

The study of human sleep: a historical perspective

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Since this is an historic meeting which will address one of the most important clinical issues in the field of sleep medicine, it is appropriate to examine how we arrived at this moment. Accordingly, I will present a brief review of the history of sleep medicine. I have addressed this topic on several previous occasions.¹⁻³ In my view the history of sleep medicine can be divided into five clearly demarcated phases. These are listed in table 1.

Phase 1: before 1952

I have designated the first phase, to some extent with tongue in cheek, as “prehistoric”. This reflects the relative lack of scientific experimentation involving sleep over the first half of the 20th century and before. The subject of dreams and dream interpretation probably received the most attention. A great deal of the early sleep literature reported observations on sleep habits and sleep characteristics in the service of comparing and contrasting the data reciprocally to data describing the waking state. During this “prehistoric” period nearly every biomedical scientist assumed that sleep occurred when sensory stimulation continuously bombarding the brain during the day was rendered insufficient to maintain a waking level of brain activity by the occurrence of the darkness and silence of night.

It seems reasonable that this perspective, often called the “passive process theory”, would have made the study of sleep seem relatively uninteresting. The notion that sleep was the brain “turned off” led to the erroneous conclusion that sleep could be regarded as an entirely homogenous state, and that a single observation could be generalised to the entire sleep period. Finally, there was no tradition of staying up at night to carry out scientific research except, of course, for astronomy.

There are some “prehistoric” scientific landmarks that are worth noting but which occurred far too early to be exploited by the field of sleep medicine. For example, Jean Jacques d’Ortous deMairan demonstrated the persistence of circadian rhythms in the absence of environmental cues in 1729. Jean Baptiste Edouard Gellineau published his landmark description of the narcolepsy syndrome in 1880. The Scottish physiologist, Richard Caton, demonstrated electrical rhythms in the

brains of animals in 1875. The early descriptions of the differences between brain wave patterns in awake and sleeping human beings by Hans Berger in 1929 only served to further fix the notion of sleep as an inactive or “idling” state.

Phase 2: 1952-1970

Phase 2 was ushered in by the observation in 1952 that binocularly synchronous rapid eye movements occurred during sleep.⁴ This observation and data demonstrating an association between the occurrence of rapid eye movements and the occurrence of dreaming finally stimulated an intense interest in the study of sleep for its own sake.

The years after World War II saw the unchallenged dominance of psychoanalysis in American psychiatry, and Sigmund Freud’s writings about dream interpretation and the underlying theoretical psychological structure of “id” and “ego” made dreaming a central issue of unparalleled significance. In this atmosphere one can appreciate the excitement generated by the demonstration of a physiological marker for the occurrence of dreaming.⁵ The first complete descriptive journey through the night in human beings—that is, continuously recording brain wave patterns and eye movement activity throughout an entire night—was carried out in the laboratory of Nathaniel Kleitman at the University of Chicago.

My personal excitement and interest in the newly discovered phenomenon of rapid eye movements (REMs) was certainly not shared by others. I toiled alone for about five years, studying as many individual subjects as possible to demonstrate the universality of the occurrence of REMs during sleep, the repetitive occurrence of distinct periods of sleep with which REMs were associated, and finally the basic sleep cycle and characteristic all-night sleep stage architecture.^{6,7} It was probably not until I demonstrated the REM deprivation/compensation phenomenon in a study⁸ published as *The effect of dream deprivation* in 1960 that other investigators began to investigate all-night sleep. The “pressure” that developed as REM sleep was prevented from occurring was widely regarded as evidence supporting Freud’s theory that dreaming functioned as a

Table 1 History of sleep medicine

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| Phase 1 | Prehistoric |
| Phase 2 | 1952-1970 Exploring sleep; discovery of REM; journey through the night |
| Phase 3 | 1971-1980 Extending medical practice to include the sleeping patient; understanding the determinants of daytime alertness |
| Phase 4 | 1981-1990 New treatments; expanding and organising sleep medicine; operational and public policy implications |
| Phase 5 | 1991-2000 Bringing the diagnosis and treatment of sleep disorders into the mainstream of society and the health care system |

