PENN SLEEP CENTER
Annual Report 2008
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I am delighted to bring you the first annual report for Penn Sleep – the Center for Sleep and Respiratory Neurobiology and the Division of Sleep Medicine in the Department of Medicine. Over the years, our structure for Sleep Medicine has evolved to reflect our commitment to Sleep Medicine as a truly interdisciplinary endeavor. The Center for Sleep and Respiratory Neurobiology is a medical school-wide center, although faculty from other schools in the University are members of the Center, as is evident in the faculty profiles. The Center is the structure to develop the academic aspects of our program. The Division of Sleep Medicine is the clinical arm of our program. It is also a multidisciplinary entity and some faculty in the Division have dual appointments in the School of Medicine. These structures closely collaborate with the Division of Sleep and Chronobiology in the Department of Psychiatry that is directed by Dr. David Dinges and the Sleep Center at the Children’s Hospital of Philadelphia, directed by Dr. Carole Marcus.

This is an exciting time for Penn Sleep. All aspects of our program are flourishing. Our faculty have published in a range of respected journals such as Nature, Nature Genetics, Annals of Internal Medicine, Journal of the American Medical Association and Journal of Neuroscience. We have the most grants from the National Institutes of Health (NIH) for sleep research of all institutions in the country (source: “Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem” National Academies Press, 2006). Our program project grant “Mechanisms of Alterations in Sleep with Age” was recently renewed for five more years of funding. We are attracting top quality trainees and our trainees are developing careers as independent investigators. A number of our trainees have K Awards from the NIH and one of our recent trainees just won the prestigious Burroughs Wellcome Award. Our clinical program is growing rapidly and we have developed the Penn Sleep Network, with 22 beds for clinical studies at five different locations. Two new clinical sleep centers are in development. We are rapidly developing information systems to link these centers. We are focusing on an outcomes-based approach to management of our patients with a variety of sleep disorders. We believe that Sleep Medicine is fundamentally a knowledge-based chronic disease management discipline, not a diagnostic discipline, and this vision motivates development of our clinical program.
The Institute of Medicine’s 2006 report, “Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem,” recommended that all academic medical centers should have an interdisciplinary sleep center and cited our program as a model. They specifically recommended that there should be Regional Comprehensive Interdisciplinary Academic Sleep Centers, which play a major role in education – both professional and public – as well as in basic and clinical research. We are continuing to build our program to be such a Regional Comprehensive Center.

Our program is strongly supported by the leadership of Penn Medicine who consider that we have a model multi-departmental interdisciplinary program. Two years ago we moved into 11,000 sq. ft. of new space for our basic science program and 16,000 sq. ft. of new, reconstructed space for our clinical program and faculty offices including space for sleep laboratories, outpatient practice and the academic program.

In this first annual report, we describe the various aspects of our programs, what our faculty do, and provide information about our training programs and our trainees. We trust that this will be informative. Any inquiries should be addressed to me at pack@mail.med.upenn.edu.
Funding for basic science research, including NIH grant awards continue to grow within Penn Sleep. NIH funding for the Center’s basic science research has grown 14% from $7.8 million in 2004 to $8.8 million in 2007. These dollars only reflect grants administered by the Sleep Center; there are also substantial portfolios of NIH grants in the Department of Psychiatry, Department of Neuroscience, Children’s Hospital and the School of Nursing.

A newly acquired program project for the Center brings together faculty from three departments for synergistic studies into the mechanisms by which aging impairs sleep and memory. Investigators leading these projects are Drs. Allan Pack (Medicine), Amita Sehgal (Neuroscience), and Ted Abel (Biology). Indeed, a major strength of the Center is its prestigious, multidisciplinary faculty coming from different departments in the University of Pennsylvania. The basic science sleep research community at Penn is considered one of the strongest and most collaborative in the country.

While investigators come from diverse departments, there is a focused emphasis of the research: understanding the molecular mechanisms regulating sleep and wakefulness, the functions of sleep at a most basic molecular level, and how aging and disease disrupt these processes. Studies are being conducted in multiple model systems, each with particular strengths for exploring sleep – C. elegans, Drosophila, and mice. Dr. David Raizen (Neurology) has recently identified a sleep-like state in C. elegans and has been appointed to the faculty in the Department of Neurology to pursue studies in this model system. He has just published his findings in Nature. Dr. Sehgal’s lab and Dr. Pack’s lab are studying sleep in Drosophila. Within the past year, these labs have identified several key proteins whose transcriptional regulation is different between sleep and wake based on microarray studies conducted by Dr. Miroslaw Mackiewicz. Dr. Nirinjini Naidoo is pursuing proteomic approaches.

New molecular mechanisms that regulate sleep are being identified. Dr. Marcos Frank (Neuroscience) is doing seminal studies on the role of sleep in synaptic plasticity during development. By examining the relevance of these molecules across different species, investigators at Penn have the ability to identify evolutionary conserved molecules regulating sleep.
At the same time, there are strong ongoing collaborations with the mouse genetics group at the Jackson Laboratory in Maine, to develop high-throughput screens for abnormal mouse sleep/wake patterns and models of specific sleep disorders. In addition, Dr. Sigrid Veasey (Medicine) has developed a major program of research on oxidative injury neurons in models of obstructive sleep apnea (OSA), work that is ready for clinical translation. Dr. Eliot Friedman (Medicine) and Dr. Cynthia Otto (School of Veterinary Medicine) are developing models to study this in Drosophila. Dr. Leszek Kubin (Schools of Veterinary Medicine and Medicine) has an active program of research studying the neurochemistry, neuroanatomy and neurophysiology of the effects of rapid eye movement (REM) sleep on the neural control of upper airway muscles using a rodent-based, pharmacological model of REM sleep.

The Center has also recently received NIH funding for an exciting new career development opportunity in the area of genomic/genetic study of respiratory diseases and sleep disorders. This opportunity is designed for those with an MD, MD/PhD or PhD degree who have demonstrated aptitude for research and a commitment to pursuing a research academic career. The program offers didactic training in genomic/genetic strategies, relevant laboratory experience and conduct of research under an experienced mentor. Individuals pursuing this can obtain a Master’s in Translational Research. Opportunities for research are available in OSA and sleep disorders, lung cancer, asthma, and other lung diseases.

“The basic science sleep research community at Penn is considered one of the strongest and most collaborative in the country.”
**PATIENT-ORIENTED RESEARCH**

*Penn Sleep has a comprehensive program of patient-oriented research and a major commitment to this area.*

We have developed important cores to support this. First, we have a Research Sleep Core, with both adult and pediatric components. These are part of the recently awarded Clinical and Translational Science Award (CTSA). The University of Pennsylvania was a recipient of a CTSA in the first round of applications. On the adult side, there are four bedrooms dedicated for sleep research and on the pediatric sleep center, two such bedrooms. These facilities are managed by experienced staff and we provide a broad range of studies: overnight sleep studies; multiple sleep latency and maintenance of wakefulness tests; actigraphy; neurobehavioral tests of function. These facilities are available to all faculty at Penn and Children’s Hospital of Philadelphia (CHOP) who have an interest in sleep research. This approach has greatly facilitated our development of a vibrant program of research in this area.

