with insomnia have greater self-ratings of role impairment, days of limited activity, days spent in bed, and higher total healthcare costs.[69] Health-related quality of life is significantly lower for individuals with insomnia than for those without.[70] Individuals with insomnia may also have higher rates of serious accidents or injuries[71] and injurious falls.[72] The economic costs of insomnia are also substantial. One recent estimate places the annual direct costs for insomnia-related problems at nearly 14 billion dollars (including 11 billion related to nursing home care).[73] Insomnia has been identified as a significant risk factor for institutionalization in the elderly in some studies.[74] Perhaps the greatest morbidity associated with insomnia is an increased risk for psychiatric disorders, described in several large, and carefully controlled, prospective studies.[63,75-79] These studies have included subjects from young adults to the elderly and follow-up intervals from 1 to 35 years. The obvious— and unanswered— question is whether early identification and intervention in insomnia could prevent this costly outcome. Despite these morbidities, insomnia does not appear to be an independent risk factor for mortality.[5,62,80]

Relatively little is known regarding the neurobiology of insomnia. One of the earliest and most enduring conceptualizations of insomnia is that of psychophysiologic arousal. For instance, individuals with insomnia may have elevated temperature and muscle tone at sleep onset,[81,82] elevated heart rate and elevated sympathovagal tone in heart rate variability,[83] and positive correlations between wake time after sleep onset and urinary norepinephrine and dopamine metabolites.[84] Studies of whole-body metabolic rate, assessed by oxygen consumption, show elevated rates for individuals with insomnia compared to healthy controls, a difference that persists 24 hours per day.[85] The psychologic arousal of insomnia is supported by higher rates of self-reported ruminations and intrusive thoughts among insomniacs. Finally, evidence for actual central nervous system hyperarousal includes EEG studies that show reduced daytime sleep propensity[86] and lower delta EEG power during sleep (usually taken as an indicator of homeostatic sleep drive) and elevated amounts of beta EEG power (usually interpreted as evidence of EEG activation or cognitive activity).[87,88] In one recent investigation of depressed patients with insomnia, beta EEG activity correlated positively with glucose metabolic rate in the medial orbitofrontal cortex, a region implicated in both behavioral and electroencephalographic activation.[89]

A comprehensive review of the efficacy of behavioral treatments for chronic primary insomnia, based on two meta analyses and 48 individual treatment studies, showed reliable improvements in the main outcome measures of latency to sleep, wake-time after sleep onset, and sleep quality.[90] Data consistently indicated that approximately 70% to 80% of insomniacs benefited from treatment. Improvements with behavioral treatment are well maintained over at least 6 months.[91] Other nonpharmacologic treatments for insomnia include phototherapy with artificial light or exposure to diffuse natural outdoor light.

Several medication classes are used for the treatment of insomnia: benzodiazepine-receptor agonists (BzRA), antidepressant drugs, antihistamines, melatonin, and various herbal remedies including valerian root extracts. Of these medications, only BzRA are formally approved for insomnia treatment in the US. Recent meta analyses confirm the effects of BzRA on sleep latency, sleep duration, number of awakenings, and sleep quality.[99-101]

Although the use of antidepressants for insomnia has increased dramatically, evidence to support their efficacy is relatively sparse. Studies with small numbers of subjects and diverse inclusion criteria suggested the beneficial effects of trazodone.[113-115] A more recent 2-week, double-blind, placebo-controlled study compared the effects of trazodone 50 mg and zolpidem 10 mg to placebo among individuals with primary insomnia,[116] and showed improvements in subjective sleep latency and sleep duration with both active drugs.

Although considerable progress has been made with regard to the epidemiology of insomnia, further work needs to be done regarding its consequences for health and role functioning. Individuals with insomnia complain not only of sleep disturbance, but of daytime consequences as well. In addition, investigations into the neurobiology of insomnia are clearly needed. This will help to define the underlying pathophysiology of insomnia in the general sense and also help to define the boundaries of specific insomnia disorders.

Chronobiology: Scientific Progress

Discovery of the biologic clock: The suprachiasmatic nucleus

Scientific progress in the area of chronobiology has been equally spectacular and complementary to the progress that has been made in sleep science over the past quarter century. Although plants and animals have long been known to possess circadian rhythms that would persist in the absence of light, the scientific investigation and understanding of these rhythms dramatically accelerated with the discovery of the suprachiasmatic nuclei (SCN) as the site of the biologic clock. In 1972, anatomic destruction of the SCN located in the hypothalamus was shown to eliminate circadian rhythms in adrenal corticosterone and drinking and locomotor activity in rats.[119,120] At this same time, Moore and Lenn identified the retinohypothalamic tract that serves the important function of connecting the SCN with the photic environment.[121] The central role played by the SCN in mediating circadian rhythmicity was further supported by the finding that individual neurons dissociated from the SCN were capable of maintaining rhythmic circadian firing patterns when cultured in vitro.[122] Eloquent studies subsequently demonstrated that circadian rhythmicity could be restored in SCN-ablated arrhythmic animals by fetal SCN transplantation.[123] In addition, transplanting fetal SCN

tissue from a mutant strain of hamsters with a short circadian rhythm of 20 hours can change the duration of the restored rhythm in wild animals from 24 to 20 hours.[124]

Molecular and genetic mechanisms regulating the biologic clock

In 1971, the first gene that encoded for a clock protein, *per*, was discovered in Drosophila.[125] Evidence supporting a central role for the *per* gene as a component of the circadian clock followed when the mRNA transcript of the *per* gene was found to oscillate in a circadian fashion as a result of transcriptional regulation.[126,127] Further progress was made with the identification of the timeless gene *tim* and the fact that the mRNA encoded by the *tim* gene oscillated in near synchrony with *per* mRNA.[128] Based on these early experiments, the concept emerged that activation of the *tim* and *per* genes results in the synthesis of their protein products TIM and PER. They then form a heterodimer in the cytoplasm and diffuse back into the nucleus inhibiting *tim* and *per* gene expression, thereby establishing the molecular oscillatory pattern needed for a circadian clock. Subsequent work has revealed additional complexity with the identification of two additional proteins, CLOCK and BMAL1, that are involved in this process.[129] Using similar molecular techniques, investigators have been able to elucidate analogous genetic and molecular mechanisms of circadian oscillation in mice.[130,131]

Recently, Kramer et al[132] reported that the rhythmic expression of transforming growth factor-alpha by the SCN serves to inhibit locomotion in mice. They went on to demonstrate that this effect was mediated by epidermal growth factor receptors located on neurons in the subparaventricular zone of the hypothalamus. This work has increased our understanding of the molecular pathway between the output of the SCN and a behavioral activity.

In the clinical arena, rapid and exciting progress is also being made. In 1999, Jones et al[133] identified three kindreds with a profound phase advance of the sleep-wake, melatonin, and body temperature rhythm in association with a very short circadian period. The inheritance of this trait was found to follow an autosomal dominant pattern with a high degree of penetrance. Within 18 months Toh et al[134] established that familial advanced sleep phase syndrome resulted from a serine to glycine mutation within the casein kinase I (varepsilon) binding region of hPER2. Therefore, a variant in human behavior (advanced sleep phase) was documented to result from a missense mutation in a clock component, hPER2, that alters circadian periodicity.

The insight gained from these studies suggests that some patients with the more common problem of delayed sleep phase syndrome may also have an underlying genetic basis but with prolonged as opposed to short circadian period. Although circadian periodicity can be changed in animals by SCN ablation and the transplantation of fetal neural tissue, less invasive methods of altering the circadian period will hopefully be developed for use in humans with abnormally fast or slow biologic clocks.

Light and melanopsin: Setting the biologic clock

Although both photic and nonphotic stimuli have been known to influence circadian rhythmicity in animals and man, light is considered to be the dominant synchronizing input.[135] In 1963, Wurtman et al[136] reported that melatonin synthesis in the pineal gland was under the inhibitory control of light. Although the retinohypothalmic tract connecting the retina to the SCN was first documented in 1971,[121] Moore et al subsequently went on to identify the neural pathway by which output from the SCN reaches the pineal gland.[137] This pioneering work completed our understanding of how light reaching the retina could produce suppression of melatonin secretion from the pineal gland. Recently, research from several laboratories has led to the discovery that there is a new class of photoreceptor cells in the mammalian retina. These retinal ganglion cells (RGC) send information on the level of luminance or irradiance to the SCN independent of the rod and cone cells that function as the photoreceptors for the visual system.[138,139] In addition, melanopsin, a photosensitive protein present in frog melanophores that functions to redistribute melanin in response to light, has been found in a subset of the RGC present in the mouse retina.[140,141] Furthermore, some of these cells have projections to the SCN.[142] Because genetically mutant mice lacking rod and cone cells in the retina and some visually blind human subjects retain the ability to have their circadian rhythms entrained by light,[143] most investigators now believe that the RGC are the actual photoreceptors responsible for photic entrainment of the SCN. Furthermore, melanopsin may be the responsible photopigment.

While these major advances in circadian neurobiology have been occurring, clinicians practicing Sleep Medicine have been using light to photically reset the biologic clock of patients with both delayed and advanced sleep phase syndromes.[144] Exposure to light has been used to adjust the circadian rhythm of night-shift workers and astronauts in order to maximize alertness and performance.[135,145,146] Human phase-response curves to light have been published with the results dependent on both the intensity and number of consecutive days of exposure.[147] Even low-intensity exposure on the order of 180 lux, typical of indoor artificial lighting, has been found to be capable of inducing phase shifts.[148] This has major implications and explains why numerous early studies of the human circadian pacemaker erroneously concluded that the intrinsic period was about 25 hours. Although these studies were all conducted in caves or laboratories free of environmental time cues, the subjects were allowed to turn lights on after awakening and lights off at bedtime. By using a forced desynchrony protocol, with subjects constantly exposed to dim light (10-15 lux), the intrinsic period of the circadian pacemaker has been found to have an average period of 24.2 hours.[149]

Summary—Developments in Sleep Science and Implications for Sleep Medicine

Advances in clinical and basic science sleep research have led to increasing recognition that disorders of sleep are highly prevalent, to a greater understanding of their pathophysiology and to the development of effective treatments for these conditions. These advances have stimulated the formation of professional and patient-focused organizations to advocate for the delivery of the highest standard of care for patients with sleep disorders, to set professional standards for delivery of care, to train physicians in Sleep Medicine and to provide the cadre of investigators that will conduct research to further advance the field of Sleep Medicine.

THE AMERICAN ACADEMY OF SLEEP MEDICINE

The American Academy of Sleep Medicine (AASM) is a pro-

fessional society that serves the needs of individual sleep medicine practitioners as well as sleep disorders centers. It provides professional standards for the practice of sleep medicine, standards for accreditation of sleep disorders centers, participates in two journals for scientific publication, encourages research through grants to investigators and educators, and has developed fellowship programs to train the next generation of sleep specialists. The development of AASM evolved through the development of a body of science in sleep and the subsequent evolution of the practice of Sleep Medicine. Figure 1 depicts the major milestones in the development of Sleep Medicine. This includes the incorporation of professional societies, the development of accreditation of centers (1975), the publication of the journal *SLEEP* (1978), board certification of practitioners (1978) and the establishment of formalized fellowship training programs (1989).

The origins of the AASM can be traced to the efforts of Dr. William Dement who provided much of the leadership and direction for the first decade of the society, in large part based on his experiences in the center he directed. The first sleep disorders center was established as a narcolepsy clinic at Stanford University in 1964. By 1970 the Stanford group had evolved into a full-service Sleep Disorders Clinic and included Drs. Dement, Mary Carskadon, Christian Guilleminault and Vincent Zarcone. The Sleep Center was envisioned to be directed by a sleep specialist, and having the ability to perform nocturnal polysomnography and multiple sleep latency tests.

By 1975 a handful of centers started examining patients during sleep. In addition to Stanford, Montefiore Medical Center in New York, Ohio State University, Baylor College in Houston, University of Cincinnati Medical Center and the University of Pittsburgh Medical School were providing overnight sleep studies. Until 1975 Sleep Medicine was deemed "experimental" and medical insurance companies routinely denied reimbursement claims. However, that year, Blue Shield of California recognized the significance of Sleep Medicine and began reimbursing patients for sleep services.

At the Edinburgh sleep conference in 1975, a group was established during a lunch meeting organized by Dr. Peter Hauri. Discussions continued later that year in Chicago. The group's leadership included Drs. Dement, Edward Bixler, Ismet Karacan, Milton Kramer, David Kupfer, Howard Roffwarg, Thomas Roth and Elliot Weitzman. They agreed that a new organization should be formed that would be sleep-center oriented with a strong medical and research direction. They named the new organization the Association of Sleep Disorders Centers (ASDC). Dr. Dement served as the President of the then ASDC for its first 12 years, and was then succeeded yearly by Drs. Thomas Roth, Philip Westbrook, Howard Roffwarg, Jon Sassin, James Walsh, Mark Mahowald, Meir Kryger, Paul Frederickson, June Fry, David White, Wolfgang Schmidt-Nowara, Gihan Kader, Stuart Quan, Daniel Buysse, John Shepard, Andrew Chesson, Conrad Iber and Michael Sateia. Thus, from its onset, the field of Sleep Medicine sought acceptance in mainstream medicine by having leaders with expertise in both scientific investigation as well as clinical practice.