“safety valve” for the release of instinctual energy. During the 1960s many investigators participated in a detailed and quantitative description of human and animal sleep including changes related to different stages of development. Perhaps the major advance was the concept of the duality of sleep—that is, sleep consists of two entirely different organismic states, REM sleep and non-REM sleep. Added to this was the elucidation of the brain stem control of sleep states including the neural mechanisms of active motor inhibition during REM sleep.

Obstructive sleep apnoea was discovered in Europe in 1965 by two separate groups, Gastant *et al*⁹ and Jung and Kuhlo.¹⁰ Kuhlo *et al* are credited with performing the first tracheostomy with the intention of bypassing airway obstruction that occurred during sleep in the upper airway of these very obese patients.¹¹ The observations a decade earlier that led to the description of the “Pickwickian syndrome”¹² included the misattribution that the associated daytime somnolence was caused by hypercapnia. It is not clear what would have happened if an Italian neurologist, Elio Lugaresi, had not become very interested in obstructive sleep apnoea which he called “hypersomnia with periodic breathing”. He pursued the problem with unusual zeal, although he did not publish his seminal study¹³ documenting an association between snoring and hypertension until 1975.

Phase 3: 1971–1980

The beginning of phase 3 occurred when Stanford sleep researchers formally extended the practice of medicine to include the sleeping patient. There was a wise physician who once said: “The practice of medicine ends when the patient falls asleep”. His intention was to draw attention to an important gap in medical practice. However, it is my impression that the disenfranchisement of the sleeping patient grew out of the general attitude that sleep represented a boundary that physicians should not cross. In other words, the practice of medicine should end when the patient falls asleep.

The Stanford University Sleep Disorders Clinic for the diagnosis and treatment of patients with sleep problems was launched in the summer of 1970. We had studied several patients with Pickwickian syndrome and noted the periodic breathing. However, our major clinical interest was managing patients with narcolepsy and developing diagnostic and treatment approaches for individuals complaining of insomnia. In the summer of 1971 Dr Vincent Zarcone and I attended the First International Congress of the APSS in Bruges, Belgium where we recruited Dr Christian Guilleminault to join us at Stanford. He arrived in January 1972 and immediately insisted we pay more attention to sleep disordered breathing.

Although we were charging patients for our services, our early survival depended almost entirely on research grants. Early in 1972 the recording of respiratory and cardiac variables as part of the all-night sleep test (later to be called “polysomnography”) became routine. Since the Stanford University Sleep Disorders

Center was well known for its research studies of narcolepsy, the Sleep Clinic received many referrals of putative narcoleptics from all over the United States. It will be no surprise that the excessive daytime sleepiness of the majority of these individuals was due to obstructive sleep apnoea. Literally within a few months, it was completely obvious to us that the diagnosis and treatment of obstructive sleep apnoea (OSA) would be a very important item in the future of sleep medicine. Furthermore, most of the OSA victims seen at Stanford in those early days were very far advanced and we were extremely impressed by the severity of the clinical complications. The case history of our first patient who received a tracheostomy and the consequent reversal of severe hypertension is described in detail elsewhere.¹⁴

By November 1972 we had organised our voluminous new clinical knowledge and were able to begin teaching others. A clinical discipline can only be said to exist if it represents an organised body of knowledge, and if this body of knowledge can be effectively taught. Accordingly, the first sleep medicine continuing medical education exercise that took place on 29 November 1972 can be designated as the birthday of the field of sleep medicine. A replica of the original brochure announcing a clinical course on “Sleep