Another facility that we have developed, under Dr. Sam Kuna’s leadership, is for centralized scoring of sleep studies from multiple locations. This facility is being used for two NIH-funded multicenter studies. CPAP (continuous positive airway pressure) Apnea Trial – North American Program (CATNAP, PI: T. Weaver), assessing outcomes of therapy with CPAP in patients with mild-to-moderate sleep apnea who are excessively sleepy; and Sleep Action for Health in Diabetes (Sleep AHEAD, PI: G. Foster) evaluating prevalence of OSA in obese Type 2 diabetics, progression of disease and effects of behaviorally induced weight loss.

Dr. Richard Schwab has developed an upper airway imaging core to facilitate analysis of three-dimensional images of the upper airway, surrounding soft tissues and craniofacial structure. This core is being used for studies in adults (Dr. Schwab) and in children (Dr. C. Marcus). It is also being used to analyze MR images collected in Iceland as part of our ongoing study of genetics of sleep apnea (Dr. T. Gislason, Dr. A. Pack, and deCODE Genetics). Currently, we have funded programs of research in several distinct areas. Tools developed at the University of Pennsylvania such as the Multivariable
Apnea Prediction (Maislin et al., Sleep 18:158-166, 1995) and Functional Outcomes of Sleepiness Questionnaire (Weaver et al., Sleep 20:835-843, 1997) are now used in patient-oriented research around the world and have been translated into many languages.

The current programs of research include:

- Alternative medicine approaches to sleep disorders (N. Cuellar)
- OSA in obese Type 2 diabetics (G. Foster/S. Kuna)
- Insomnia and other disorders in older adults (N. Gooneratne)
- Screening strategies for OSA (I. Gurubhagavatula)
- Metabolic syndrome and OSA in children (A. Kelly, L. Brooks)
- New strategies for diagnosis of sleep apnea (S. Kuna)
- Pathophysiology of childhood OSA (C. Marcus)
- Pediatric parasomnias (A. Mason)
- Genetics of sleep and OSA (A. Pack)
- Sleep disorders in women (G. Pien)
- Narcolepsy and other disorders of excessive sleepiness (A. Rogers)
- Outcomes of therapy for sleep apnea (T. Weaver)

Finally, important new initiatives in patient-oriented research have recently been developed. First, we are building a program of research in the cardiovascular consequences of sleep apnea. We have recently obtained funding to study the relative role of obesity and OSA in cardiovascular disease, insulin resistance (PI: F. Samaha, Chief of Cardiology at the VA Medical Center). Second, under the direction of Dr. Sam Kuna, we are developing a new program in Health Care Delivery Research in OSA. This effort is based at the Sleep Center at the VA Medical Center. Third, we are aggressively pursuing development of research programs in the genetics of sleep and its disorders, under the direction of Dr. Pack. New R01 grants have been awarded to Dr. Grace Pien to study development of sleep apnea with menopause and to Dr. Indira Gurubhagavatula to study screening for sleep apnea in commercial drivers.
Clinical care for the full spectrum of sleep disorders is provided by the outpatient practices and diagnostic sleep laboratories of the Penn Sleep Centers. The outpatient practices formerly located at the Hospital of the University of Pennsylvania and Penn Presbyterian Medical Center have recently merged and now occupy a new state-of-the-art-facility at 3624 Market Street in West Philadelphia, as part of Penn Medicine’s expanding clinical campus. The Penn Sleep Centers also maintain an active outpatient practice at Penn Medicine at Radnor. Sleep laboratories accredited by the American Academy of Sleep Medicine are in operation at 3624 Market St. (four beds), the University Sheraton Hotel at 36th and Chestnut Sts. (eight beds), Audubon (two beds) and Doylestown Hospital (four beds). We also have four beds at the VA Medical Center that we help manage. Thus, we have a total of 22 clinical beds. Our laboratories are owned by the University of Pennsylvania but managed in collaboration with Neurocare Inc. under a management service agreement with the University of Pennsylvania Health System.

Since the Division of Sleep Medicine was established in 2001, there has been dramatic growth in clinical activity. As shown on the accompanying figures, the number of patient visits has increased approximately five-fold from fiscal year 2002 to the present. Similarly, the number of sleep studies performed has increased from 1,324 in 2001 to 5,500 studies in 2007.
Faculty in the Division of Sleep Medicine, the clinical arm of our program, includes specialists in Pulmonary Medicine, Neurology, Geriatrics and Psychology. These physicians work closely with colleagues in Otorhinolaryngology and Oral and Maxillofacial Surgery. Recent clinical initiatives include collaboration with the Bariatric Surgery Program in the pre-operative evaluation of gastric-bypass patients for OSA and collaboration with Cardiology in the identification and treatment of congestive heart failure patients with sleep apnea. Over the last two years there has been an increasing emphasis on monitoring and improving patient adherence to CPAP, achieved via both direct patient contact and improved technology. A program utilizing cognitive-behavioral therapy for the treatment of insomnia began in the spring of 2006 directed by Dr. Phil Gehrman.

These programs and increasing patient volume have created the need for improvement in data management. New information systems and a comprehensive database for all Sleep Center programs are in development. Our information systems allow studies to be uploaded to a dedicated server from any location facilitating scoring and interpretation of data. New information systems are being developed to track outcomes of therapy.

Refinements in data management, growth in programs and support staff, and our new physical plant will enhance our ability to treat our patients, provide an appropriate setting for the training of residents and sleep fellows, and facilitate recruitment of patients for clinical research.
As in the Center for Sleep and the Sleep Medicine Division, the fellowship training program has a strong multidisciplinary focus. The program has been accredited by the Accreditation Council for Graduate Medical Education (ACGME) and the American Academy of Sleep Medicine. Fellows who began their training after July 2007 are required to complete the 12-month ACGME clinical sleep medicine fellowship followed by two years (three if desired) of a postdoctoral research fellowship in sleep medicine. The length of our sleep fellowship is longer than needed to qualify for ABMS certification, but we are committed to providing a strong sleep-related research experience that prepares physicians for a career in academic medicine.

The program accepts trainees who have completed training in Internal Medicine, Neurology, Otolaryngology, Pediatrics, Psychiatry and Pulmonary Medicine. We currently have eight physicians in the fellowship program who completed fellowship/residency training in Pulmonary (4), Neurology (1), Psychiatry (1), Internal Medicine (1), and Developmental Pediatrics (1).

Located within the Department of Medicine, the Sleep Division has nine full-time faculty members. The clinical and research sleep laboratories at three adjacent hospitals (Hospital of the University of Pennsylvania (HUP), the Children’s Hospital of Philadelphia (CHOP), and the Philadelphia Veterans’ Affairs Medical Center (VA)) evaluate patients with a full range of sleep disorders. The Center for Sleep and Respiratory Neurobiology serves as the research arm of the training program. Its 43 faculty members are drawn from the above clinical departments as well as basic science departments, including Genetics and Neuroscience. Each fellow forms a mentorship committee that provides advice and guidance during the training process. Given the multidisciplinary structure of the program, the fellowship curriculum is tailored to allow each trainee to concentrate on his/her particular area of specialization.