In the formative years of the ASDC, its purpose was five fold: (1) to establish, update, and maintain standards for the evaluation and treatment of human sleep and sleep-related disorders, (2) to establish and review a standard diagnostic classification of such disorders, (3) to establish an examination process for specialists in Sleep Medicine, (4) to provide a forum for the exchange of information on such disorders, and (5) to promote the role of sleep and sleep-related disorders in clinical medicine. In addition it was to represent this discipline in relation to professional health organizations, federal and local regulatory bodies, and federal and private health insurers.

The ASDC appointed a Nosology Committee in February of 1976 to begin the task of creating a diagnostic system for sleep and arousal disorders that would include all conditions encountered clinically. Chaired by Dr. Howard Roffwarg, the committee consisting of Drs. Peter Hauri, David Kupfer, Vincent Zarcone, Robert Clark, Christian Guilleminault, Laughton Miles, Helmut Schmidt, and Frank Zorick published the completed work of 137

Societies	**Milestones**	
Association for the Psychophysiological Study of Sleep (APSS)	**1964**	**Stanford Narcolepsy Center**
	1968	**Manual for Scoring Sleep**
	1970	**Stanford Sleep Center**
Association of Sleep Disorders Centers (ASDC)	**1975**	**5 Centers**
		PSGs Reimbursed
	1977	**ASDC Center Accreditation**
	1978	**Journal SLEEP**
		Certification in Sleep Medicine
Clinical Sleep Society (CSS)	**1984**	
Association of Professional Sleep Societies (APSS)	**1986**	
American Sleep Disorders Association (ASDA)	**1987**	
Associated Professional Sleep Societies	**1988**	
	1989	**ASDA Fellowship Training Programs**
American Board of Sleep Medicine(ABSM), National Sleep Foundation (NSF)	**1991**	**International Classification of Sleep Disorders (ICSD-1)**
Sleep Medicine Education & Research Foundation (SMERF),	**1998**	
American Academy of Sleep Medicine (AASM)	**1999**	
American Sleep Medicine Foundation (ASMF)	**2003**	**Behavioral Sleep Medicine Certification**
	2005	**International Classification of Sleep Disorders (ICSD-2)**
		Journal of Clinical Sleep Medicine (JCSM)

Figure 1—Milestones in the Development of Sleep Medicine in the United States.

pages as the autumn issue of *SLEEP* in 1979. A complete revision, begun in 1985 under the direction of Dr. Michael Thorpy, ended with the publication of a stand-alone volume, the 400-page *The International Classification of Sleep Disorders: Diagnostic and Coding Manual (ICSD)*, in 1990. Dr. Hauri now chairs a committee that has nearly completed a revision of the *ICSD, ICSD-2,* scheduled for publication in 2005.

As part of its goal to establish and maintain standards for the evaluation and treatment of sleep disorders, the ASDC from its inception began to accredit sleep centers. The Accreditation Committee, previously the Certification Committee, accredited the first sleep center at Montefiore Hospital in New York on April 27, 1977. Over the years, the Accreditation Committee has edited and revised the accreditation guidelines, officially known as the *Standards for Accreditation*, numerous times. Each center has its application reviewed by the committee and then undergoes a site visit. Following a favorable site visit and approval by the Board of Directors, full accreditation status, which is not contingent upon membership, is granted for a period of 5 years. To date, the AASM has accredited 710 facilities—610 centers, 75 laboratories, and 25 satellites.

In the fall of 1984, the ASDC announced the formation of a new organization for individuals interested in the clinical aspects of sleep and sleep disorders—the Clinical Sleep Society (CSS). Individuals who had passed the examination in Clinical Polysomnography were made Fellows of the CSS. The CSS Steering Committee, comprised of Drs. Phillip Westbrook, Martin Cohn, Helio Lemmi and Ralph Pascualy, launched a recruitment drive directed primarily at pulmonologists, neurologists, and psychiatrists, and membership reached 339 by the close of the year. In September of 1987, the ASDC-CSS reorganized to form the American Sleep Disorders Association (ASDA) with two branches of membership: centers and individuals. Mrs. Carol Westbrook became the first Executive Director of the new organization that was located in Rochester, MN. She was followed several years later by Ms. Carolyn Hiller. In 1996, the Association hired Mr. Jerome Barrett to serve as its Executive Director and in 1999 the ASDA changed its name to the American Academy of Sleep Medicine (AASM). In 2002, the national office was moved to Chicago. The rapid growth in AASM membership (Figure 2) subsequent to 1984 is a testimony to the vitality of the field of Sleep Medicine and the increasing recognition of the impact of sleep disorders on health of the general public.

In addition to accreditation, other activities of AASM have helped to define its role in professional standards, research and education. The AASM established a Standards of Practice Committee in 1989 that published the first practice parameters paper in *SLEEP* in 1992. The AASM has since published 17 additional papers and 10 position statements. As a result of the efforts by an ASDA taskforce co-chaired by Drs. Helmut Schmidt and Andrew Jamieson, the American Medical Association (AMA) recognized Sleep Medicine as a self-designated practice specialty on January 1, 1995, and subsequently granted the AASM (then ASDA) a seat in the AMA House of Delegates on January 1, 1997. Dr. Paul Fredrickson served as the first delegate and has been succeeded recently by Dr. Jamieson. In November of 1997, the AASM (then ASDA) was awarded accreditation as a sponsor of continuing medical education for physicians by the Accreditation Council for Continuing Medical Education (ACCME). Recently, the AASM has decided to publish a new journal, the *Journal of Clinical Sleep Medicine,* which will focus on publishing papers and providing continuing education applicable to Sleep Medicine practitioners, Its first editor is Dr. Stuart Quan. In addition, as discussed in subsequent sections, the AASM has played pivotal roles in the publication of the journal *SLEEP*, the formation of 2 non-profit foundations and a very successful annual scientific meeting.

Today, the AASM with over 5000 members, is the leading professional organization promoting the specialty of Sleep Medicine, advocating for excellence in clinical care for patients with sleep disorders, providing education pertaining to sleep disorders for its members, other health professionals, patients and the public, and contributing funding for sleep research.

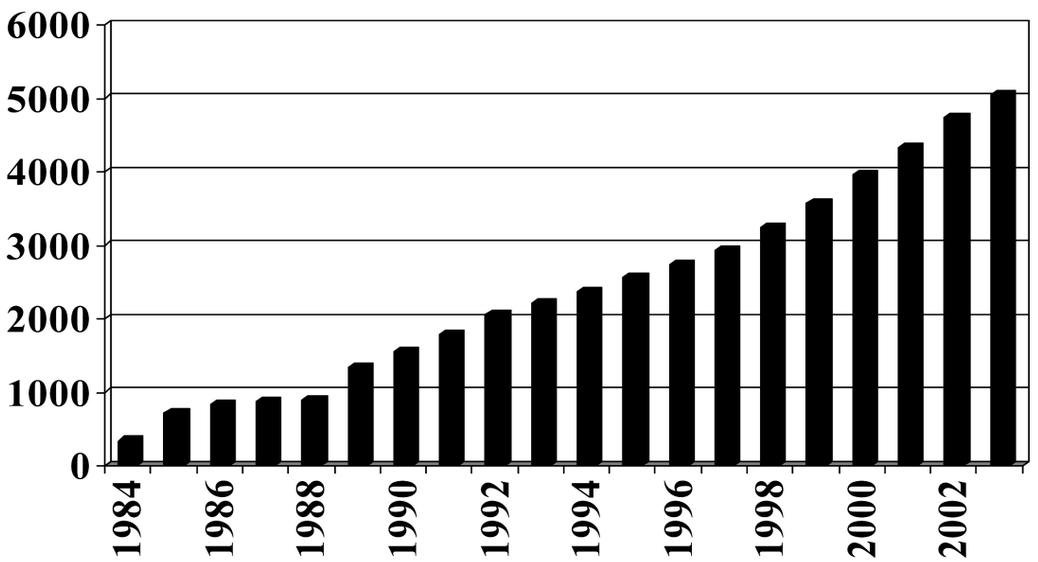

Figure 2—Membership of the Clinical Sleep Society (1984-1986), American Sleep Disorders Association (ASDA) 1987-1998 and American Academy of Sleep Medicine (AASM) 1999 – 2003.

THE SLEEP RESEARCH SOCIETY

The origin of the Sleep Research Society (SRS) dates to 1961, when a small group of sleep researchers met at the University of Chicago, to share ideas and data. The dates, locations and host scientists for the first decade of meetings were as follows:

1961 - Chicago, IL, Drs. Nathaniel Kleitman, Allan Rechtschaffen and William Dement
1962 - Chicago, IL, Drs. Nathaniel Kleitman, Allan Rechtschaffen and William Dement
1963 - New York, NY, Dr. Charles Fisher
1964 - Stanford, CA, Dr. William Dement
1965 - Washington, DC, Dr. Frederick Snyder
1966 - Gainesville, FL, Dr. Wilse Webb
1967 - Los Angeles, CA, Dr. Anthony Kales
1968 - Denver, CO, Dr. Robert Emde
1969 - Boston, MA, Dr. Allan Hobson
1970 - Santa Fe, NM, Drs. Jack Rhodes and Johann Stoyva

The group's meetings initially were informal. In late 1962, the group selected its first Secretary-Treasurer, Dr. Joseph Kamiya, to coordinate communication but kept its informal character by deciding against having other officers. In 1964, the Society chose the name, "Association for the Psychophysiological Study of Sleep". The abstracts of papers presented at annual meetings were limited to single-page mimeographs. Shorter versions of the meeting abstracts from 1968 to 1971 were published in the journal Psychophysiology. In 1972, Dr. Michael Chase began the annual publication of *Sleep Research* that included full-page abstracts and a bibliography of articles published during the year. In 1998, the journal *SLEEP*, took over publication of the abstracts from the annual meeting which by then had evolved into the current combined meeting with the AASM.

The Society came into being during an expansionary period of electrophysiological measurements after the discovery of the electroencephalogram by Dr. Hans Berger in 1929. Increasingly, electrographic methods were being adapted for continuous monitoring of brain waves as pioneered by early electroencephalographers such as Dr. A. L. Loomis and colleagues in order to describe relationships between central nervous system activity and behavior. Applying longer term continuous electrophysiological monitoring to humans and animals with the addition of electrographic measures of eye movements and postural muscle activity led to striking discoveries that sleep was not a homogenous state of quiescence. The early pioneers of sleep research included Drs. Nathaniel Kleitman, William Dement, Allan Rechtschaffen, Eugene Aserinsky and Michel Jouvet. Collectively, their work sowed the seeds that grew into the fields of sleep research and sleep medicine.

One of the most influential documents produced by early sleep researchers was the 1968 "A Manual of Standardized Technology Techniques and Scoring Systems for Sleep Stages of Human Subjects" co-authored by Drs. Allan Rechtschaffen and Anthony Kales. This allowed objective comparisons of data among multiple laboratories throughout the world; it transformed sleep research from a descriptive, to an experimental science. In due course, manuals for recording the sleep of cats, rats and human infants immeasurably advanced the rigor and reproducibility of research findings. Selected, but representative, areas of knowledge developed by sleep research and some early investigators associated with these areas included:

- Ontogenetic changes in sleep architecture: Drs. Danielle Jouvet, Arthur Parmelee and Howard Roffwarg
- Sleep in diverse species of animals: Drs. Truett Allison, Harold Zepelin, Jerome Seigel
- Relationship of REM sleep to dreaming: Drs. Charles Fisher, Robert Van De Castle, Rosalind Cartwright, and David Foulkes
- Physiological and endocrinological changes during sleep: Drs. Walter Baust, Ismet Karacan, Christian Guilleminault, John Sassin, Michael Chase, and John Orem
- Objective evaluation of the therapeutic efficacy of sedative hypnotic drugs: Drs. Anthony Kales, Gerald Vogel, and Thomas Roth
- Relationship between 24-hour wakefulness-sleep cycles and circadian rhythms: Drs. Elliot Weitzman, Wilse Webb, Daniel Kripke, and Merrill Mitler
- Computational and instrumentation approaches: Drs. Ross Adey, Harmon Agnew, Ralph Berger, Ardie Lubin, Jack Smith, Turan Itil
- Assessment of daytime sleepiness and the multiple sleep latency test: Drs. Mary Carskadon, William Dement, Merrill Mitler, Thomas Roth, Phillip Westbrook, Sharon Keenan

The history of the SRS is inextricably tied to objective and scientifically reproducible measurements of sleep and wakefulness. The need for such measurement is broad and has involved important interactions between the SRS and a variety of governmental organizations. Most discoveries in the field of sleep research were made possible by research funding from governmental sources including the National Institutes of Health (NIH) and the Department of Defense (e.g., Army, Navy and Air Force biomedical research organizations). Beginning in the early 1970s, the Food and Drug Administration developed guidelines for the evaluation of hypnotic efficacy. In 1979, the Surgeon General's Office created Project Sleep to further focus governmental attention on sleep research and sleep disorders. In 1990, the Institute of Medicine prepared a research briefing entitled "Basic Sleep Research." The Institute of Medicine recognized that limited training of young sleep researchers and funding for sleep research on animals threatened the continuation of basic sleep research in the United States. At that time, attacks by animal rights groups on several basic sleep research programs were a threat to impede research in the field. Finally, stimulated by a report from a congressional commission, the National Center on Sleep Disorders Research (NCSDR) was created within the NIH in 1993. One of the first actions of the NCSDR was to write a national sleep research plan. Members of the SRS played pivotal roles in all of these activities.