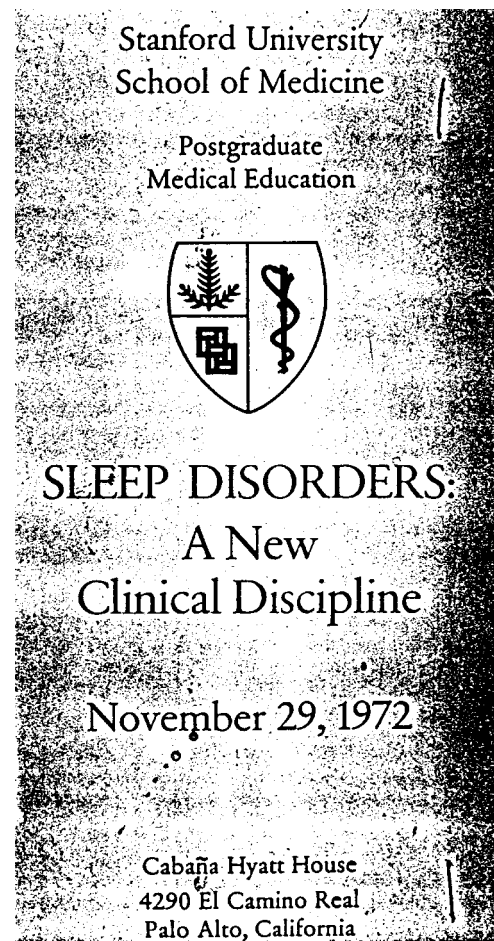


Figure 1 A replica of the original brochure announcing a clinical course on “Sleep Disorders: a New Clinical Discipline”.

Disorders: a New Clinical Discipline” is displayed in fig 1.

The 1970s can be regarded as the period of defining the field of sleep medicine. Polysomnography was refined and standardised as the major clinical test. The defining parameters of obstructive sleep apnoea were established and first published in 1976.¹⁵ The American Sleep Disorders Association (ASDA) was formed in 1975 to represent scientists and clinicians dealing with sleep disorders. The early tasks of ASDA were developing additional standards of practice and organising the first examination which has evolved into the American Board of Sleep Medicine. Dr Mary Carskadon and her colleagues took on the task of understanding and quantifying the major nocturnal determinants of daytime sleepiness including frequent arousals.¹⁶ Her work led directly to the development of the Multiple Sleep Latency Test (MSLT).¹⁷ The phase 3 decade was capped by the launching of the scientific journal *Sleep* and the publication of the first diagnostic classification of sleep disorders in the entirety of Issue 1, Volume 2 of the journal in 1979.

Throughout the 1970s the only effective treatment for severe OSA was chronic tracheostomy. This approach and the constraints it imposed on patients was obviously a barrier to the expansion of sleep medicine and was not considered an acceptable treatment for patients who were not classified as severely ill. One major regret I still carry from this early period is that we lacked the resources to conduct meticulous longitudinal outcome studies of all the severely ill OSA patients who refused treatment.

Phase 4: 1981–1990

Phase 4 is clearly marked by the introduction of alternative treatments for OSA. Uvulopalatopharyngoplasty (UPPP) was introduced into the United States by Dr Shiro Fujita in 1981.¹⁸ This surgical procedure enjoyed major popularity for a few years until adequate numbers of polysomnographic evaluations showed it to be relatively ineffective in curing or greatly ameliorating sleep disordered breathing. What is currently the treatment of choice—nasal continuous positive airway pressure (CPAP)—was introduced by Colin Sullivan and his colleagues also in 1981.¹⁹ The dramatic effectiveness of nasal CPAP and its relative ease of delivery was probably crucial in an accelerated expansion of the diagnosis and treatment of OSA and other sleep disorders in the United States and other countries, and a “legitimisation” of sleep disorders medicine, at least among many pulmonary specialists, neurologists, and psychiatrists. Phase 4 of our history was capped by the publication of the first true textbook *Principles and Practice of Sleep Medicine* in 1989.²⁰