The clinical training program is in collaboration with CHOP. Thus, we train both adult and pediatric sleep medicine physicians. The clinical fellowship program is co-directed by
Drs. Ilene Rosen (Medicine) and Alex Mason (Pediatrics). It is a comprehensive one-year program that consists of two tracks, an adult and a pediatric sleep medicine track. We are also committed to training physician-scientists. Thus, we seek applicants who have this goal and anticipate that fellows interested in research training in sleep medicine will spend three years in our program – one clinical year and at least two years in research. Fellows see adult patients at our clinical facility at 3624 Market Street as well as our community-based outpatient facility, Penn Medicine at Radnor. Pediatric patients are evaluated by fellows at the Sleep Center at CHOP. Fellows also do rotations through the Sleep Center at the VA, under the direction of Dr. Kuna. Fellows do inpatient consults at both HUP and CHOP.

New clinical training programs are also in development. We have become an accredited training site for behavioral sleep medicine to train clinical psychologists in cognitive-behavioral therapy for insomnia and other programs. This new program was developed by Drs. Jodi Mindell (Pediatrics) and Phil Gehrman (Medicine). We are also working with our colleagues in Pulmonary and Critical Care Medicine to develop a new combined Pulmonary/Sleep Medicine fellowship program. This will, we believe, fill an important national need.

Our comprehensive Sleep Medicine Lecture Series covers all aspects of sleep medicine. This is primarily held in the summer months. During the rest of the year we have a weekly Clinical Case Conference (case presentation followed by presentation of latest information on the topic). There is a fortnightly Research-in-Progress Conference. We also have a monthly Sleep Medicine Journal Club. Currently we have added video-conferencing facilities to our conference room so that other sleep medicine programs can join our educational activities. This is another step leading toward our goal of being a Regional Comprehensive Interdisciplinary Sleep Center.
The mission at the Sleep Center at CHOP is to provide comprehensive diagnostic evaluation and management to pediatric patients of all ages, using a family-centered approach; provide education and treatment for patients, medical trainees and practitioners, and the general community; and develop research to lead to a better understanding of normal and abnormal sleep during childhood and development. The Sleep Center at CHOP continues to be highly productive in both the clinical and research arenas.

A new Sleep Laboratory opened in December 2005. The expanded laboratory, located on the seventh floor of the main building is 2,295 square feet in size, and has six beds, two of which are dedicated to research. Each room is spacious enough for parents to spend the night with the child, and has a private bathroom with shower. The lab is equipped with new, state-of-the-art equipment. The staff has expanded to include 11 polysomnography technicians. The Sleep Center at CHOP was accredited by the American Academy of Sleep Medicine in January 2006. The Sleep Clinic continues to see more than 1,000 children a year with a wide variety of sleep complaints.

The faculty of the Sleep Center was enhanced by the addition of Lisa Meltzer, PhD. Dr. Meltzer is a psychologist whose research interest is in the sleep of caregivers of children with chronic disease. She joins the multidisciplinary faculty, which includes pulmonologists Drs. Marcus and Brooks, neurologists Drs. Mason and Brown, and psychologist Dr. Mindell. Dr. Mason completed a Master of Science in Clinical Epidemiology (MSCE) degree from Penn’s Center for Clinical Epidemiology and Biostatistics.

The General Clinical Research Center Sleep Core was established in 2005, and is directed by Dr. Mason. Research grants to the center include “Oxyhemoglobin Desaturation and Vasculopathy in Sickle Cell Disease” (PIs, Drs. Marcus and Mason), “Pediatric Obstructive Sleep Apnea and Metabolic Syndrome” (PI, Dr. Kelly of Endocrinology in conjunction with Sleep Center faculty), “Impact of Sleep Disruptions on Children with Autism Spectrum Disorders and Their Caregivers” (J. Christian Gillin Research Grant, Sleep Research Society, Dr. Meltzer) and “Pediatric Sleep Disordered Breathing Screening & Diagnostics Methods And Devices” (Respironics, Dr. Marcus).
In other faculty highlights, Sleep Center Associate Director Dr. Mindell was co-chair of the Second Annual Pediatric Sleep Medicine Conference and Dr. Marcus was elected onto the American Thoracic Society Pediatric Program Committee. Drs. Mindell and Marcus participated in the development of the International Classification of Sleep Disorders 2 and Dr. Marcus participated in the task force for the revision of the Rechtschaffen and Kales manual. Sleep center faculty members continue to participate on NIH study sections and the Sleep Research Society Board of Directors. Faculty members gave numerous scientific and educational presentations at meetings including the Associated Professional Sleep Societies (APSS), American Thoracic Society (ATS), the American Academy of Pediatrics (AAP), SuperCME, the American Academy of Sleep Medicine (AASM) Advanced Sleep Medicine Course, the Northeast Sleep Society, the American Society of Pediatric Otolaryngology, the American Academy of Craniofacial Pain. Dr. Marcus received the Annenberg Award for contributions to the field of Sudden Infant Death Syndrome and apnea. There were 24 publications from the Sleep Center faculty, including two books by Dr. Mindell (“Take Charge of Your Child’s Sleep: The All-in-One Resource for Solving Sleep Problems in Kids and Teens,” and “Sleeping Through the Night: How Infants, Toddlers, and Their Parents Can Get a Good Night’s Sleep”).
The Veteran’s Integrated Services Network (VISN) Eastern Regional Sleep Center at the Philadelphia VAMC is a state-of-the-art four bed facility that opened in February 2003.

The center is staffed by a multidisciplinary team of sleep specialists and is accredited by the American Academy of Sleep Medicine. The Sleep Center serves as an academic resource to medical students, residents and fellows at the University of Pennsylvania. Medical students and physicians-in-training rotate through the outpatient sleep disorders clinics to learn how to evaluate, diagnose and manage patients with a wide range of sleep disorders.