The SRS remains a unique and multidisciplinary society with researchers from psychology, physiology, endocrinology, neural sciences, pharmacology, chronobiology, pulmonology and other fields that contribute to the study of sleep. Sleep research and medicine has an established research base, and our member scientists continue to explore new frontiers. Although early records of membership in the Association for the Psychophysiological Study of Sleep and the SRS are not available, the SRS has evolved into a complex organization of over 900 members (Figure 3). The SRS Board of Directors now includes 12 sitting members and is aided by a number of committees. In all that it does, the SRS strives to promote understanding of the processes of sleep and its disorders through research, the training of practitioners of research and the dissemination of the fruits of their efforts to the scientific and medical communities as well as the general public.

THE ASSOCIATED PROFESSIONAL SLEEP SOCIETIES

Organizational Development and Structure

On January 13, 1986, the ASDC and the SRS, along with the Association of Polysomnographic Technologists (APT), formed a federation — the Association of Professional Sleep Societies (APSS). This acronym replicated the original one used by the first organization of sleep researchers, the Association for the Psychophysiological Study of Sleep (i.e., APSS), subsequently to become the SRS. The stated goals of the APSS were: to sponsor and organize a single Annual Meeting; to represent the interests of the professional sleep societies to the government, to the private sector, and to the public; and to oversee and coordinate the distribution of the professional publications of the three member societies: *SLEEP*, *Sleep Research*, and the *Journal of the Association of Polysomnographic Technologists*. A few years later the APT withdrew from the APSS partnership leading to yet another name change to Associated Professional Sleep Societies. Intentionally, the APSS acronym remained. Most people associate APSS with the name of Annual Meeting of the professionals in the field of Sleep Medicine and Sleep Research. The APSS, from inception until 2001, was a partnership between the SRS and the AASM and was run by a Joint Operating Committee (JOC) under an agreement that allowed each society 1 vote in making policy decisions. Consequently, all decisions had to be made by consensus between the two societies. For liability purposes following the September 11, 2001 attacks, the APSS changed its legal status, but not its name or purpose, from a partnership to a Limited Liability Company with a Board of Directors and President. The APSS was and remains responsible for the care and management of two primary assets of the AASM and the SRS; the APSS Annual Meeting and the journal, *SLEEP*.

Evolution and Growth of the Annual Scientific Meeting

Evolution of the scientific meeting

As recounted in the development of the SRS, meetings related to sleep science began in 1961 predominantly under the sponsorship of the SRS's predecessor, the Association for the Psychophysiological Study of Sleep. Beginning in 1981 the ASDC held its first annual meeting that shared basic scientific and clinical science related to the growing field of Sleep Medicine. Although initial attendance was sparse, with only 150 attendees, it proved a need existed. In subsequent years, the ASDC held joint meetings with the American College of Chest Physicians, Academy of Head and Neck Surgery and the SRS.

In June 1986 after the creation of the initial 3 society federation, the first APSS meeting was held in Columbus, Ohio hosted by the Division of Sleep Medicine at Ohio State University with a local program committee chaired by Dr. Helmut Schmidt. Important contributions also were made by Mr. Jon Hollett of the Ohio State University Center for Continuing Medical Education. This was to be the last "sleep meeting" hosted by a single institution. Subsequent meetings were organized nationally by the APSS. By all accounts the first meeting was a resounding success. Meeting registration was 739 persons and was supported by 32 exhibitors. Additionally, the meeting was held in conjunction with the first "National Sleep and Health Awareness Week", an event that since 1998 has been promoted by the National Sleep Foundation.

In 1987 the ASDA and the SRS met independently for the last time because the SRS had a previous commitment to have a meeting outside the U.S. every fourth year. The ASDA met in September 1987 in San Francisco, California, the only time an annual meeting was not held in June. The APSS meeting resumed in 1988 in San Diego, California. In two short years attendance had jumped from 739 to 1,030 and exhibitor support had increased from 32 to 40. The early success of the APSS meeting can directly be attributed to the tireless efforts of many volunteers. Staff during these early years consisted of only four dedicated individuals, led by Mrs. Carol Westbrook, then ASDC Executive Director. Furthermore, at that time, there was no technology available to ASDA and SRS members or the staff, which made the effort and success all the more impressive.

Abstract submissions also are generally used as a gauge for measuring growth of a discipline. In 1986, there were 300 abstracts presented at the first APSS meeting and by 1989 this grew to 448. Over the next 15 years abstract submissions have climbed to approximately 1,000 per year. While the growth at first glance may not appear all that impressive, a change in policy for submitting abstracts significantly reduced the growth rate. In 1997, then Scientific Program Chair, Dr. Jerome Siegel found that many of the best sleep scientists were submitting as many as 10 abstracts per year. Consequently, he instituted a controversial policy change to

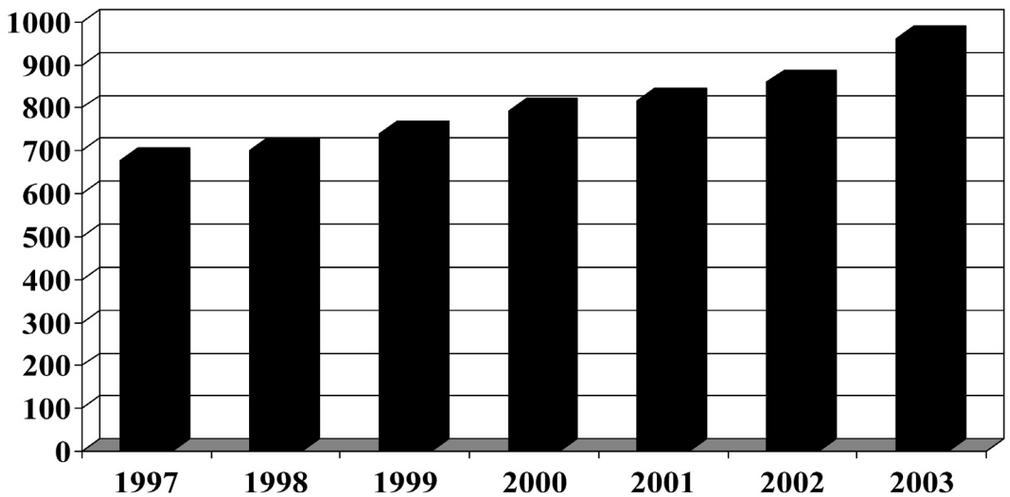

Figure 3—Membership of the Sleep Research Society

limit submissions to no more than two abstracts as lead author.

Another major step for the APSS came in 1999. At this time, publication of the meeting abstracts moved from *Sleep Research* to a supplemental issue of the journal *SLEEP*. *SLEEP* has continued to publish the supplemental issue annually allowing easy access to the meeting abstracts to both the scientific and clinical communities.

The APSS Annual Meeting is now the largest gathering of sleep professionals in the world, and the premiere event for the field. Attendance now is over 5,000 registrants. In addition to attracting researchers and clinicians from across the United States, 17 percent of attendees are international, which reflects the global nature of the field.

Development of the meeting program

Beginning with the first APSS meeting in 1986, the annual meeting is planned and coordinated through a Scientific Program Committee. For the first 6 years, the Scientific Program Committee was chaired by Dr. Thomas Roth who during his tenure built a solid foundation for the content of subsequent meetings. The following have served since Dr. Roth as Program Chair: Drs. Jerome Siegel, Ruth Benca, David White, Ronald Szymusiak, and David Gozal. Each Program Chair and all Program Committee members have dedicated considerable time, provided valuable input, and imparted beneficial knowledge in order to ensure the success of the APSS Annual Meeting. Undoubtedly, this concerted effort ensures the vitality of the APSS Annual Meeting and enables its continued success.

Currently, the Program Committee with equal representation from the AASM and SRS annually creates a scientific program that presents new discoveries in the field, offers valuable educational forums for all attendees, and also identifies areas for growth and development. At the 2004 Annual Meeting, more than 940 abstracts, 237 speakers, 51 meet-the-professor sessions, 20 symposia and three clinical workshops were featured and represent the most comprehensive scientific program to date. Moreover, the Annual Meeting provides an opportunity for members of both organizations to gather and exchange knowledge and discuss relevant topics in the field.

THE JOURNAL *SLEEP*

A journal dedicated to sleep research was originally proposed in 1973 by the Association for the Psyhophysiological Study of Sleep (APSS). However, the idea was soundly rejected that year and it was not until 1977 that the concept reemerged and was endorsed by a small majority. However, the APSS would not raise dues to support the journal, would not direct funds to it, and to avoid apparent conflicts, would not allow advertising by the pharmaceutical industry. Despite these solvency issues, a search began for an editor-in-chief and eventually Dr. Christian Guilleminault was selected with Dr. William Dement serving as a co-Editor. An APSS Publication Board was formed and chaired by Dr. Eliott Weitzman with the directive that an issue of the journal was to be published within 18 months.

Dr. Guilleminault, as he initiated the Journal, set up a number of "ground rules" including:

1) The need for peer review of all submissions.
2) There would be no charge for publication.
3) Submission in English was suggested but not required, and
4) Free editing was provided to non-English speaking authors.

This offer of free "editing" proved to be a major undertaking, most of which was handled by Ms. Mary Smith, the first editorial assistant. Finding a publisher also proved to be a challenge as the society (APSS) wanted to control/own the Journal, but not assume financial responsibility for it. Raven Press emerged as the only viable candidate, and, despite their unwillingness to support a half-time editorial position, was selected. The original relationship with Raven was complex as they kept all advertising revenue, while APSS collected fees from the membership subscribing to the Journal. On the other hand, Drs. Guilleminault and Dement handled all administrative/editorial activities and officially owned the journal with full financial responsibility for it. In addition, the Journal was to have a maximum of 100 pages per issue and three issues had to be completed before the first would be published.

These conditions proved to be quite a challenge to Dr. Guilleminault and his colleagues. Despite these hurdles many aggressive young investigators and senior ones as well supported this journal with their science. Prominent examples included studies by Drs. Ralph Lydic and John Orem on the upper airway

Table 1—APSS meeting location, attendance, number of exhibitors and abstracts

Year	City	Attendance	Exhibitors	Abstracts
1986	Columbus, OH	739	32	287
1988	San Diego, CA	1030	40	402
1989	Washington, DC	1363	42	448
1990	Minneapolis, MN	1342	47	410
1991	Toronto, Canada	1576	48	469
1992	Phoenix, AZ	1670	48	410
1993	Los Angles, CA	1737	54	412
1994	Boston, MA	2210	56	505
1995	Nashville, TN	2612	68	546
1996	Washington, DC	2557	68	584
1997	San Francisco, CA	2903	70	787
1998	New Orleans, LA	3097	86	618
1999	Orlando, FL	3113	92	582
2000	Las Vegas, NV	3821	89	703
2001	Chicago, IL	4028	98	797
2002	Seattle, WA	4122	111	760
2003	Chicago, IL	4800	115	1144
2004	Philadelphia, PA	5031	112	945

of the cat,[150] papers on sleep deprivation by Drs. Christopher Frederickson and Alan Rechtschaffen,[151] basic studies of REM sleep induction by Dr. N. Sitaram and colleagues,[152] and a study of genetic factors in canine narcolepsy by Dr. Arthur Foutz and co-workers.[153] The journal also benefited from the lack of recognition of the obstructive sleep apnea syndrome, thus leading to a number of submissions on this topic that had difficulty finding a niche elsewhere. The first issue was published in January 1978 with the plan to have 4 issues per year.

Over its first several years a number of important scientific concepts emerged from the pages of *SLEEP*. Dr. Loyd Glenn and co-workers demonstrated hyperpolarization of motoneurons during REM sleep.[154] Dr. Murray Johns established the Epworth Sleepiness Scale.[155] The methods and normal values for the Multiple Sleep Latency Test were defined.[156] Dr. Carlos Schenck and colleagues described "REM Behavior Disorder",[43] while the concept of chronotherapy emerged from Dr. Charles Czeisler and co-workers.[157] At the end of five years, *SLEEP* was established sufficiently in the scientific community such that the editors no longer had to attend numerous scientific meetings to solicit papers for the Journal.

At this point, a number of changes occurred. First, ownership of the Journal moved from Drs. Guilleminault and Dement to three societies (the SRS, the European Society for Sleep Research and the ASDC). Second, advertising revenues allowed for the hiring of a 50% editorial assistant which, at the time, was a major step forward. However, despite considerable progress, without the firm financial backing of the societies, Raven Press would not allow an increase in the number of issues, which remained at four until volume 10 in 1987. That year the number of issues increased to six.

In the early 1990's, it was decided that there was adequate material for 8 and subsequently 10 issues per year. In addition, the decision was made to move publication from the Raven Press to the Allen Press, which would serve as a printing company not a publisher. This meant that all proofing had to be handled by the Editor and his now 75% assistant. In 1996, the Journal temporarily progressed to 12 issues per year.

In 1996, for a variety of reasons, the APSS, which now managed the Journal, made the decision to publish the Journal from its office in Rochester rather than having virtually all operations handled at Stanford. At this same time the decision was also made to have a regular rotation of Editors with 5-year terms. As a result, a search committee year was organized (chaired by Dr. Emmanuel Mignot) and in the summer of 1997, Dr. Thomas Roth was chosen Editor-in-Chief of the Journal. Thus on January 1, 1998, Dr. Roth assumed responsibility for the scientific content of the Journal and Mr. Jerome Barrett, Executive Director of the then ASDA, handled all operational and financial issues.