Phase 5: 1991, now, and into the 21st century

We are now well into what I have designated phase 5 which is the effort to bring issues involving sleep physiology, sleep deprivation,

and sleep disorders, particularly obstructive sleep apnoea, completely into the mainstream of medical practice and the public health arena in the United States, and to whatever extent possible, in other industrialised nations. Pre-monitory events to phase 5 were the establishment of an office for the American Sleep Disorders Association in Washington DC and the advocacy efforts that led to the enabling legislation for a National Commission on Sleep Disorders Research. We can date the onset of phase 5 to the beginning of the Commission’s study on the impact of sleep deprivation and sleep disorders on American society in March 1990.

As we here address the stunningly important topic of cardiovascular disease in the human race and the exciting possibility that sleep disordered breathing may be an important causal factor, we also co-exist with an amazing societal paradox. In recent years we have learned that pervasive sleep deprivation and undiagnosed sleep disorders are arguably one of our largest health problems. The single disorder we are addressing in this symposium—obstructive sleep apnoea—is now known to afflict around 30 million people in the United States and millions more worldwide. The study by Young *et al*²¹ on working adults suggested a prevalence of 24% in men and 9% in women across the full range of severity. Our outreach work suggests that even higher percentages exist in clinical populations, particularly primary care, and certain other non-clinical groups.^{22, 23} Yet today with enormous amounts of scientific and clinical knowledge together with effective treatments that are readily available, there are large primary care patient groups in which no sleep disorder diagnoses including OSA can be found, as well as in the vast majority of American citizens.²⁵ It seems reasonable to assume that, if OSA is unrecognised in its advanced stages, it becomes disabling and eventually lethal. If recognised and treated, even those who are near to death can often be saved and restored to normal health. In one primary clinic where physicians learned to recognise these illnesses, the number of patients with OSA being managed jumped from zero to more than 800 in the course of a few years.

The “amazing paradox” is that our society does not know these things. The benefits of hard learned knowledge about normal and pathological sleep have not been effectively passed on to the general public and practising physicians. The National Commission on Sleep Disorders Research found a pervasive failure of education about sleep, sleep deprivation, and sleep disorders in every component of American society. This included observations gathered from every level in the educational system including a thorough study of American medical schools.²⁴

In order to resolve the paradox the National Commission made several recommendations to the Congress of the United States. The following material containing the recommendations and their rationale is taken from the

Commission's final report "Wake Up America! A National Sleep Alert".²⁵

Recommendations of the National Commission on Sleep Disorders Research to the Congress of the United States submitted in September 1992

The National Commission on Sleep Disorders Research has proposed several key recommendations which will launch a long range national plan to create an environment in which research findings and education programmes will lead to early diagnosis and prevention of sleep disorders, and reduce the impact of these disorders and pervasive sleep deprivation on the health and welfare of America.

ESTABLISH A NATIONAL CENTRE

Our nation needs an accountable structure to coordinate education and research on sleep and sleep disorders. There are excellent growing programmes of sleep research in several of the NIH Institutes. However, coordinated management and accountability are necessary to ensure that the findings of basic and clinical research are applied widely for the benefit of all our citizens, and that serious gaps in research are continually identified and effectively addressed.

Each of the problems identified by the Commission had, as its root cause, the absence of specific accountability for the resolution of the problems. The Commission believes that greater public, scientific, policy making, clinical, and administrative attention must be focused on the study of sleep disorders and their effects on society, and cost effective preventive solutions must be found.

Accordingly, the Commission recommends to the Congress of the United States the simple, but inestimably important, initial step of the creation of a national focus for sleep research. It recommends the creation of a Federal entity whose mission is (a) to foster the scientific understanding of sleep and sleep disorders, (b) to translate sleep related knowledge into improvement of health and productivity throughout our society, (c) to provide leadership, focus, and coordination in devising and implementing an effective education campaign aimed at all health professionals, industry, policy makers, and the general public, (d) to provide guidelines and blueprints to increase research and clinical manpower, (e) to support and cooperate with other institutes in meeting these needs, and (f) to harness the best scientific and clinical expertise to continually update the research agenda and the national plan.