Clinical research projects include “Predictors of adherence to CPAP therapy in OSA” (PI, A. Sawyer, RN, MScN, CS) is funded by a VISN 4 VA Stars & Stripes Pilot Project. The purpose of this project is to identify pre-treatment predictors of adherence to CPAP treatment. “Imagery rehearsal therapy in veterans with PTSD-related sleep disturbance,” (PI, R. Ross, MD, PhD), funded by a VA Merit Review Award, is a randomized controlled trial to determine if imagery rehearsal therapy (IRT), a form of cognitive behavioral treatment, is effective treatment for patients with post-traumatic stress disorder. “Cost effective strategy for the management of veterans with sleep apnea” (PI, S.T. Kuna, MD) is a randomized controlled trial to compare home versus in-laboratory testing of patients with suspected obstructive sleep apnea. Funded by the VA’s Health Services Research and Development, the study will determine if the two clinical pathways result in similar patient adherence to CPAP and functional outcomes on CPAP treatment. “Effectiveness of CPAP treatment in hypertensive patients with OSA” (PI, I. Gurubhagavatula, MD, MPH) is another randomized control trial to determine if CPAP treatment lowers arterial blood pressure in patients with systemic hypertension and OSA. This study is funded by grants from the American Heart Association and the NIH.
The University of Pennsylvania School of Nursing has one of the largest concentrations of nurses studying sleep in the country. Dr. Terri Weaver, the first nurse researcher at Penn to study sleep, recruited Dr. Ann E. Rogers in 1998, and Dr. Norma Cuellar a few years later. Recently, Drs. Barbara Reigel and Nancy Tkacs have begun studying sleep in their populations of interest (congestive heart failure and diabetes). Post-doctoral students, supervised by Drs. Rogers and Weaver have investigated topics ranging from sleep in HIV-positive patients and sleep in patients with lung cancer, to sleep and obesity in pediatric patients, as well as sleep in patients with COPD or diabetes mellitus. Faculty research is also wide-ranging, with projects focusing on the management of sleep disorders, sleep in other medical disorders, and the effects of staff nurse fatigue on patient safety.

Ongoing research projects at the School of Nursing include a large, multi-center project, headed by Dr. Weaver focusing on identifying the factors associated with CPAP non-compliance. Dr. Cuellar’s funded research focuses on the impact of RLS on quality of life. In addition to documenting the high prevalence of RLS among diabetic patients, she is conducting a randomized control trial evaluating the efficacy of valerian for the management of RLS.
The Unit for Experimental Psychiatry, Division of Sleep and Chronobiology is a multi disciplinary group of investigators focused on establishing the nature of the physiological and neurobehavioral changes engendered by sleep loss and circadian rhythmicity. Basic human translational research within the laboratory characterizes the relationship between the biological basis (e.g., genetics) of sleep need and circadian physiology, and their control of waking neurobehavioral functions and health, as reflected in mood, physiological alertness, cognitive functions, quantitative EEG/EOG, cerebral blood flow, endocrine, immune, and inflammatory responses. Research is also conducted on ways to assess effective interventions for and countermeasures to these changes. Experiments utilizing healthy adult volunteers are conducted in a specially equipped Sleep and Chronobiology Laboratory and in the NIH General Clinical Research Center, both at HUP. The Unit also explores neurobehavioral functioning in response to stress, memory enhancement and distortion, and various pathologies of sleep and wakefulness (e.g. Circadian sleep disorders, hypersomnolence syndromes, insomnias, and insufficient sleep syndromes).

The Unit’s overarching goal is to discover new ways to effectively prevent and treat neurobehavioral, neuroendocrine, neuroimmune and psychophysiological impairments from sleep loss and related stressors, and their adverse effects on health, behavior, and safety, using novel behavioral, pharmacological, and technological countermeasures. Research is currently funded by NIH, NASA and National Space Biomedical Research Institute, Air Force Office of Scientific Research, and Department of Homeland Security.
ALLAN I. PACK, MB, CHB, PHD  
Center Director; Professor of Medicine;  
Chief, Division of Sleep Medicine, Department  
of Medicine.

Dr. Pack is pursuing research on genetics/genomics of sleep apnea. His laboratory is conducting studies in *Drosophila* and mice and translating these findings to humans. To study the genetics of sleep apnea, he has initiated a linkage/association study in Iceland in collaboration with Dr. Thorarinn Gislason (University of Iceland) and Dr. Kari Stefansson (deCODE Genetics). A particular focus of Dr. Pack’s work is to evaluate whether there are genetic determinants to outcomes of sleep apnea, in particular, sleepiness. Studies are ongoing to evaluate molecular mechanisms of sleepiness and sleep promotion using both hypothesis-driven and discovery science. Techniques being used include behavioral/sleep studies in *Drosophila* and mice, RT-PCR, Western analysis of protein, expression profiling, laser microcapture dissection, and immunohistochemistry. Dr. Pack is committed to research training and directs the postdoctoral research-training grant funded by the National Heart, Lung and Blood Institute.

TED ABEL, PHD  
Associate Professor of Biology; Director,  
Biological Basis of Behavior Program.

Dr. Abel’s research interests include the molecular basis of sleep/wake regulation using genetically modified mice and examining the role of sleep in memory storage. The biological function of sleep has remained elusive, but studies suggest that one function of sleep may be to mediate memory storage. Dr. Abel’s lab has recently begun to use genetic, electrophysiological and behavioral approaches to understand the regulation of sleep and the role of sleep in memory storage—with interesting findings. First, sleep appears to be critical for the storage of hippocampus-dependent memories, and sleep is increased following training. Second, sleep appears to be regulated by many of the same molecular processes that regulate memory storage, including the transcription factor CREB (cyclic AMP-response element binding protein) and the PKA signaling pathway. By using conditional genetic approaches and microarray studies, they can elucidate the machinery underlying sleep and define the role of sleep in the consolidation of long-term memory. Thus, our genetic approaches to study the role of specific signal transduction pathways in neuronal function may ultimately lead to an understanding not only of the mechanisms of memory storage, but also the function of sleep, providing insight into how the processes of memory and sleep are disrupted by aging as well as neurological and psychiatric disorders.

LEE BROOKS, MD  
Attending Pulmonologist, Sleep Center at CHOP.

Dr. Brooks is pursuing research on the metabolic consequences of sleep apnea in children. In collaboration with Dr. Andrea Kelly of pediatric endocrinology, he is attempting to determine whether there is an association between the metabolic syndrome (impaired fasting glucose, central obesity, dyslipidemia and hypertension) and OSA in children, and the physiologic causes for any such relationship. With Dr. Lorraine Katz and others, he is attempting to determine the extent that insulin resistance in children can be improved by treatment of their OSA. Dr. Brooks is also pursuing studies of the effects of sleep disorders on learning in elementary and middle school children.
Dr. Brown is interested in the interaction of sleep and neurological disease in children. There are several model areas of clinical interest, particularly the effects of sleep disorders and disturbances of the sleep-wake cycle in epilepsy and ADHD. Childhood epilepsy has important effects on alertness, attention and behavior. Some seizures and epilepsy syndromes are seen primarily in drowsiness or sleep; these may mimic primary sleep disorders like parasomnias. Sleep resistance, sleep-onset insomnia and poorly consolidated sleep are more commonly found in children with ADHD than control populations. Obstructive sleep apnea and periodic leg movements of sleep are often under-recognized but treatable causes of hyperactivity and inattentiveness. Similarly, other childhood neurological disorders (i.e., Tourette syndrome, autism, mental retardation, Prader-Willi syndrome, Smith-Magenis syndrome, etc.) have important interactions with sleep through primary disturbances of sleep, drug interactions and other mechanisms. Dr. Brown’s lab is developing collaborations to investigate aspects of sleep in these special pediatric populations.