During Dr. Roth's five years at the helm of the Journal, many changes occurred. He first streamlined the review process and in 1998, first published the abstracts from the Associated Professional Sleep Societies meeting (APSS). That same year a web site was established and in 2000 all current and previous issues of *SLEEP* were archived on it. Although the impact factor for the Journal had been rising, under Dr. Roth there was a substantial further increment to a value approaching 4.0 in his last year.

In the spring and summer of 2002 another search committee was organized, under the chairmanship of Dr. Robert McCarley, and a new Editor-in-Chief was sought. On this occasion, Dr. David White was selected for a six-year term as Editor-in-Chief with the new stipulation that future Editors would overlap with their predecessor for a year to maximize smooth transitions.

Under Dr. White's leadership a number of changes occurred. His first decisions were to select and delegate Associate Editors to oversee the review of submitted manuscripts, appoint a team of Deputy Editors to help with decisions regarding policy and direction, and reestablish an Editorial Board for the Journal. With the help and support of Ms. Jennifer Markkanen, AASM Assistant Executive Director, Dr. White transitioned the review process to an electronic format using ScholarOne. This led to a remarkable improvement in review time which, by 2004, had decreased to approximately 30 days. He also began adding editorials to each issue of the Journal, publishing reviews on a variety of topics, and increased, to some extent, the size of the Journal. This led to a substantial increase in the number of submitted manuscripts. Thus, at the time of this printing, the Journal is published 8 times per year with plans to go to 12 issues by 2005. It currently receives about 400 submitted manuscripts per year.

ACADEMY OF DENTAL SLEEP MEDICINE

The Academy of Dental Sleep Medicine (ADSM) was founded as the Sleep Disorders Dental Society in 1991 by eight dentists with an interest in treating patients with sleep-disordered breathing. What began as monthly conference calls between colleagues discussing clinical applications of oral appliance therapy for treatment of upper airway obstructive pathology has developed into an international network of dentists, physicians, oral and maxillofacial surgeons, and researchers interested in advancing the practice and knowledge of this field. The primary purpose of the Academy is to foster increased knowledge regarding oral appliance therapy and upper airway surgery in patients with sleep-related breathing disorders and obstructive sleep apnea to the dental and medical professions, as well as to the general public.

Throughout the 1990's the ADSM grew in size and scope, providing continuing education through its annual meeting, and providing a forum for exchange between its members. Significant advances within the body of research and professional literature during this time interval contributed to the legitimization of (and appreciation of) oral appliance therapy for treatment of OSA, and the annual meeting quickly established a worldwide reputation for providing cutting-edge scientific research within this field.

In 1998, the ADSM established a certification program in dental sleep medicine as a means for dentists with an interest and expertise in the field to be recognized as possessing the knowledge and skills necessary to interface with physician colleagues in the management of sleep patients. The certification process tests competency in sleep medicine, oral appliance therapy and upper airway surgery, and certification indicates to patients, professional colleagues and organizations in both medicine and dentistry that one has met baseline established criteria in these areas. The ADSM Certification Committee administered its first examination in 1999 and has offered an examination each year thereafter.

In 2002, the ADSM transferred its national office headquarters to Westchester, Illinois and contracted its management with the AASM. The move brought the ADSM physically closer and tightened organizational affiliation not only with the AASM, SRS, APT, and APSS, but also with groups such as the American Dental Association, Academy of General Dentistry and the

American Association of Oral and Maxillofacial Surgeons.

In recent years, the ADSM has experienced strong growth and development. There are currently over 650 members of whom 105 have passed the certification examination. International membership has grown significantly with 70 dentists from 22 countries having joined. The Academy recently has assisted in fostering and establishing sister academies in Europe, Asia, and Australia. The ADSM also is involved in the legislative and policy arenas, providing support on a state- by-state basis for practitioners of this new and emerging field.

THE AMERICAN BOARD OF SLEEP MEDICINE

The first examination in clinical polysomnography was given in Cincinnati in 1978 under the direction of Drs. Mary Carskadon, Christian Guilleminault, Peter Hauri, Milton Kramer and Thomas Roth. Twenty-one candidates passed the exam and certificate #1 in clinical polysomnography was awarded to Dr. William Dement on April 6, 1978. The examinations for 1978 and 1979 consisted of a series of true and false type questions and an oral examination with senior clinicians and researchers examining each other.

Beginning with the 1980 examination co-chaired by Drs. Schmidt and Guilleminault, major changes were instituted. The Part I examination was designed to cover the basic sciences and clinical aspects of sleep and sleep disorders in two sections of multiple choice questions that could be statistically analyzed, allowing year-to-year comparisons. The oral form of the examination (Part II) was replaced by a format that included the review of two full polysomnograms and an MSLT, followed by questions requiring both essay type and short answers on scoring and clinical decision making. It was felt that face-to-face examinations among a relatively small pool of candidates, typically familiar with each other, would affect the grading process and could make adverse decisions less likely and also difficult to defend legally. A coding system was initiated with the code only broken after all final decisions were made by the full examination committee. In addition, until 1985, Dr. Schmidt insisted that all hand-written responses by candidates were transcribed by his secretary to avoid potential candidate identity recognition. A polysomnographic record fragment section was created for Part II with case vignettes and an entirely multiple choice format. In 1988, this was shifted to Part I, which was held in early fall while Part II was shifted to early spring. The questions and their performance history in prior exams were maintained on 5" x 8" cards organized by major topics in boxes, thus leading to the name "Shoe Box" or Helmut S. Schmidt Award given yearly for meritorious service to the American Board of Sleep Medicine (ABSM). Much of the exam evolution occurring in the 1980's can be credited to the efforts of Dr. Schmidt. Additionally from 1980-1989, Professor Donald J. Smeltzer of the Department of Psychiatry at Ohio State University provided hundreds of hours of invaluable assistance in statistics and exam item creation—expertise he gained from directing the national pre-certification practice examination for psychiatric residents.

The 1980's witnessed tremendous growth in the applicant examination pool, During these years, the exam coordination and process was supported by Dr. Schmidt's chief technologist, Ms. Linda R. Fortin. Those responsibilities transferred in 1986 to Ms. Kathy Brutinel of the ASDA office in Rochester. Dr. Schmidt became chair of the examination committee in 1982, and in 1985 began to press for a legally independent examination board. At its November 17, 1990 meeting, the American Sleep Disorders Association unanimously voted to create the ABSM. The first board of directors meeting of the ABSM was held in Dublin, OH on April 27 and 28, 1991 with Dr. Helmut Schmidt serving as its first President. Up to that time, 514 individuals had passed the examination: 33.8% neurologists, 30% pulmonologists, 15.6% psychiatrists, 4.5% other physicians, and 16.5% Ph.D.'s.

The history of the Board's first 13 years is a story of exponential growth in the number of diplomates, expanding recognition, increasing professionalism, and developments in the forefront of examination technology. Subsequent presidents of the ABSM were Drs. Wolfgang Schmidt-Nowara (1991-1994), Michael S. Aldrich (1994-1997), Barbara Phillips (1997-2000), Michael H. Silber (2000-2003) and Nancy C. Collop (2003-2006). Figure 4 shows the dramatic growth in the number of individuals certified in Sleep Medicine as Diplomates of the ABSM. By 2002 this number had more than quadrupled to 1,945. Of the diplomates certified in 2002 or earlier, 54% were pulmonologists, 25.5% neurologists, 7% Ph.Ds, 6.5% psychiatrists, 3.5% internists, 2% pediatricians, and 1% other specialists including otolaryngologists. Successful examinees were initially given the title of Board Certified Sleep Specialist (BCSS), but later this name was changed to Diplomate of the ABSM. By 2003, 2,324 certificates had been issued. In order to encourage the growth of sleep medicine internationally, in 1999, the ABSM allowed candidates from outside the United States and Canada to take the examination, awarding successful examinees with the title of ABSM Certified International Sleep Specialist.

Increasing recognition of the ABSM and growing respect for its certification followed. The AASM required directors of AASM accredited sleep centers to be certified by the ABSM. The State of California agreed in 1998 that the ABSM met standards equivalent to boards affiliated with the American Board of Medical Specialties (ABMS) and allowed ABSM diplomates to advertise their qualification. Increasing professionalism accompanied the Board's growth. Credentialing procedures became more rigorous, depending on objective criteria rather than subjective judgment. Although the preferred route to accreditation was always completion of a fellowship in Sleep Medicine, the majority of candidates qualified under one of two waivers, allowing for varying combinations of training and experience. These waivers were finally eliminated in 2004. Over the years the Board was ably served by a number of Examination Coordinators. However, with increasing growth, the ABSM reorganized its administrative structure. In 2001, Mr. Jerome Barrett was appointed Executive Director and has remained in this position, providing experienced leadership as well as serving as an important liaison to the AASM. A conflict of interest policy, introduced in 2000, resulted in directors and examiners no longer participating in board review courses.

The Part I examination remained relatively unchanged over the years, consisting of 3 booklets of multiple choice questions covering the basic sciences of sleep, clinical sleep medicine, and interpretation of polysomnogram fragments and other material. However, the Part II examination has evolved. As paper polysomnograms became less commonly used in clinical practice, the examination was converted with the first fully computerized examination being offered in 2003. This consisted of a

series of clinical cases with partial polysomograms, multiple sleep latency tests and other relevant data with candidates typing short answers to questions. This format has placed the ABSM at the forefront of groups pioneering innovative computerized examinations. With the elimination of the waivers, the ABSM has decided to fuse the two parts of the examination in 2005, offering a single day, one part computerized examination incorporating the format of both current parts.

Despite its growth in reputation and numbers of diplomates, it became evident by the late 1990s that the ABSM as a freestanding board would not be recognized as fully legitimate by organized medicine. Because sleep medicine requires only one year of post-residency fellowship training, the ABSM was ineligible to join the ABMS as an independent board. Following several years of preparatory discussions a historic meeting dubbed the "sleep summit" was held in Philadelphia in 2002. It was attended by the American Board of Internal Medicine (ABIM), the American Board of Psychiatry and Neurology (ABPN), the American Board of Pediatrics (ABP), the ABSM, the AASM, the Accreditation Council for Graduate Medical Education (ACGME) and a number of national professional societies. A consensus plan was developed for the establishment of a new multidisciplinary subspecialty examination in Sleep Medicine to be jointly offered by the ABIM, the ABPN and the ABP. Following further successful negotiations, a plan for this examination was submitted to the ABMS in early 2004. It is hoped that the first new examination will be offered no later than 2007. At that time, the ABSM will cease offering the current test.

SLEEP MEDICINE FELLOWSHIP TRAINING

Physician Training

In 1988, the AASM formed the Sleep Medicine Fellowship Training Committee. While the committee composition has varied over time, all members are board certified sleep practitioners and researchers, with mixed primary specialty representation (e.g. pulmonary, neurology, psychiatry physicians and PhDs, primarily psychologists). The committee was initially charged with developing formal guidelines for the comprehensive training of physicians in Sleep Medicine. Prior to this, Sleep Medicine training largely consisted of self-directed or loosely mentored experiences. Largely these experiences occurred within neurophysiology or pulmonary fellowships. Trainees then, as now, had divergent backgrounds ranging from internal medicine, pulmonary, psychiatry, neurology, and pediatrics. Thus, specific needs varied with the trainee, and program capabilities and focus paralleled the primary specialty field providing that training. Training duration and exposure were similarly heterogeneous. Nevertheless, dedicated training in Sleep Medicine did occur in a few centers across the United States, notably Stanford University, the University of Pennsylvania, the University of Chicago and Harvard University.

During its initial years, the Sleep Medicine Fellowship Training Committee concentrated on developing guidelines to ensure comprehensive training in clinical, technical and research aspects of sleep medicine. This task was made more challenging given the multidisciplinary characteristics of the field, and the diverse backgrounds of both trainees, and programs. Eventually, guidelines were developed that recommended a training standard comparable to other specialty training in medicine. Specific content areas included basic neurological sleep mechanisms, chronobiologic mechanisms, cardiovascular, pulmonary, endocrine and gastrointestinal sleep physiology, specific disorders of sleep, psychopharmacology of sleep, as well as the operation of polysomnographic equipment, polysomnographic interpretation and troubleshooting. Furthermore, it was recognized that based on their previous experience, the needs of trainees would be different, and this would necessitate some curriculum flexibility by training programs. In some cases in order to provide exposure to the entire field of Sleep Medicine, programs would be required to provide educational experiences or enlist the assistance of faculty outside their primary area of emphasis. As a result of these initial efforts, in 1989 the Committee granted AASM fellowship accreditation to its first two programs: Stanford University in California and the Center for Sleep and Wake in New York. In ensuing years, accreditation has been granted to a number of other programs. The accreditation period was for five years, and programs were then evaluated at the end of that time period for re-accreditation.