The Commission recommends that the Congress authorise the establishment of and appropriate sufficient funds to support a national centre for research and education on sleep and sleep disorders to be housed within an existing NIH Institute. The Centre's activities will complement the sleep and sleep disorder related research currently undertaken by the various National Institutes of Health and, through its own award authority, shall encourage and support gap-filling and crosscutting research,

and develop new research programmes and educational/training initiatives in the field.

TRAINING AND CAREER DEVELOPMENT

The Commission identified a serious absence of career and training opportunities for young investigators interested in the field of sleep. Research is essential for cures and better treatments of sleep disorders. Students need to be exposed to sleep medicine in school; additional laboratories and resources are needed to support doctoral and postdoctoral candidates in sleep science.

The Commission recommends that substantially increased levels of Federal support be directed to the NIH, the Centers for Disease Control, and other agencies specifically for sleep and sleep disorder research training and career development opportunities.

EDUCATION OF HEALTH PROFESSIONALS

Consistent with its mandate to improve the public health, the Public Health Service supports excellent research and promotes the dissemination of research findings to the public through the conduit of the health professionals. At present the American public is *not* receiving the benefits of new findings on sleep disorders. There is an urgent need for physicians, nurses, and all health care professionals to be able to identify and refer or treat patients with sleep disorders. Because primary care physicians represent the first line of treatment for most citizens, special emphasis should be placed on improving the quality and extent of their training in sleep and sleep disorders.

The Commission recommends that Congress encourage and support broader awareness of and training in sleep and sleep disorders spanning the full range of health care professions, particularly at the primary care level.

AN EDUCATED AMERICA

The nationwide low level of awareness of the nature and impact of sleep disorders and sleep deprivation is a national emergency. Witnesses asked repeatedly: "How many preventable deaths are going to occur this year?" "Why don't we do something right now?" "Why don't we save as many lives as possible now—not years or decades from now?" The Commission has concluded that the American public has been inappropriately denied the benefits of the research knowledge its tax dollars have supported. This situation must be remedied without delay.

Critically important to the National Centre's mission are the development and implementation of a major public awareness and education campaign about sleep and sleep disorders and the stimulation of greater knowledge of and training in sleep and sleep disorders among health care professionals. Among the primary goals of this campaign are to heighten public awareness and understanding of sleep and sleep disorders including, but not limited to, such issues as the ramifications of sleep deprivation, the nature of sleep disorders, the promotion of healthful behaviours regarding sleep, and the recognition of when a sleep

problem will benefit from intervention by a qualified health care professional. The Commission believes that such a public awareness/education campaign can effect behaviour change, thereby ultimately reducing family dysfunction, lost educational opportunities, accidents, lost income, disability, and lost lives.

The Commission recommends that a major public awareness/education campaign about sleep and sleep disorders be undertaken immediately by the Federal government.

1997 update: progress in implementing the commission's recommendations

Each year, the lives of millions of American men, women, and children are disturbed, disrupted, or destroyed by sleep deprivation and sleep disorders. With an incidence and prevalence of staggering proportions, both sleep disorders and sleep disturbances associated with other medical problems exact a tremendous toll on our nation's population. The costs of a sleepy society include lost lives, lost income, disability, lost educational opportunities, accidents, and family dysfunction; other costs raise the toll much higher. The effect on health and the quality of life for millions of individuals and families is incalculable.

The study of the National Commission was the first effort to gauge fully the nature and magnitude of the problems related to sleep in American society. Having done this, it recommended several inexpensive, do-able initiatives which would enable policy makers to make rapid progress in solving them. Given the gigantic numbers, the extremely low costs of effective societal interventions, and the possibility of a restoration of health and quality of life for so many Americans, the current situation should be viewed as unacceptable.