Maja Bucan, PhD
Professor of Genetics; Chair, Genomics and Computational Biology Graduate Group.

Advances in the identification of genes causing complex disease, such as psychiatric disorders, have been modest. Current focus is on the identification of endophenotypes – biochemical, physiological or behavioral components of a clinical syndrome. The goal of the behavioral screen is to identify mouse mutants that can serve as animal models for human psychiatric disorders or more specifically, to identify genes/SNPs known to cause behavioral anomalies in mice and then use them as candidate genes in human genetics. A screen for behavioral mutations resulted in more than five single gene mutations causing anomalies in rest-activity behavior (Earlybird, Rooster, Bedlem, etc.). One of these mutations, Earlybird, associated with abnormal sleep and circadian behavior, is caused by dominant negative mutations in Rab3A. By showing that mutations in Rab3A cause behavioral anomalies in mice, we predict that not only Rab3A but more than 70 genes known to be involved in synaptic transmission should be considered as candidate genes for behavioral/psychiatric anomalies in humans.

Charles Cantor, MD
Clinical Associate Professor of Neurology and Medicine; Medical Director, Penn Sleep Centers.

Dr. Cantor oversees the clinical program of the Penn Sleep Centers which has outpatient practice sites at 3624 Market Street and Penn Medicine at Radnor, as well as sleep laboratory facilities in three University City locations, and in Audubon and Doylestown, PA. His clinical interests include sleep disturbances in Parkinson’s disease and other extrapyramidal disorders, narcolepsy, adult parasomnias, and restless legs syndrome (RLS). He is currently participating in clinical research on sleep quality in Parkinson’s disease and the effects of gastric bypass surgery on obstructive sleep apnea. He is collaborating in these studies with colleagues in the Movement Disorders Center and in the Bariatric Surgery Program at Penn.

Diego Contreras, PhD
Associate Professor of Neuroscience.

The focus of Dr. Contreras’ lab is the generation and synchronization of rhythms that characterize the waking and sleep states as well as the transition from certain sleep patterns into seizure activity. Using intracellular and optical recordings in vivo, they address questions concerning the cellular mechanisms of rhythm generation in cerebral cortex and thalamus. Using genetically modified mice, they try to understand the role of particular ionic channels expressed in specific populations of cortical and thalamic cells for their transition into epileptic patterns. With the aid of realistic computer models of cortical and thalamic networks (in collaboration with Dr. Roger Traub in the department of physiology at SUNY Brooklyn), they explore a hypothesis concerning the role of different intrinsic electrophysiological properties, synaptic arrangements, and the presence of gap junctions for the generation of sleep rhythms and their transitions to epilepsy.
NORMA CUELLAR, RN, DSN
Assistant Professor of Nursing.

Dr. Cuellar is currently involved in a variety of research projects related to the gerontological aspects of sleep, complimentary and alternative medicine, and RLS. She recently completed two studies; the first looked at older adults and compared symptoms of primary and secondary RLS and was published in the September issue of the *Journal of the American Geriatric Society*. The second project examined the prevalence of RLS in Type 2 diabetics and outcomes of sleep and glycemic control and has been accepted for publication in *Diabetes Educator* and is in review at another sleep journal. She also recently completed a study examining the use of valerian (an herb used for centuries for anxiety and as a sleep aid) on sleep in persons with RLS which was a pilot for her K01 award through the National Institute of Nursing Research that was awarded in May 2007.

RICHARD O. DAVIES, DVM, PHD
Professor of Physiology, School of Veterinary Medicine.

Current investigations center on the neural mechanisms underlying the obstructive apneas/hypopneas that occur during sleep, especially rapid eye movement (REM) sleep. For this, animal models of REM sleep are used to study the changes in the control of motoneuronal activity to various respiratory muscles (both upper airway and respiratory pump muscles) that accompany REM sleep. A REM sleep-like state, is induced bringing about a profound suppression of activity in motoneurons to most respiratory muscles. There is a differential suppression of respiratory motoneuronal activity, with a pattern similar to natural REM sleep. The role of the two aminergic systems of the brainstem in the motor and reflex control of upper airway motoneurons (hypoglossal, pharyngeal, laryngeal) and the relation of these systems to the atonia of REM sleep is currently being investigated using a variety of complementary neurophysiological, neuroanatomical and neuropharmacological techniques.

DAVID F. DINGES, PHD
Professor of Psychology; Director, Unit for Experimental Psychiatry, Department of Psychiatry.

The primary focus of Dr. Dinges’ research is on identifying the manner in which sleep and the endogenous circadian pacemaker interact to control wakefulness and waking neurobehavioral and physiological functions. Laboratory experiments are directed at the dual goals of establishing the nature of the physiological and neurobehavioral changes engendered by sleep loss and circadian rhythmicity, and testing the effectiveness of countermeasures to these changes. Current research areas include experimentally identifying the effects of chronic sleep loss on neurocognitive functions and physiological profiles; determining the essential physiological features of recovery sleep; and evaluation of novel behavioral, technological and pharmacological countermeasures to sleep deprivation and circadian rhythm disturbances.

VICTOR FENIK, PHD
Research Investigator, School of Veterinary Medicine.

Dr. Fenik is interested in neuropharmacological mechanisms of airway motor atonia during sleep apnea. He exploits a carbachol model of REM sleep in anesthetized rats. In this model, respiratory activity of hypoglossal motoneurons (important upper airway dilators) is dramatically depressed during the carbachol-induced REM sleep-like episodes. The most exciting finding is that the hypoglossal depression can be reversibly abolished by simultaneous antagonism of serotonergic and noradrenergic receptors in and around hypoglossal nucleus. Techniques used include microinjections, electrophysiology and neuroanatomy.

MARCOS FRANK, PHD
Assistant Professor of Neuroscience.

Dr. Frank investigates the function, development and regulation of neonatal sleep. To address sleep function, he studies the role of sleep in the development of circuitry in primary visual cortex using a combination of sleep recording, electrophysiology and intrinsic optical imaging of cortical signals. In particular, Dr. Frank is interested in determining how sleep modifies cortical plasticity.
during critical developmental periods, and whether or not sleep provides an important source of endogenous stimulation to developing circuits. He is also extending his interest to examine the effects of perinatal drug use on the ontogenesis of sleep architecture and sleep regulatory mechanisms. Dr. Frank’s work is supported by funding from the National Institute of Mental Health.

**LEE GOLDBERG, MD**
Associate Professor of Medicine, Division of Cardiology, Department of Medicine; Director, Heart-Lung Transplant Program.

Dr. Goldberg is interested in the associations between sleep-disordered breathing and cardiovascular disease. In collaboration with the Center for Sleep and the NIH-funded Clinical Translational Research Center, Dr. Goldberg is the principal investigator of an international, multi-center intervention trial for patients with central sleep apnea and heart failure. In addition, Dr. Goldberg has worked with investigators in the School of Nursing to understand the impact of sleep-disordered breathing on the behavior, quality of life and outcomes of patients with heart failure.