In reality, although the full one year training program was the model for comprehensive Sleep Medicine training and paralleled

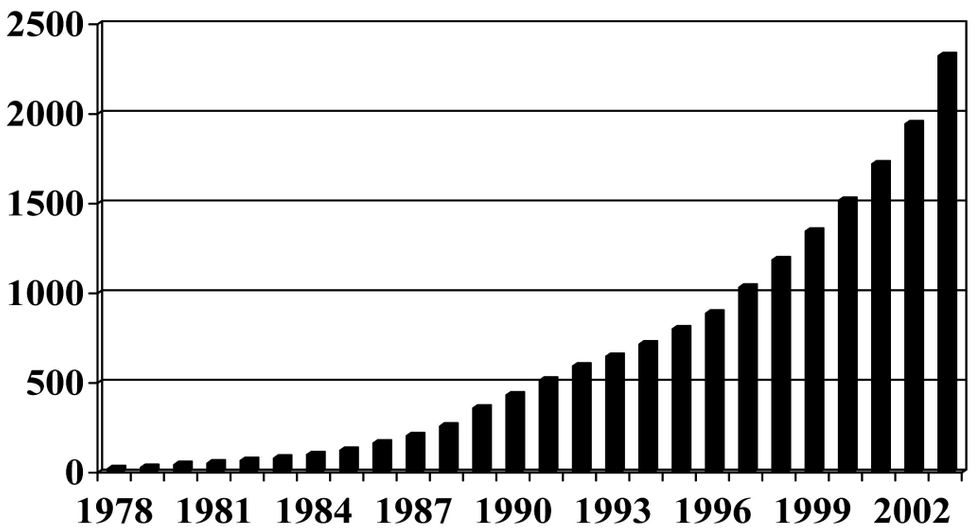

Figure 4—Total number of individuals certified in Sleep Medicine by the ABSM

specialty training in other disciplines, most sleep medicine training was being provided in alternative paradigms. Many trainees were receiving their Sleep Medicine training as a component of their fellowships in pulmonary medicine or neurophysiology. This represented an additional challenge to the Sleep Medicine Fellowship Training Committee. In order to ensure comparable training to one-year Sleep Medicine fellowships, the AASM charged the Committee to develop more specific guidelines to improve the quality of Sleep Medicine training within existing non-sleep fellowship programs. An alternative track (also known as level 2 fellowship) mechanism thus was established. In such programs, 6 months credit was given to trainees for relevant pulmonary or neurophysiology training and experience. However, such programs then needed to also furnish 6 months of dedicated Sleep Medicine training focusing on content areas that are not ordinarily components of pulmonary or neurophysiology training. Most alternative track fellowships developed within pulmonary programs and ultimately several of these became full one-year sleep fellowships.

Board eligibility is an obvious goal of the individual completing Sleep Medicine training. The American Board of Sleep Medicine (ABSM) requires its candidates to have the equivalent of one year of formal fellowship training in Sleep Medicine. During the initial years of the examination, most applicants met these requirements through a clinical waiver, with limited formal training. However, with time, the impact of growing numbers of fellowships, both unaccredited and accredited, led to more candidates from Sleep Medicine fellowships applying for the ABSM examination. This is reflected by data from candidates for the ABSM examination. By 1995, 43% of candidates applied under a clinical experience waiver, 27% had some clinical training and 30% had completed a full year of training. Many of the full year fellowships, however, were not standardized or accredited. Nevertheless, a total of 31 sleep fellowship programs had been accredited by the AASM by 2002. To encourage the accreditation process and thus further standardize training in the field, the ABSM decided to phase out the clinical waiver option by 2003, and to require a full year of Sleep Medicine training in an AASM-accredited fellowship by the year 2005. This decision resulted in increased efforts by many institutions to develop new fellowships, or to bring existing fellowships up to the accreditation standards of the AASM.

In 2002, as part of its strategic initiatives to increase acceptance of Sleep Medicine as an independent medical specialty, the AASM applied to the Accreditation Council on Graduate Medical Education (ACGME) for the establishment of Sleep Medicine training programs within the ACGME. This application was favorably reviewed within the ACGME, and in spring 2003 the ACGME appointed a Sleep Medicine Working Group (SMWG). The SMWG was comprised of members representing the AASM, the American Boards of Internal Medicine and its subspecialty Pulmonology board, Pediatrics, Psychiatry and Neurology, as well as the ACGME. Using current Sleep Medicine fellowship requirements as a template, the SMWG developed training requirements for ACGME approved 1 year Sleep Medicine fellowships. These initial training requirements were approved in June 2004 and the ACGME currently is accepting applications for accreditation. These new fellowships will be open to trainees who have completed residency programs in Internal Medicine, Neurology, Pediatrics, Otolaryngology or Psychiatry. As a result of the ACGME's action, the AASM is phasing out its own accreditation program and the role of the AASM Sleep Medicine Fellowship Training Committee has now changed to facilitating and encouraging programs to apply for ACGME accreditation. The new fellowships will be eligible for direct and indirect federal graduate medical education funding, and trainees will be eligible to sit for the new American Board of Medical Specialties examination in Sleep Medicine that is currently in development. It also is expected that ACGME accreditation will encourage further growth of the number of Sleep Medicine training programs that are available and thereby enhance recognition and expansion of the field.

Ph.D. Training

From the beginning, Ph.D.'s have been major contributors to the science and clinical practice of Sleep Medicine. In the clinical arena, their contributions have been particularly noteworthy in the area of Behavioral Sleep Medicine (BSM). The focus of BSM is on the evaluation and treatment of insomnia, especially cognitive behavioral therapy, the evaluation and treatment of circadian rhythm disorders and parasomnias, as well as improving the compliance of patients with various treatment measures such as positive airway pressure for sleep disordered breathing. Recognizing that the needs for the training of PhDs in Sleep Medicine are different from those for physician training, the AASM Fellowship Training and Behavioral Sleep Medicine Committees developed guidelines for Ph.D. training in Sleep Medicine. The first review course in Behavioral Sleep Medicine was offered by the AASM in April 2004. To meet an anticipated demand for qualified Behavioral Sleep Medicine practitioners, the AASM approved a plan by the Behavioral Sleep Medicine Committee to offer a new examination in Behavioral Sleep Medicine for psychologists as well as physicians with training in this field. The first examination was given in 2003 by a committee led by Dr. Edward Stepanski resulting in 31 candidates being certified.

It is the expectation of the AASM that training and certification in Behavioral Sleep Medicine will encourage continued entry of qualified Ph.D.'s into the field of Sleep Medicine as members of the health care team providing care for patients with sleep disorders.

NATIONAL COMMISSION ON SLEEP DISORDERS RESEARCH

Recognition of the morbidity and public health impact of sleep disorders and sleep deprivation not only led to the development of sleep medicine, but also dramatically increased the number of pressing research questions related to the disorders. Existing institutional structure and public policies, however, impeded growth of the field. The two major barriers were limited funding of clinical sleep research by the National Institutes of Health (NIH), and difficulty in obtaining reimbursement from Medicare and insurance companies for sleep medicine services. Several visits to NIH and the Health Care Finance Administration (HCFA, now the Centers for Medicare and Medicaid Services) by the officers of the Association of Sleep Disorders Centers brought little progress and no clear solutions. In 1985 the ASDC took an initial step toward organized government affairs activity by retaining the services of a Washington representative, Mr. Dale Dirks of the Health and Medicine Council of Washington, and

ASDC representatives began to make Congressional visits and to present testimony before Congressional committees.

Progress was slow, as both the NIH and HCFA are constantly deluged with requests for increased funding. In the summer of 1988, ASDC president Dr. William Dement and Mr. Dale Dirks, visited the office of Senator Edward Kennedy, then Chairman of the Committee on Health, Education, Labor and Pensions which has jurisdiction over the Department of Health and Human Services and the NIH. In a meeting with Senator Kennedy's health liaison, Dr. Mona Sarfaty, authorization by the Committee of a national institute for sleep disorders was requested. Dr. Sarfaty asked about how many individuals were practicing sleep medicine around the United States at that time and politely chuckled at the answer. "Your small numbers do not justify such a major legislative step," she said, "but one route to a more mainstream presence would be the creation of a national commission that would study the impact of your field in society and report the results to the Congress along with recommendations."

In November 1988, legislation creating the National Commission on Sleep Disorders Research was included within the NIH reauthorization bill. The relevant sections of the legislative mandate follow:

a) conduct a comprehensive study of the present state of knowledge of the incidence, prevalence, morbidity, and mortality resulting from sleep disorders, and of the social and economic impact of such disorders;
b) evaluate the public and private facilities and resources (including trained personnel and research activities) available for the diagnosis, prevention, and treatment of, and research into such disorders; and
c) identify programs (including biological, physiological, behavioral, environmental, and social programs) by which improvement in the management and research into sleep disorders can be accomplished.

Because of the government's practice of insuring ethnic, geographic, and gender balance for federal appointments, it took nearly a year and a half to select, invite, and receive acceptance from the commissioners. The first meeting of the National Commission on Sleep Disorders Research was on March 28, 1990 in Bethesda, Maryland. The ten appointed commissioners included six representatives of the sleep research/medicine community (Drs. William C. Dement, Mary A. Carskadon, Norman H. Edelman, June M. Fry, James P. Kiley, Debra J. Myers) and four from related private and government agencies (Mssrs. Joseph A. Piscopo, Floyd J. Brinley, Jr., Jehu C. Hunter, Felix Strumwasser).

The National Institute on Aging (NIA) was selected as the lead Institute, and Dr. Andrew Monjan, who managed NIA's sleep research portfolio, became the able Executive Secretary of the Commission. Dr. Dement was elected Chairman and Dr. James K. Walsh was appointed as Special Advisor.

Although Secretary of Health and Human Services Dr. Louis Sullivan chartered the Commission at $400,000 per annum, he also stated that this should come from contributions by individual Institutes. At the first meeting, the Director of the NIH reported that no Institute was willing to make a contribution because it would reduce their ability to fund research. This was a considerable shock to the Commissioners. Dr. Dement considered resigning because he did not see how the Commission could fulfill its daunting and sizable mission without funding. Fortunately Carnegie Corporation President, Dr. David A. Hamburg, recognized the importance of the opportunity. Carnegie made a grant to Stanford University, making possible employment of a Commission manager and establishment of a Commission office at Stanford. The manager from late 1988 to the end of 1992 was Ms. Molly Haselhorst, who ably assisted the Commission chair and coordinated many Commission activities.

The Commission gathered voluminous data from the scientific literature and expert interviews during 1990 and 1991. Additionally eight public hearings in various locations around the United States provided unique and compelling input from individuals impacted by sleep disorders and sleep deprivation. For those Commissioners who cared for and interacted with sleep disorder patients, these tragic and touching reports confirmed their belief that strong public policy recommendations were warranted. For Commissioners not personally involved with the victims of sleep deprivation and disturbances, the witnesses' testi-

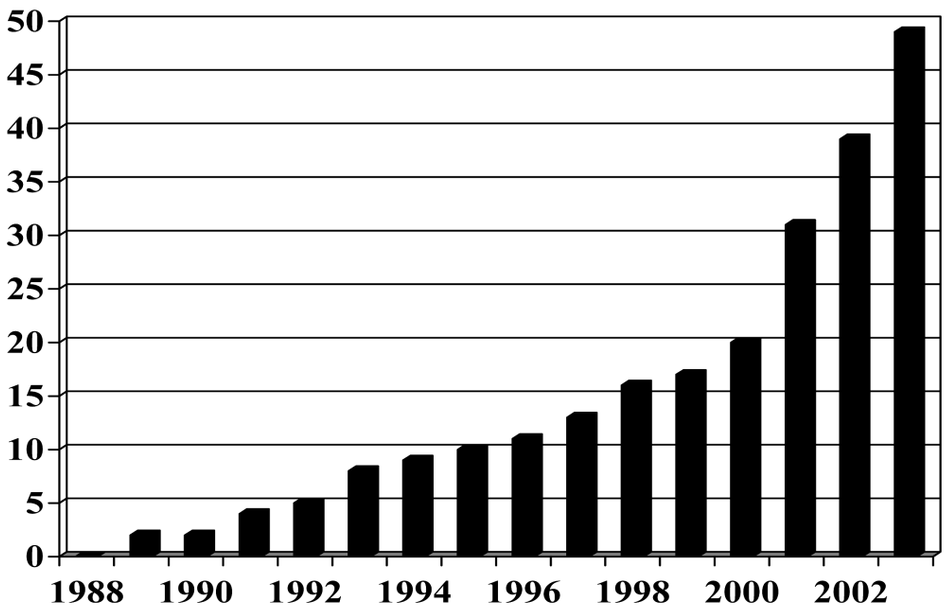

Figure 5—Growth in the total number of AASM accredited fellowship training programs in Sleep Medicine

monies attached the reality of human suffering to the numbers and dollar signs of scientific reports. They too were ready to act. Perhaps most important was the public hearing in Portland, Oregon, where the Commission's activities captured the attention of Senator Mark O. Hatfield. Senator Hatfield's chief of staff chaired the Portland hearing, and from that moment the Hatfield office stayed in very close touch with the Commission.

The final report of the National Commission was submitted to Congress in October 1992. It contained six recommendations (abbreviated below):

1. the establishment and funding of a national center for research and education on sleep and sleep disorders, housed within an existing NIH Institute
2. expansion of federal support for sleep research and health services
3. the establishment of offices on sleep and sleep disorders within all federal departments and agencies
4. substantially increased support for all federal agencies currently engaged in sleep and sleep disorders research
5. encourage and support training in sleep and sleep disorders
6. a major public awareness/education campaign about sleep and sleep disorders be undertaken immediately

On November 4, 1992, Senator Hatfield convened a field hearing of the Senate Appropriations Committee in Portland, Oregon, and a number of Commission members, patients, and other sleep professionals attended and testified. At the end of the day, Senator Hatfield characterized America as a "vast reservoir of ignorance" about sleep, and announced, "When I return to Washington, the first business of the Senate of the United States will be legislation to establish a National Center on Sleep Disorders Research, as recommended in your report."