The National Center on Sleep Disorders Research was established within the National Heart Lung Blood Institute of NIH. The enabling legislation was introduced and passed in 1993. Unfortunately, the National Center and other initiatives recommended by the Commission ran afoul of Congressional budget cutting, and designated funds have never been provided for them. In spite of the lack of designated financial support, there has been modest progress. For example, the National Center on Sleep Disorders Research has supported eight teaching awards although the original intention was to support only three. However, as I have pointed out, the serious societal problems that were identified by the Commission still exist. In 1998, six years after the National Commission on Sleep Disorders Research submitted its final report to the Congress of the United States, pervasive sleep deprivation and untreated and mistreated sleep disorders remain arguably the biggest health problem in America.

Conclusion

Recently, 852 consecutive patients completed a validated questionnaire (148 refused, usually being in too much of a hurry) as they exited from the Stanford University Primary Care Clinic. Although no patient had a previous diagnosis of OSA, the survey indicated that

about 200 patients were afflicted with this problem at a level of severity usually requiring treatment. This study is not published and we are not, for our present purposes, concerned that the results are absolutely accurate. However, the symptoms of at least a few were flagrant. We do not know if these patients were genuinely not recognised, or if they were deliberately ignored. If Stanford University primary care doctors are not recognising OSA, can we assume that all other doctors are? I say the answer is a resounding no. We have now embarked on a study where we are accurately diagnosing and evaluating severity in every single patient in three or four primary care settings. The numbers could be as high as 10 000, certainly 5000, which should give a good indication of the prevalence of OSA and other sleep disorders in typical primary care populations. The hope is that primary physicians can then no longer ignore the problem.

I will end with a couple of things. First of all, the research on sleep apnoea and cardiovascular disease is very exciting. Nonetheless, good science involves a great deal of scepticism. It is not yet a proven fact that OSA plays a causal role in cardiovascular disease. However, even if we are not 100% convinced by the end of this meeting that OSA *causes* cardiovascular disease, we finally must come to terms with the value of improving the quality of life. There is no quality of life for those who are disabled by excessive sleepiness all day long, day after day after day.

The second point to consider is how sleep medicine, and particularly the management of OSA, will finally be integrated into the mainstream? Will it be a specialty practised by one or several specialists or will the diagnosis and treatment of sleep disorders be practised mainly in primary care and family practice settings. Assume it is finally proven that OSA causes heart disease and stroke and everybody believes it. What will happen then? I will give you the example of poliomyelitis. When I was a youngster, every summer we lived in terror of polio. Who would be stricken? You always knew someone. Our parents worried constantly. When the polio vaccine finally became available, everyone knew about polio. We were eager to get the vaccine. On the other hand, we live in a society where a similar awareness and concern about OSA does not exist.

I think it behoves all of us to get our society ready for these exciting new findings that we are going to hear about and the implications of which for medical practice may be just over the horizon. A massive national awareness campaign and effective penetration of the educational system at all levels, particularly medical school, is the only answer.

I showed a slide of a 44 year old man who was diagnosed and treated for severe OSA at the Stanford University Sleep Disorders Clinic in 1974. He had a tracheostomy. Today, more than two decades later, he remains healthy and active. In his all night sleep test he showed serious cardiac arrhythmias, severe oxygen desaturation, and a very high apnoea index. He had intractable high blood pressure and he

repeatedly fell asleep in the most extraordinary circumstances. To date, we have given him 24 additional years of life and who knows how many more. I have no doubt about this whatsoever. Had he not been treated, he would surely have fallen asleep behind the wheel, or he would have succumbed to a fatal arrhythmia. Today he feels fine, his blood pressure is controlled, and he is alive, energetic and alert. There is an enormous amount of good yet to be done. Let's do it!

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