**NALAKA GOONERATNE, MD, MSCE**
Assistant Professor of Medicine, Division of Geriatric Medicine, Department of Medicine.

Dr. Gooneratne’s research interests are centered on studying the nature of sleep disorders in the elderly. While many older adults complain of difficulties with sleep, it is an area about which modern medicine has only a limited understanding. He has received funding through a National Institute on Aging Mentored Research Career Development Award and a National Center for Complementary and Alternative Medicine Research Award, which have supported research examining the role of melatonin, a hormone secreted by the pineal gland, in sleep in the elderly. Dr. Gooneratne also has a strong interest in the attitudes of senior citizens towards their sleep problems and how their background/ethnicity informs their decisions. Dr. Gooneratne also runs a Sleep Disorders Clinic for seniors in an effort to address the medical needs of these patients.

**INDIRA GURUBHAGAVATULA, MD, MPH**
Assistant Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Polysomnography is an expensive technology that requires that the patient has access to a sleep laboratory with trained personnel to conduct and interpret the sleep study. Dr. Gurubhagavatula’s studies explore the relative accuracies of alternative, simpler strategies for identifying cases of obstructive sleep apnea. Her research focuses on screening high risk populations in particular, such as occupational drivers who may otherwise be at risk for fall-asleep accidents. She also evaluates the relative costs of different screening strategies, and whether screening for sleep apnea can be justified on the basis of a detailed cost analysis. Dr. Gurubhagavatula also studies whether or not persons identified with sleep apnea benefit from treatment in terms of their cardiovascular risk profile. Her research has been funded by grants from the National Institutes of Health. Her clinical interests include diagnosis and management of various sleep disorders, including OSA, periodic limb movements during sleep and restless legs syndrome, narcolepsy and REM behavior disorder.

**SUSAN HERMAN, MD**
Assistant Professor of Neurology; Director of the Epilepsy Monitoring Unit and EEG Laboratory, HUP.

Dr. Herman conducts clinical research on the interaction of sleep and epilepsy. A major interest is determining the distribution of partial seizures during the sleep-wake cycle, and how sleep differentially affects seizures arising from the temporal versus frontal lobes. She is involved in the development of new digital analysis tools for sleep electroencephalography. Dr. Herman is board-certified in neurology and clinical neurophysiology. She has authored several papers and chapters about the sleep-epilepsy interaction.

**LESZEK KUBIN, PHD**
Research Professor of Physiology, Department of Animal Biology, School of Veterinary Medicine.

The research in Dr. Kubin’s laboratory is concerned with the central neural mechanisms of sleep-disordered breathing. The neurochemistry, neuroanatomy and neurophysiology of the effects of rapid eye
movement (REM) sleep on the neural control of upper airway muscles is studied using a rodent-based, pharmacological model of REM sleep. Other studies address the role of inhibitory mechanisms localized in the posterior hypothalamus in the homeostatic regulation of sleep and cardiorespiratory response to sleep deprivation. Studies are also being conducted to determine whether chronic intermittent hypoxia similar to that experienced by obstructive sleep apnea patients leads to changes in the expression of hypothalamic transcription factors and receptors important for metabolic regulation.

SAMUEL T. KUNA, MD
Associate Professor of Medicine, Pulmonary, Allergy and Critical Care Division, Department of Medicine; Chief, Pulmonary, Critical Care & Sleep Section, Philadelphia VA Medical Center.

Dr. Kuna’s primary clinical and research interests concern the causes and treatment of sleep apnea syndrome. Dr. Kuna is medical director of the Veterans Integrated Service Network (VISN) 4 Eastern Regional Sleep Center at the VA Medical Center, where he is also director of the Pulmonary and Critical Care Division. He is conducting clinical research at the VA Medical Center on the ambulatory management of patients with obstructive sleep apnea and working with other members of the Penn Sleep Center on the heritability of sleep homeostasis. Dr. Kuna is medical director of the Centralized PSG Reading Laboratory at the Clinical Research Center for Sleep. This program standardizes the recording and analysis of sleep recordings in four ongoing multicenter randomized control trials including: Sleep AHEAD - the effect of weight loss on sleep-disordered breathing in obese individuals with Type 2 diabetes (Dr. Gary Foster, PI, Weight and Eating Disorders Center, Temple University), and CATNAP - the effect of CPAP treatment on functional outcomes in patients with milder obstructive sleep apnea who are excessively sleepy (Dr. Terri Weaver, PI, Penn School of Nursing). Dr. Kuna collaborates on Dr. Michael Brennick’s research on the effects of obesity on pharyngeal airway mechanics that is using innovative MRI techniques to track tissue movement in the pharyngeal walls in rodents.

LAWRENCE LEVIN, DDS, DMD
Associate Professor of Oral Surgery/Pharmacology; Chief, Division of Oral and Maxillofacial Surgery; Chief, Division of Dentistry at CHOP.

Dr. Levin’s expertise involves the use of oral appliances and orthognathic surgery in the management of obstructive sleep apnea. He also serves as clinical instructor in the oral and maxillofacial surgery and dentofacial deformity clinics. His research interests include clinical trials for postoperative analgesics. His clinical interests include pediatric oral and maxillofacial surgery, dental implantology, and surgical correction of dentofacial deformity.

IRWIN LEVITAN, PHD
David J. Mahoney Professor and Chair of Neuroscience.

Dr. Levitan studies the long term regulation of neuronal excitability and synaptic transmission. The molecular mechanisms that nerve cells use to modulate the activity of individual ion channels contribute to long term changes in neuronal function and ultimately in behavior. The essence of his approach is a combination of biochemistry, molecular biology, genetics and electrophysiology, at the level of individual neurons, synapses and ion channels. The lab studies the electrophysiological properties of native channels in neurons, and of cloned channels expressed in heterologous host cells, using patch recording techniques.

MIROSŁAW MACKIEWICZ, PHD
Research Assistant Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Dr. Mackiewicz is pursuing research on the molecular determinants of sleep homeostasis. A particular focus of his work is to establish spatial and temporal patterns of gene expression in sleep regulatory areas of the brain, as well as to uncover functional classes of genes affected by increasing durations of wakefulness. He has utilized high-throughput genomic techniques such as gene expression profiling with microarrays. Studies are carried out in mice including transgenic
mutants. He is developing techniques to do expression profiling in small numbers of neurons from specific, identified neuronal populations. Dr. Mackiewicz is also engaged in research on the identification of potential target genes for the transcription factor CREB using in vitro and in vivo models in combination with genomic and bioinformatics approaches.

GREG MAISLIN, MS, MA
Adjunct Associate Professor of Statistics in Medicine, Division of Sleep Medicine, Department of Medicine.