The Commission had previously decided that a center within an institute would be the best solution, and its recommendation was modeled on a study of the National Center for Medical Rehabilitation Research. This Center was housed in the National Institute for Child Health and Human Development, and it had a line-item annual budget. It was therefore anticipated that a line-item budget would be appropriated for the National Center on Sleep Disorders Research.

The difficult choice at that time was which institute should house the NCSDR. A small committee, which included Drs. William Dement, James Walsh, Allan Pack and Mr. Dale Dirks, then visited the Director of each of the five NIH Institutes that were funding substantial sleep research grants. These were the National Institute of Mental Health (NIMH), the National Institute of Neurological Disease and Stroke, the National Institute of Aging (NIA), the National Heart, Lung and Blood Institute (NHLBI), and the National Institute of Child Health and Human Development.

The only Institute Director expressing enthusiasm and support for the opportunity to incorporate the NCSDR into his Institute was Dr. Claude Lenfant of the National Heart, Lung and Blood Institute. Accordingly, NHLBI became the first choice. At that point, some in the sleep community advocated that the center should not be placed in the NHLBI but rather in the NIMH despite a lack of interest and support from the NIMH Director and staff. This caused a major delay in submitting the legislation, during which Congress passed the Budget Reconciliation Act of 1993 in response to concerns about the budget deficit. Among other things, this Act eliminated direct funding of agencies below the level of Institute. Accordingly, line item funding was withdrawn from the National Institute on Medical Rehabilitation Research, and when the legislation was finally passed creating the National Center on Sleep Disorders Research no specific funding appropriation was made. It is to the everlasting credit of the NHLBI and its Director that the National Center has functioned so well in promoting research and achieving a heightened visibility for the field in the United States.

As a historical footnote, Senator Hatfield wrote a letter requesting Senator Kennedy to include his legislation to establish a National Center on Sleep Disorders Research in the 1993 NIH reauthorization bill, and Kennedy requested supporting signatures from at least three additional senators. Those signing were Senator Jeff Bingaman of New Mexico, Senator Paul Simon from Illinois, and Senator John Chafee from Rhode Island.

An advisory board was appointed and met for the first time on August 10, 1994. The inaugural members of the National Center on Sleep Disorders Research Advisory Board (NCSDR) included Drs. Rosalind Cartwright, Wayne Crill, J. Christian Gillin, Debra Myers, Allan Pack, Barbara Phillips, Thomas Roth, James Walsh and Mr. Bobby Heagerty and Ms. Joyce Lewis and Mrs. Carol Westbrook. At the first meeting Dr. Roth was elected Chair of the Advisory Board, and Drs. Walsh and Pack were selected, respectively, as Chairs of the Education and Research Sub-committees. Plans were then made to create the first national plan for sleep research.

Dr. James Kiley served as the first Director of the NCSDR until 1999 after which Dr. Michael Twery served as acting Director in 2000 followed by Dr. Carl Hunt's appointment as Director in January 2001. Total NIH sleep research funding has increased from 76 million in 1996 to an estimated 203 million in 2003.

THE ASSOCIATION OF POLYSOMNOGRAPHIC TECHNOLOGISTS AND BOARD OF REGISTERED POLYSOMNOGRAPHIC TECHNOLOGISTS

Led by Mr. Peter McGregor with the encouragement of Dr Elliott Weitzman, the Association of Polysomnographic Technologists (APT) was created by a group of technologists attending a meeting of the Association for the Psychophysiological Study of Sleep in 1978. The purpose of the organization was to provide a structure for communication among those entering the new field of polysomnographic technology and to promote educational opportunities and professional identity within the discipline. Mr. McGregor served as the first APT president followed by Dr. Sharon Keenan, Mr. Cameron Harris, Mr. Todd Eiken, Ms. Pam Minkley, Mr. Robert Turner, Mr. Kelly Million and Ms. Rose Anne Zumstein.

Since its inception the APT has met conjointly with the various iterations of the APSS providing a unique opportunity for interaction between physicians, scientists and technologists. More recently the organization has produced annual courses each spring and fall to supplement the annual APSS meeting.

In acknowledgment of the need to provide education for patients, the APT sponsored the development of a network of patient support groups known as Alert, Well and Keeping Energetic (AWAKE). This program later became affiliated with the American Sleep Apnea Association. Recently the APT has become active politically as it deals with issues related to Respiratory Care licensure and polysomnographic testing.

Organizers of the APT recognized the need for a certification examination for polysomnographic technologists as one of their first

orders of business. In 1978, the APT created a committee to develop an exam. This led to the development of the American Board of Registered Polysomnographic Technologists (ABRPT) which subsequently shortened its name to Board of Registered Polysomnographic Technologists (BRPT) as it is named today. The first chair of the BRPT was Mr. Moshe Reitman. Others who have held that responsibility are Ms. Cynthia Mattice, Mr. David Franklin, Ms. Robin Foster, Ms. Andrea Patterson, Mr. Greg Landholt, Mr. Gary Hansen, Mr. Dan Herold and Ms. Bonnie Robertson.

Originally the BRPT was defined as a standing committee of the APT. Circumstances change, however, and by the late 1990's it was propitious for the APT and the BRPT to become separate entities. In 2000 the BRPT commenced operations independently from the APT. Mr. Cameron Harris was the first president and has been followed in that role by Ms. Marietta Bibbs and Mr. Mark DiPhillipo.

One of the biggest steps forward for the BRPT began in 1989. The APT contracted with Applied Measurement Professionals to use formal test development and administration methods to bring the RPSGT exam process in line with current certification testing practices. Such a relationship has continued with various testing professionals and in 2002 the BRPT became accredited by the National Commission for Certifying Agencies.

In June of 1979 the first exam was administered. Eight technologists became the first individuals to hold the Registered Polysomnographic Technologist (RPSGT) credential. At first the number of RPSGTs grew slowly, reaching 500 in 1991. Then growth accelerated exceeding 1000 by 1994 and 5000 by 2002. Today more than 6000 have earned the RPSGT credential.

HISTORY OF THE SLEEP FOUNDATIONS: NATIONAL SLEEP FOUNDATION AND AMERICAN SLEEP MEDICINE FOUNDATION

In the late 1980's the leadership of the American Sleep Disorders Association (now the American Academy of Sleep Medicine) identified a need for coordinated education efforts about sleep throughout many components of society. The concept of a national foundation evolved, to provide information about sleep and its disorders to the public, healthcare professionals, patients, the media and government agencies, and to raise funds to support education, training, and research in sleep. That concept became the National Sleep Foundation (NSF).

NSF was established in 1990 with a $100,000 unrestricted grant from the ASDA. The first NSF Board of Directors consisted of recognized sleep specialists, sleep disorder patients, and lay volunteers experienced in the nonprofit health agency field guiding the new foundation. Dr. Thomas Roth was the first NSF President and Mrs. Carol C. Westbrook served as its executive director. Dr. Roth announced the official formation of NSF on June 20, 1991 as an independent organization with charitable, 501(c)(3) status, and opened its doors in Los Angeles. NSF sponsored a Gallup Survey and announced that more than 35 million Americans suffer varying degrees of insomnia, recognizing it as America's most common sleep problem. In its first year of operation, NSF responded to more than 18,000 people who requested information about sleep and sleep disorders. Early efforts also included primary care physician tutorials on diagnosing and treating insomnia, a newsletter for healthcare professionals, and a public information campaign on the problem of drowsy driving: Drive Alert. Arrive Alive.

Over the next 12 years, the activities and programs of NSF grew as the Foundation pursued new ideas and partnerships. Individuals with Board of Directors' leadership roles have included Drs. Ronald Krall, Allan Pack, Lorraine Wearley, and Mr. John Hoag,. The NSF insomnia program and Drive Alert, Arrive Alive have been joined by comprehensive focus on sleep hygiene, sleep disorders and by public education initiatives on women and sleep, sleep and travel, sleep and pain, sleep and aging and shift work. NSF's annual Sleep in America poll has drawn extensive media attention since 1995, as it reflects the sleeping habits of America's adults and children.

The re-establishment of National Sleep Awareness Week in 1998 has generated an array of activities that involve federal, state and local organizations to promote and advocate healthy sleep. NSF has added a number of valuable communication tools, including the newsmagazine *SLEEPm*atters, the weekly e-mail newsletter NSF Alert, and its web site, which attracts more than 120,000 visitors each month. NSF's office relocated to Washington, DC in 1994 and over the subsequent decade, the NSF has funded 15 "Pickwick" fellows to conduct research in sleep science and medicine. Total funding has exceeded 1.2 million to date. The aim of the NSF, currently under the direction of current Board Chairman Dr. James K. Walsh and CEO Mr. Richard Gelula, is "waking America to the importance of sleep."

Sensing a need for increased support for educational, basic and clinical research in Sleep Medicine, the AASM established the Sleep Medicine Education and Research Foundation in 1998. Dr. Wolfgang Schmidt-Nowara was the guiding force in establishing the Foundation that was affectionately known as the SMERF. He served as its first President followed by Drs. Daniel Buysse and John Shepard. The name of the Foundation was changed to the American Sleep Medicine Foundation in 2003.

By design, the Board of Directors of the AASM and ASMF are identical. Because the Academy has been the major financial contributor to the Foundation to date, this structure ensures that the Foundation will direct its research and education programs into areas considered to be a priority for the field of Sleep Medicine by the Academy. In 1999 the Foundation funded it first two grants. These grants provided researchers at Stanford and the University of Pennsylvania the resources to obtain preliminary data that would support applications to NIH for clinical studies related to the treatment of obstructive sleep apnea with nasal CPAP. These two programs have been successful in obtaining multi-year, multi-million dollar funding.

The Foundation reviews 15-25 grant applications per year. Most of these grants are submitted for Faculty Career Advancement Awards and are reviewed by the members of the research committee of the AASM. These grants provide research funding for young faculty over a period of 2 years. The goal is to help these individuals achieve success in obtaining independent funding from more traditional sources such as the NIH. In 2004, the Foundation funded its first 2- year grant to support educational research. Since 1999 the Foundation has provided funding for 28 grants at a cost of slightly over $2 million dollars.

THE FUTURE OF SLEEP MEDICINE

Although this brief historical review chronicles the development of sleep science and sleep organizations in the United States, it nevertheless fails to recognize the innumerable individual contri-

butions of the thousands of researchers, educators, students, technicians, and practitioners whose collective efforts have culminated in the establishment of Sleep Medicine as an important field of medical practice. Patients whose lives have been adversely affected by disorders of sleep have also contributed to this effort. They have formed patient oriented organizations that function to provide patient education/services, disseminate information to the public and raise money for the support of sleep research. The Restless Legs Foundation, the American Sleep Apnea Association, the Narcolepsy Network and the American Insomnia Association are all contributing to the evolution of Sleep Medicine. The rate of progress has been incredible when we reflect on the fact that REM sleep was discovered only a half century ago and that Centers devoted to the diagnosis and treatment of disorders of sleep were organized only in the past quarter century.

As demand for the diagnosis and treatment of disorders of sleep continues to grow, a critical mass of sleep practitioners, educators and researchers will develop within Sleep Centers across the country. This will undoubtedly lead to the establishment of independent sections, divisions and/or departments of Sleep Medicine as has already occurred at Harvard and the University of Pennsylvania.

Growth in subspecialty areas of medical practice has often occurred in response to the needs of individuals and society. In the 1920s and 30s the practice of Pulmonary Medicine was limited primarily to the treatment of tuberculosis and other pulmonary infections. Growth in this field accelerated rapidly with the emergence of lung cancer and chronic obstructive pulmonary disease as major clinical problems in the 1950s after a sufficient number of years of tobacco exposure had occurred in the general population. In this context, the related epidemics of obesity, diabetes, coronary artery disease and obstructive sleep apnea can be viewed as fundamental drivers of the subspecialty practices of Bariatric Surgery, Endocrinology, Cardiology and Sleep Medicine.

While the technological success of our society in producing abundant food and reducing physical activity has contributed to the epidemic of obesity, the development of artificial lighting has contributed greatly to the problem of sleep deprivation. We are now able to run factories, stores and the Internet 24/7; thereby, increasing the efficiency of economic activity. However, we have not been able to adapt human circadian rhythms and need for sleep to meet either the economic demands of society or the socially desired preferences of individuals that result in insufficient sleep. On demand sleep and/or alertness will likely become a major goal and challenge for the field of Sleep Medicine. Pharmacological treatments are available but have limited efficacy. Adjusting the timing of light exposure effectively shifts circadian rhythms but it is slow and difficult to regulate. New methods, technologies and treatments must be developed to meet the demands for alertness and sleep. Perhaps, studies of nocturnally active, diurnally inactive rodents will reveal how we can reverse the sleep-wake pattern in humans for those in whom it would be advantageous such as night-shift workers. Further into the future, as mankind explores space, we may even need to alter the period of the current circadian rhythm to adapt humans for life on other planets with rotational periods of less or greater than 24 hours. Sleep science and Sleep Medicine will undoubtedly strive to provide solutions to the problems faced by individuals and society in ways that we have never before even dreamed.

REFERENCES

1. Rechtschaffen A, Bergmann BM, Everson CA, et al. Sleep deprivation in the rat: X. Integration and discussion of the findings. Sleep 1989;12:68-87.
2. Everson CA. Sustained sleep deprivation impairs host defense. Am J Physiol 1993;265(5 Pt 2):R1148-54.
3. Bonnet MH. Sleep deprivation. In: Kryger MH, Roth T, Dement W, eds. Principles and Practice of Sleep Medicine. 3rd ed. Philadelphia: WB Saunders Co; 2000:53-71.
4. Kripke DF, Simons RN, Garfinkel L, et al. Short and long sleep and sleeping pills. Is increased mortality associated? Arch Gen Psychiatry 1979;36:103-16.
5. Kripke DF, Garfinkel L, Wingard DL, et al. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59:131-6.
6. National Commission on Sleep Disorders Research. Wake up America: a national sleep alert. 1993;1:15-74.
7. Knipling R, Wang J. Revised estimates of the U.S. drowsy driver crash problem size based on general estimates system case reviews. Association for the Advancement of Automotive Medicine, 39th Annual Proceedings 1995;Oct. 16-18.
8. American Sleep Disorders Association. International Classification of Sleep Disorders, Revised: Diagnostic and Coding Manual. Rochester, MN: American Sleep Disorders Association; 1997.
9. Partinen M, Hublin C. Epidemiology of sleep disorders. In: Kryger MH, Roth T, Dement W, eds. Principles and Practice of Sleep Medicine. 3rd ed. Philadelphia: WB Saunders Co; 2000:558-79.
10. Beninati W, Harris CD, Herold DL, et al. The effect of snoring and obstructive sleep apnea on the sleep quality of bed partners. Mayo Clin Proc 1999;74:955-8.
11. Caton R. The electric currents of the brain. Br Med J 1875;2:278.
12. Berger H. Über das elektroenkephalogramm des menschen. Arch Psychiatr Nervenkr 1929;97:6-26.
13. Loomis AL, Harvey EN, Hobart GA. Cerebral states during sleep as studied by human brain potentials. J Exper Psychol 1937;21:127-44.
14. Aserinsky E, Kleitman N. Regularly occurring episodes of eye mobility and concomitant phenomena during sleep. Science 1953;118:273-4.
15. Dement WC, Kleitman N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility and dreaming. Electroencephalogr Clin Neurophysiol 1957;9:673-90.
16. Gelineau GBE. De la narcolepsie. Lancette Fr 1880;53:626-8.
17. Vogel G. Studies in the psychophysiology of dreams, III: the dream of narcolepsy. Arch Gen Psychiatry 1960;3:421-8.
18. Juji T, Satake M, Honda Y, et al. HLA antigens in Japanese patients with narcolepsy. All the patients were DR2 positive. Tissue Antigens 1984;24:316-9.
19. Matsuki K, Grumet FC, Lin X, et al. DQ (rather than DR) gene marks susceptibility to narcolepsy. Lancet 1992;339(8800):1052.
20. Mignot E, Lin X, Arrigoni J, et al. DQB1*0602 and DQA1*0102 (DQ1) are better markers than DR2 for narcolepsy in Caucasian and black Americans. Sleep 1994;17(8 Suppl):S60-7.
21. Mignot E, Hayduk R, Black J, et al. HLA DQB1*0602 is associated with cataplexy in 509 narcoleptic patients. Sleep 1997;20:1012-20.
22. de Lecea L, Kilduff TS, Peyron C, et al. The hypocretins: hypothalamus-specific peptides with neuroexcitatory activity. Proc Natl Acad Sci USA 1998;95:322-7.
23. Sakurai T, Amemiya A, Ishii M, et al. Orexins and orexin receptors: a family of hypothalamic neuropeptides and G protein-coupled receptors that regulate feeding behavior. Cell 1998;92:573-85.
24. Marcus JN, Aschkenasi CJ, Lee CE, Chemelli RM, Saper CB, Yanagisawa M, Elmquist JK. Differential expression of orexin receptors 1 and 2 in the rat brain. J Comp Neurol. 2001; 18:435:6-25.
25. Kilduff TS, Peyron C. The hypocretin/orexin ligand-receptor system: implications for sleep and sleep disorders. Trends Neurosci

2000;23:359-65.
26. Lin L, Faraco J, Li R, et al. The sleep disorder canine narcolepsy is caused by a mutation in the hypocretin (orexin) receptor 2 gene. Cell 1999;98:365-76.
27. Chemelli RM, Willie JT, Sinton CM, et al. Narcolepsy in orexin knockout mice: molecular genetics of sleep regulation. Cell 1999;98:437-51.
28. Nishino S, Ripley B, Overeem S, Lammers GJ, Mignot E. Hypocretin (orexin) deficiency in human narcolepsy. Lancet. 2000;355(9197):39-40.
29. Thannickal TC, Moore RY, Nienhuis R, Ramanathan L, Gulyani S, Aldrich M, Cornford M, Siegel JM. Reduced number of hypocretin neurons in human narcolepsy. Neuron. 2000;27:469-74.
30. Peyron C, Faraco J, Rogers W, et al. A mutation in a case of early onset narcolepsy and a generalized absence of hypocretin peptides in human narcoleptic brains. Nat Med 2000;6:991-7.
31. Phillips B, Young T, Finn L, et al. Epidemiology of restless legs symptoms in adults. Arch Intern Med 2000;160:2137-41.
32. Ruottinen HM, Partinen M, Hublin C, et al. An FDOPA PET study in patients with periodic limb movement disorder and restless legs syndrome. Neurology 2000;54:502-4.
33. Turjanski N, Lees AJ, Brooks DJ. Striatal dopaminergic function in restless legs syndrome: 18F-dopa and 11C-raclopride PET studies. Neurology 1999;52:932-7.
34. Trenkwalder C, Walters AS, Hening WA, et al. Positron emission tomographic studies in restless legs syndrome. Mov Disord 1999;14:141-5.
35. Bucher SF, Seelos KC, Oertel WH, et al. Cerebral generators involved in the pathogenesis of the restless legs syndrome. Ann Neurol 1997;41:639-45.
36. Bara-Jimenez W, Aksu M, Graham B, et al. Periodic limb movements in sleep: state-dependent excitability of the spinal flexor reflex. Neurology 2000;54:1609-16.
37. Winkelmann J, Wetter TC, Collado-Seidel V, et al. Clinical characteristics and frequency of the hereditary restless legs syndrome in a population of 300 patients. Sleep 2000;23:597-602.
38. Desautels A, Turecki G, Montplaisir J, et al. Identification of a major susceptibility locus for restless legs syndrome on chromosome 12q. Am J Hum Genet 2001;69:1266-70.
39. O'Keeffe ST, Gavin K, Lavan JN. Iron status and restless legs syndrome in the elderly. Age Ageing 1994;23:200-3.
40. Sun ER, Chen CA, Ho G, et al. Iron and the restless legs syndrome. Sleep 1998;21:371-7.
41. Earley CJ, Connor JR, Beard JL, et al. Abnormalities in CSF concentrations of ferritin and transferrin in restless legs syndrome. Neurology 2000;54:1698-700.
42. Allen RP, Barker PB, Wehrl F, et al. MRI measurement of brain iron in patients with restless legs syndrome. Neurology 2001;56:263-5.
43. Schenck CH, Bundlie SR, Ettinger MG, et al. Chronic behavioral disorders of human REM sleep: a new category of parasomnia. Sleep 1986;9:293-308.
44. Hendricks JC, Morrison AR, Mann GL. Different behaviors during paradoxical sleep without atonia depend on pontine lesion site. Brain Res 1982;239:81-105.
45. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. Brain 2000;123 (Pt 2):331-9.
46. Boeve BF, Silber MH, Ferman TJ, et al. REM sleep behavior disorder and degenerative dementia: an association likely reflecting Lewy body disease. Neurology 1998;51:363-70.
47. Ferman TJ, Boeve BF, Smith GE, et al. REM sleep behavior disorder and dementia: cognitive differences when compared with AD. Neurology 1999;52:951-7.
48. Boeve BF, Silber MH, Ferman TJ, et al. Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord 2001;16:622-30.
49. Schenck CH, Bundlie SR, Mahowald MW. Delayed emergence of a parkinsonian disorder in 38% of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. Neurology 1996;46:388-93.
50. Eisensehr I, Linke R, Noachtar S, et al. Reduced striatal dopamine transporters in idiopathic rapid eye movement sleep behaviour disorder. Comparison with Parkinson's disease and controls. Brain 2000;123 (Pt 6):1155-60.
51. Albin RL, Koeppe RA, Chervin RD, et al. Decreased striatal dopaminergic innervation in REM sleep behavior disorder. Neurology 2000;55:1410-2.
52. Burwell C, Robin E, Whaley R, et al. Extreme obesity associated with alveolar hypoventilation: A Pickwickian syndrome. Am J Med 1956;21:811-8.
53. Gastaut H, Tassinari CA, Duron B. Polygraphic study of the episodic diurnal and nocturnal (hypnic and respiratory) manifestations of the Pickwickian syndrome. Brain Res 1965;2:167-86.
54. Remmers JE, deGroot WJ, Sauerland EK, et al. Pathogenesis of upper airway occlusion during sleep. J Appl Physiol 1978;44:931-8.
55. Sullivan CE, Issa FG, Berthon-Jones M, et al. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1981;1(8225):862-5.
56. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230-5.
57. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
58. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283:1829-36.
59. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med 2001;163:19-25.
60. Ganguli M, Reynolds CF, Gilby JE. Prevalence and persistence of sleep complaints in a rural older community sample: the MoVIES project. J Am Geriatr Soc 1996;44:778-84.
61. Mellinger GD, Balter MB, Uhlenhuth EH. Insomnia and its treatment. Prevalence and correlates. Arch Gen Psychiatry 1985;42:225-32.
62. Foley DJ, Monjan AA, Brown SL, et al. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep 1995;18:425-32.
63. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-84.
64. Ohayon MM. Prevalence of DSM-IV diagnostic criteria of insomnia: distinguishing insomnia related to mental disorders from sleep disorders. J Psychiatr Res 1997;31:333-46.
65. Foley DJ, Monjan A, Simonsick EM, et al. Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. Sleep 1999;22 Suppl 2:S366-72.
66. Katz DA, McHorney CA. Clinical correlates of insomnia in patients with chronic illness. Arch Intern Med 1998;158:1099-107.
67. Dodge R, Cline MG, Quan SF. The natural history of insomnia and its relationship to respiratory symptoms. Arch Intern Med 1995;155:1797-800.
68. Kuppermann M, Lubeck DP, Mazonson PD, et al. Sleep problems and their correlates in a working population. J Gen Intern Med 1995;10:25-32.
69. Simon GE, VonKorff M. Prevalence, burden, and treatment of insomnia in primary care. Am J Psychiatry 1997;154:1417-23.
70. Zammit GK, Weiner J, Damato N, et al. Quality of life in people with insomnia. Sleep 1999;22 Suppl 2:S379-85.
71. Balter MB, Uhlenhuth EH. New epidemiologic findings about insomnia and its treatment. J Clin Psychiatry 1992;53 Suppl:34-9;