Mr. Maislin has served as director of the biostatistics core for the Center for Sleep and Respiratory Neurobiology since 1990. He has collaborated with Dr. Pack and other center investigators for many years and has been involved in applying statistical methods to address sleep research questions since 1988. His current areas of interest in statistics include methods for randomized clinical trials, Bayesian biostatistics, and non-linear mixed models for longitudinal data. He is currently active in sleep research involving efficacy of CPAP treatment for apnea, population screening for apnea, excessive daytime sleepiness and insomnia in the elderly, differential vulnerability to partial and total sleep deprivation, and in the heritability of differential vulnerability to sleep deprivation and other sleep-related phenotypes.

CAROLE MARCUS, MBBCH
Professor of Pediatrics; Director, Sleep Center at CHOP.

Dr. Marcus’ research is focused on understanding the pathophysiology of childhood obstructive sleep apnea, and the developmental aspects of ventilatory and upper airway control. Studies have concentrated on clinical research across the age spectrum, evaluating upper airway collapsibility during sleep, as well as arousal mechanisms. In addition, in concurrent studies, she is evaluating other aspects of sleep-disordered breathing, including diagnostic techniques and treatment, with an emphasis on noninvasive ventilation.

THORNTON B. ALEXANDER MASON, MD, PHD
Assistant Professor of Neurology, Sleep Center at CHOP.

Dr. Mason’s research interests include genetic influences on pediatric sleep and sleep disorders. One focus involves periodic limb movements in sleep (PLMS). Although family studies suggest a genetic basis for some cases of PLMS occurring with restless legs syndrome, no associated genes or gene products have been identified. Some data support a paucity of PLMS among normal children and a high prevalence of PLMS in children with Williams Syndrome, a human developmental disorder caused by a microdeletion of multiple genes in a distinct region of chromosome 7.

JODI A. MINDELL, PHD
Adjunct Professor of Pediatrics; Associate Director, Sleep Center at CHOP.

Dr. Mindell’s research focuses on the assessment and non-pharmacologic treatment of sleep problems in infants and toddlers. Furthermore, she is currently working on several projects investigating the prescribing practices of pediatricians and child psychiatrists for sleep problems in children and adolescents. Dr. Mindell’s clinical interests include the treatment of pediatric sleep disorders, with a primary focus on behavioral issues of infants and toddlers.

ADRIAN R. MORRISON, DVM, PHD
Professor Emeritus of Animal Biology; Director, Laboratory for Study of the Brain in Sleep, School of Veterinary Medicine.

Dr. Morrison has long been interested in the mechanisms underlying REM sleep. The laboratory’s investigations, together with those of the laboratory of Michel Jouvet from Lyon, France, were instrumental in the recognition of REM Sleep Behavior Disorder. The laboratory has studied this condition experimentally in cats, rats and clinically in the School of Veterinary Medicine’s hospital. The laboratory’s current focus is the role of the amygdala in the control of REM onset and its maintenance.
NIRINJINI NAIDOO, PHD  
Research Assistant Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Dr. Naidoo’s research focuses on the molecular mechanisms of sleep regulation. She uses both the mouse and Drosophila models in her studies using biochemical and proteomic approaches to study the cellular responses to sleep deprivation. She has recently established that the endoplasmic reticulum is a critical sensor of perturbations that result from sleep deprivation and that a cellular protective pathway, the unfolded protein response, is induced when mice or Drosophila are sleep deprived. In addition, Dr. Naidoo is studying age-related changes in cellular protective pathways in response to sleep deprivation. She has also recently begun studying the role of the synaptic scaffolding protein, Homer, in sleep-wake behavior. Studies include determining the sleep-wake phenotypes of a Drosophila, loss of function Homer transgenic and mouse Homer1 knockouts.

CINDY OTTO, DVM, PHD  
Associate Professor of Critical Care, School of Veterinary Medicine.

Dr. Otto’s research focus is on the effects of hypoxia, in particular cyclical intermittent hypoxia, on cellular responses, particularly inflammatory responses. Her laboratory has established a method to tightly control and cycle oxygen in cultured cells. The laboratory is currently investigating the effects on nitric oxide synthesis. Recent advances in the laboratory have led to novel findings in macrophages exposed to intermittent hypoxia. This line of work has been extended to evaluate the effects of intermittent hypoxia on survival in Drosophila. The main focus is the role of nitric oxide and inflammation in decreasing survival associated with exposure to intermittent hypoxia. In addition, Dr. Otto’s laboratory, in collaboration with Dr. James Baumgardner in the Department of Anesthesiology and Critical Care, is actively investigating the implications of cyclical intermittent hypoxia in acute lung injury.

GRACE PIEN, MD, MSCE  
Assistant Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Dr. Pien’s research interests focus on sleep disorders in women. She has recently completed a project examining the risk factors for sleep-disordered breathing in pregnant women and the impact of sleep-disordered breathing on maternal-fetal health. Dr. Pien is currently conducting a longitudinal study of sleep-disordered breathing in middle-aged women, and of the mechanisms that lead to increased risk for obstructive sleep apnea in women after menopause. Her clinical interests include obstructive sleep apnea and sleep disorders in women. She is the recipient of several prestigious academic awards, including an NIH Research Project Grant, Mentored Patient-Oriented Research Career Development Award and a Scientist Development Award from the American Heart Association.

DAVID RAIZEN, MD, PHD  
Assistant Professor of Neurology.

Dr. Raizen joined the Center after completing an MD/PhD dual degree program followed by a neurology residency. His scientific interests include the genetic basis of sleep regulation and the relationship between sleep and development. He chose to address these problems in the nematode C. elegans, because of this animal’s powerful genetics and its simple, well-defined nervous system. For the past two years, he has been characterizing quiescent behavior as a model for sleep. He has been making measurements of behavior during lethargus, a known quiescent period that occurs immediately prior to each larval molt. This period is interesting because it correlates with a time of a high degree of nervous system change. Furthermore, he has shown that the worm is capable of movement during its predicted lethargus period, indicating that the behavioral quiescence is under nervous system regulation. He finds that mechanical stimulation of the worm during its predicted lethargus does not eliminate the quiescence; it only delays it. This finding suggests that the quiescent behavior during lethargus, like sleep, is controlled by a homeostatic process.
Ann E. Rogers, PhD, RN
Associate Professor of Nursing.

Dr. Rogers’ research currently focuses on the relationship of staff nurse fatigue and patient safety. Of particular interest are the effects of their work schedules, particularly extended shifts (12 hours or longer) and sleep duration. Dr. Rogers’ unique data-set includes over 22,000 days of data about the work hours, sleep patterns, errors, and drowsy driving episodes collected from 895 randomly selected full-time hospital staff nurses. She and Dr. David Dinges in Penn’s Department of Psychiatry are examining the effect of sleep duration on errors and recovery sleep obtained in a naturalistic setting. Because the majority of hospital staff nurses in the United States now work 12-hour shifts, the study is being replicated in Australia where 12-hour nursing shifts are uncommon. Drs. Jill Dorrian and Drew Dawson from the University of South Australia are collaborating with Dr. Rogers on this project. Measures include daily recordings of mood, work schedules, sleep times, errors, drowsiness at work and when driving home, as well as actigraphy recordings.