discussion 40-2.
72. Koski K, Luukinen H, Laippala P, et al. Risk factors for major injurious falls among the home-dwelling elderly by functional abilities. A prospective population-based study. Gerontology 1998;44:232-8.
73. Walsh JK, Engelhardt CL. The direct economic costs of insomnia in the United States for 1995. Sleep 1999;22 Suppl 2:S386-93.
74. Pollak CP, Perlick D. Sleep problems and institutionalization of the elderly. J Geriatr Psychiatry Neurol 1991;4:204-10.
75. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? A study in inner London. Br J Gen Pract 1993;43(376):445-8.
76. Eaton WW, Badawi M, Melton B. Prodromes and precursors: epidemiologic data for primary prevention of disorders with slow onset. Am J Psychiatry 1995;152:967-72.
77. Breslau N, Roth T, Rosenthal L, et al. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biol Psychiatry 1996;39:411-8.
78. Chang PP, Ford DE, Mead LA, et al. Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study. Am J Epidemiol 1997;146:105-14.
79. Weissman MM, Greenwald S, Nino-Murcia G, et al. The morbidity of insomnia uncomplicated by psychiatric disorders. Gen Hosp Psychiatry 1997;19:245-50.
80. Althuis MD, Fredman L, Langenberg PW, et al. The relationship between insomnia and mortality among community- dwelling older women. J Am Geriatr Soc 1998;46:1270-3.
81. Freedman RR, Sattler HL. Physiological and psychological factors in sleep-onset insomnia. J Abnorm Psychol 1982;91:380-9.
82. Monroe LJ. Psychological and physiological differences between good and poor sleepers. J Abnorm Psychol 1967;72:255-64.
83. Bonnet MH, Arand DL. Heart rate variability: sleep stage, time of night, and arousal influences. Electroencephalogr Clin Neurophysiol 1997;102:390-6.
84. Vgontzas AN, Tsigos C, Bixler EO, et al. Chronic insomnia and activity of the stress system: a preliminary study. J Psychosom Res 1998;45(1 Spec No):21-31.
85. Bonnet MH, Arand DL. 24-Hour metabolic rate in insomniacs and matched normal sleepers. Sleep 1995;18:581-8.
86. Stepanski E, Zorick F, Roehrs T, et al. Daytime alertness in patients with chronic insomnia compared with asymptomatic control subjects. Sleep 1988;11:54-60.
87. Merica H, Gaillard JM. The EEG of the sleep onset period in insomnia: a discriminant analysis. Physiol Behav 1992;52:199-204.
88. Perlis ML, Smith MT, Andrews PJ, et al. Beta/gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. Sleep 2001;24:110-7.
89. Nofzinger EA, Price JC, Meltzer CC, et al. Towards a neurobiology of dysfunctional arousal in depression: the relationship between beta EEG power and regional cerebral glucose metabolism during NREM sleep. Psychiatry Res 2000;98:71-91.
90. Morin CM, Hauri PJ, Espie CA, et al. Nonpharmacologic treatment of chronic insomnia. An American Academy of Sleep Medicine review. Sleep 1999;22:1134-56.
91. Morin CM, Stone JMK. Psychological management of insomnia: a clinical replications series with 100 patients. Behav Ther 1994;25:291-309.
92. Campbell SS, Dawson D, Anderson MW. Alleviation of sleep maintenance insomnia with timed exposure to bright light. J Am Geriatr Soc 1993;41:829-36.
93. Guilleminault C, Clerk A, Black J, et al. Nondrug treatment trials in psychophysiologic insomnia. Arch Intern Med 1995;155:838-44.
94. Horne JA. The effects of exercise upon sleep: a critical review. Biol Psychol 1981;12:241-90.
95. Kubitz KA, Landers DM, Petruzzello SJ, et al. The effects of acute and chronic exercise on sleep. A meta-analytic review. Sports Med 1996;21:277-91.
96. King AC, Oman RF, Brassington GS, et al. Moderate-intensity exercise and self-rated quality of sleep in older adults. A randomized controlled trial. JAMA 1997;277:32-7.
97. Horne JA, Reid AJ. Night-time sleep EEG changes following body heating in a warm bath. Electroencephalogr Clin Neurophysiol 1985;60:154-7.
98. Dorsey CM, Lukas SE, Teicher MH, et al. Effects of passive body heating on the sleep of older female insomniacs. J Geriatr Psychiatry Neurol 1996;9:83-90.
99. Nowell PD, Mazumdar S, Buysse DJ, et al. Benzodiazepines and zolpidem for chronic insomnia: a meta-analysis of treatment efficacy. JAMA 1997;278:2170-7.
100. Holbrook AM, Crowther R, Lotter A, et al. Meta-analysis of benzodiazepine use in the treatment of insomnia. CMAJ 2000;162:225-33.
101. Soldatos CR, Dikeos DG, Whitehead A. Tolerance and rebound insomnia with rapidly eliminated hypnotics: a meta-analysis of sleep laboratory studies. Int Clin Psychopharmacol 1999;14:287-303.
102. Kales A, Bixler EO, Scharf M, et al. Sleep laboratory studies of flurazepam: a model for evaluating hypnotic drugs. Clin Pharmacol Ther 1976;19(5 Pt 1):576-83.
103. Mitler MM, Seidel WF, van den Hoed J, et al. Comparative hypnotic effects of flurazepam, triazolam, and placebo: a long-term simultaneous nighttime and daytime study. J Clin Psychopharmacol 1984;4:2-13.
104. Scharf MB, Roth T, Vogel GW, et al. A multicenter, placebo-controlled study evaluating zolpidem in the treatment of chronic insomnia. J Clin Psychiatry 1994;55:192-9.
105. Walsh JK, Vogel GW, Scharf M, et al. A five week, polysomnographic assessment of zaleplon 10 mg for the treatment of pimary insomnia. Sleep Med 2000;1:41-9.
106. Elie R, Ruther E, Farr I, et al. Sleep latency is shortened during 4 weeks of treatment with zaleplon, a novel nonbenzodiazepine hypnotic. Zaleplon Clinical Study Group. J Clin Psychiatry 1999;60:536-44.
107. Pecknold J, Wilson R, le Morvan P. Long term efficacy and withdrawal of zopiclone: a sleep laboratory study. Int Clin Psychopharmacol 1990;5 Suppl 2:57-67.
108. Kummer J, Guendel L, Linden J, et al. Long-term polysomnographic study of the efficacy and safety of zolpidem in elderly psychiatric in-patients with insomnia. J Int Med Res 1993;21:171-84.
109. Oswald I, French C, Adam K, et al. Benzodiazepine hypnotics remain effective for 24 weeks. Br Med J (Clin Res Ed) 1982;284(6319):860-3.
110. Allen RP, Mendels J, Nevins DB, et al. Efficacy without tolerance or rebound insomnia for midazolam and temazepam after use for one to three months. J Clin Pharmacol 1987;27:768-75.
111. Schlich D, l'Heritier C, Coquelin JP, et al. Long-term treatment of insomnia with zolpidem: a multicentre general practitioner study of 107 patients. J Int Med Res 1991;19:271-9.
112. Maarek L, Cramer P, Attali P, et al. The safety and efficacy of zolpidem in insomniac patients: a long-term open study in general practice. J Int Med Res 1992;20:162-70.
113. Montgomery I, Oswald I, Morgan K, et al. Trazodone enhances sleep in subjective quality but not in objective duration. Br J Clin Pharmacol 1983;16:139-44.
114. Scharf MB, Sachais BA. Sleep laboratory evaluation of the effects and efficacy of trazodone in depressed insomniac patients. J Clin Psychiatry 1990;51 Suppl:13-7.
115. Parrino L, Spaggiari MC, Boselli M, et al. Clinical and polysomnographic effects of trazodone CR in chronic insomnia associated with dysthymia. Psychopharmacology (Berl) 1994;116:389-95.
116. Walsh JK, Erman M, Erwin CW, et al. Subjective hypnotic efficacy of trazodone and zolpidem in DSMIII-R primary insomnia. Hum Psychopharmacol 1998;13: 191-198.
117. Hajak G, Rodenbeck A, Adler L, et al. Nocturnal melatonin secre-

tion and sleep after doxepin administration in chronic primary insomnia. Pharmacopsychiatry 1996;29:187-92.
118. Hohagen F, Montero RF, Weiss E, et al. Treatment of primary insomnia with trimipramine: an alternative to benzodiazepine hypnotics? Eur Arch Psychiatry Clin Neurosci 1994;244:65-72.
119. Moore RY, Eichler VB. Loss of a circadian adrenal corticosterone rhythm following suprachiasmatic lesions in the rat. Brain Res 1972;42:201-6.
120. Stephan FK, Zucker I. Circadian rhythms in drinking behavior and locomotor activity of rats are eliminated by hypothalamic lesions. Proc Natl Acad Sci USA 1972;69:1583-6.
121. Moore RY, Lenn NJ. A retinohypothalamic projection in the rat. J Comp Neurol 1972;146:1-14.
122. Welsh DK, Logothetis DE, Meister M, et al. Individual neurons dissociated from rat suprachiasmatic nucleus express independently phased circadian firing rhythms. Neuron 1995;14:697-706.
123. DeCoursey PJ, Buggy J. Restoration of circadian locomotor activity in arrhythmic hamsters by fetal SCN transplants. Comp Endocrinol 1988;7:49-54.
124. Ralph MR, Foster RG, Davis FC, et al. Transplanted suprachiasmatic nucleus determines circadian period. Science 1990;247(4945):975-8.
125. Konopka RJ, Benzer S. Clock mutants of Drosophila melanogaster. Proc Natl Acad Sci U S A 1971;68:2112-6.
126. Hardin PE, Hall JC, Rosbash M. Feedback of the Drosophila period gene product on circadian cycling of its messenger RNA levels. Nature 1990;343(6258):536-40.
127. Hardin PE, Hall JC, Rosbash M. Circadian oscillations in period gene mRNA levels are transcriptionally regulated. Proc Natl Acad Sci U S A 1992;89:11711-5.
128. Sehgal A, Rothenfluh-Hilfiker A, Hunter-Ensor M, et al. Rhythmic expression of timeless: a basis for promoting circadian cycles in period gene autoregulation. Science 1995;270(5237):808-10.
129. Darlington TK, Wager-Smith K, Ceriani MF, et al. Closing the circadian loop: CLOCK-induced transcription of its own inhibitors per and tim. Science 1998;280(5369):1599-603.
130. Gekakis N, Staknis D, Nguyen HB, et al. Role of the CLOCK protein in the mammalian circadian mechanism. Science 1998;280(5369):1564-9.
131. Sangoram AM, Saez L, Antoch MP, et al. Mammalian circadian autoregulatory loop: a timeless ortholog and mPer1 interact and negatively regulate CLOCK-BMAL1-induced transcription. Neuron 1998;21:1101-13.
132. Kramer A, Yang FC, Snodgrass P, et al. Regulation of daily locomotor activity and sleep by hypothalamic EGF receptor signaling. Science 2001;294(5551):2511-5.
133. Jones CR, Campbell SS, Zone SE, et al. Familial advanced sleep-phase syndrome: A short-period circadian rhythm variant in humans. Nat Med 1999;5:1062-5.
134. Toh KL, Jones CR, He Y, et al. An hPer2 phosphorylation site mutation in familial advanced sleep phase syndrome. Science 2001;291(5506):1040-3.
135. Czeisler CA, Khalso SBS. The human circadian timing system and sleep-wake regulation. In: Kryger MH, Roth T, Dement W, eds. Principles and Practice of Sleep medicine. 3rd ed. Philadelphia: W.B. Saunders Co., 2000:353-375.
136. Wurtman RJ, Axelrod J, Phillips LS. Melatonin synthesis in the pineal gland: control by light . Science 1963;142:1071-3.
137. Moore RY, Heller A, Wurtman RJ, et al. Visual pathway mediating pineal response to environmental light. Science 1967;155(759):220-3.
138. Freedman MS, Lucas RJ, Soni B, et al. Regulation of mammalian circadian behavior by non-rod, non-cone, ocular photoreceptors. Science 1999;284(5413):502-4.
139. Berson DM, Dunn FA, Takao M. Phototransduction by retinal ganglion cells that set the circadian clock. Science 2002;295(5557):1070-3.
140. Provencio I, Rodriguez IR, Jiang G, et al. A novel human opsin in the inner retina. J Neurosci 2000;20:600-5.
141. Hattar S, Liao HW, Takao M, et al. Melanopsin-containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. Science 2002;295(5557):1065-70.
142. Gooley JJ, Lu J, Chou TC, et al. Melanopsin in cells of origin of the retinohypothalamic tract. Nat Neurosci 2001;4:1165.
143. Czeisler CA, Shanahan TL, Klerman EB, et al. Suppression of melatonin secretion in some blind patients by exposure to bright light. N Engl J Med 1995;332:6-11.
144. Chesson AL Jr, Littner M, Davila D, et al. Practice parameters for the use of light therapy in the treatment of sleep disorders. Standards of Practice Committee, American Academy of Sleep Medicine. Sleep 1999;22:641-60.
145. Eastman CI, Stewart KT, Mahoney MP, et al. Dark goggles and bright light improve circadian rhythm adaptation to night-shift work. Sleep 1994;17:535-43.
146. Terman M, Terman JS. Light Therapy. In: Kryger MH, Roth T, Dement W, eds. Principles and Practice of Sleep Medicine. 3rd ed. Philadelphia: WB Saunders Co; 2000:1258-74.
147. Jewett ME, Kronauer RE, Czeisler CA. Phase-amplitude resetting of the human circadian pacemaker via bright light: a further analysis. J Biol Rhythms 1994;9:295-314.
148. Boivin DB, Duffy JF, Kronauer RE, et al. Dose-response relationships for resetting of human circadian clock by light. Nature 1996;379(6565):540-2.
149. Czeisler CA, Duffy JF, Shanahan TL, et al. Stability, precision, and near-24-hour period of the human circadian pacemaker. Science 1999;284(5423):2177-81.
150. Orem J, Lydic R. Upper airway function during sleep and wakefulness: experimental studies on normal and anesthetized cats. Sleep. 1978;1:49-68.
151. Frederickson CJ, Rechtschaffen A. Effects of sleep deprivation on awakening thresholds and sensory evoked potentials in the rat. Sleep. 1978;1:69-82.
152. Sitaram N, Moore AM, Gillin JC. Induction and resetting of REM sleep rhythm in normal man by arecholine: blockade by scopolamine. Sleep. 1978;1:83-90.
153. Foutz AS, Mitler MM, Cavalli-Sforza LL, Dement WC. Genetic factors in canine narcolepsy. Sleep. 1979;1:413-21.
154. Glenn LL, Foutz AS, Dement WC. Membrane potential of spinal motoneurons during natural sleep in cats. Sleep. 1978;1:199-204
155. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991;14:540-5.
156. Carskadon MA, Dement WC, Mitler MM, Roth T, Westbrook PR, Keenan S. Guidelines for the multiple sleep latency test (MSLT): a standard measure of sleepiness. Sleep 1986;9:519-24
157. Czeisler CA, Richardson GS, Coleman RM, Zimmerman JC, Moore-Ede MC, Dement WC, Weitzman ED. Chronotherapy: resetting the circadian clocks of patients with delayed sleep phase insomnia. Sleep. 1981;4:1-21.