Ilene M. Rosen, MD, MSCE
Assistant Professor of Medicine, Division of Sleep Medicine, Department of Medicine; Director, Sleep Fellowship Program; Associate Program Director, Internal Medicine Residency Program, Department of Medicine.

Dr. Rosen has published studies on the effects of lack of sleep on residents’ performances in the New England Journal of Medicine, Annals of Internal Medicine and JAMA. Her clinical interests cover a variety of sleep disorders including circadian rhythm disorders, delayed sleep phase syndrome, idiopathic hypersomnolence, narcolepsy, restless leg syndrome, and sleep apnea.

Frederick F. Samaha, MD
Associate Professor of Medicine, Cardiovascular Division; Chief of Cardiology, VA Medical Center.

Dr. Samaha’s group has conducted several trials comparing a low-carbohydrate to a conventional low fat diet in patients with a high prevalence of either metabolic syndrome or diabetes. The results have been published in several prestigious journals including the New England Journal of Medicine, and Annals of Internal Medicine. Dr. Samaha’s group also looked at the effect of these diets on lipoprotein subfractions and C-reactive protein, which was published in the American Journal of Medicine. The metabolic syndrome is highly prevalent in patients with OSA, and may have a direct causal relationship. Dr. Samaha currently has NIH funding to compare the effects of CPAP therapy, weight loss therapy, or both, on inflammatory markers and other metabolic risk factors in patients with obesity and moderate to severe sleep apnea. This study will be in collaboration with Penn School of Medicine colleagues Drs. Gary Foster (Temple University), Allan Pack, Indira Gurubhagavatula, Karen Teff, Thomas Wadden, and Daniel Rader.

Sharon Schutte-Rodin, MD
Clinical Associate Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Dr. Schutte-Rodin is the Clinical Outcomes Program Director of the Penn Sleep Centers. Her clinical interests include the evaluation and treatment of all sleep disorders including OSA, disorders of sleepiness such as narcolepsy, insomnia, restless legs syndrome, periodic limb movement disorder, parasomnias, and circadian rhythm disorders. In addition to practicing clinical sleep medicine, Dr. Schutte-Rodin has special interests in database development and monitoring measures of clinical effectiveness and quality improvement and clinical outcomes. A particular focus has been device technology and compliance monitoring of CPAP. Recent clinical research has
included apnea and reflux, apnea and glaucoma, chronic insomnia, and CPAP tracking devices. Dr. Schutte-Rodin is currently chairperson for the American Academy of Sleep Medicine Task Force for the Evaluation and Treatment Guidelines for Chronic Insomnia. She has been a medical policy consultant for Independence Blue Cross for more than ten years.

RICHARD J. SCHWAB, MD
Associate Professor of Medicine, Department of Medicine; Co-Director, Penn Sleep Center.

Dr. Schwab’s research has focused on the pathogenesis of obstructive sleep apnea utilizing novel upper airway imaging techniques. His studies help elucidate the role of the motion of key structures of the upper airway in mediating airway closure. By examining dynamic state-related changes in the upper airway and soft tissue structures surrounding the upper airway he has begun to understand the biomechanics of apneic events. He has studied patients with both magnetic resonance imaging and electronic beam computed tomography during wakefulness and sleep. Several novel findings have resulted from these studies: 1) the anatomic significance of the lateral pharyngeal walls in mediating airway caliber in normals and apneics; and 2) the characterization of the changes in upper airway caliber during the respiratory cycle and the importance of end-expiratory airway narrowing. Dr. Schwab collaborates closely with members of the Departments of Radiology and Biomechanical and Computer Engineering. They have developed state-of-the-art computer graphics-based analysis software to help model in three dimensions the biomechanical interrelationships between the soft tissue structures and the upper airway. They have multiple Sun workstations dedicated to three dimensional image analysis. Utilizing these techniques, Dr. Schwab and his colleagues plan to develop a biomechanical model of the upper airway.

AMITA SEHGAL, PHD
Professor of Neuroscience.

The goal of Dr. Sehgal’s research is to understand the molecular basis of circadian behavior, the best known example of which is the sleep/wake cycle. Dr. Sehgal’s laboratory and others have used the fruit fly, Drosophila melanogaster, to identify and characterize a molecular clock that drives rhythms of behavior and physiology. Mechanisms as well as molecules that comprise this molecular clock are conserved in mammals and have been implicated in at least one human circadian/sleep disorder. Efforts in the laboratory are focused on understanding the basic clock mechanism, the entrainment of the clock to environmental stimuli, such as light, and the pathways that transmit signals from the clock and produce rhythmic outputs. In addition, Dr. Sehgal’s laboratory is using the fly model to understand the function of sleep, as well as the control of sleep by non-circadian mechanisms, i.e., by the homeostatic mechanisms that drive the need to sleep independently of the circadian clock.

DAVID STANTON, MD, DMD
Associate Professor of Oral Surgery and Pharmacology, School of Dental Medicine.

Dr. Stanton is a graduate of both the University of Pennsylvania School of Medicine and the School of Dental Medicine. He is the program director of the Oral and Maxillofacial Surgery residency program and course director of the third-year oral surgery course at Penn Dental Medicine. He has lectured nationally on several of his fields of interest, including cosmetic facial surgery, obstructive sleep apnea, and maxillofacial trauma. His research interests include OSA, hair transplantation and facial trauma. He is currently a member of the examination committee of the American Board of Oral and Maxillofacial Surgery. He is also a section editor for the Oral & Maxillofacial Surgery Self Assessment Tool (OMSSAT), the national in-service training examination for Oral & Maxillofacial Surgery residency programs.
SIGRID C. VEASEY, MD
Associate Professor of Medicine, Division of Sleep Medicine, Department of Medicine.

Research in the laboratory of Dr. Veasey focuses on the elucidation of mechanisms underlying brain injury in obstructive sleep apnea (OSA). It is now apparent that some individuals with OSA have refractory wake impairments, mild cognitive impairment and peripheral nerve dysfunction. Using murine models of sleep apnea oxygenation patterns, her lab has identified a key enzymatic source of superoxide injury, NADPH oxidase. This work was recently published in the Journal of Neuroscience, as a featured article. Most recently her group has identified the neural dysfunction as endoplasmic reticulum injury and translational attenuation. The group has found that solubrinal, a small molecular protein phosphatase inhibitor, can prevent much of the endoplasmic injury and apoptosis in this model. This latest work was presented in November at the Society for Neuroscience international meeting. Future endeavors will examine differential susceptibility to hypoxia/reoxygenation brain injury. It is anticipated that this work will lead to the development of therapies to prevent neural injury and impairment in OSA.

TERRI WEAVER, PHD, RN, CS
Professor of Nursing; Chair, Biobehavioral and Health Sciences Division, School of Nursing.

Dr. Weaver’s interdisciplinary research focuses on characterizing outcomes associated with sleep disorders and their treatment, particularly treatment adherence. She developed the first instrument to measure functional status in disorders of excessive sleepiness. She recently completed a study designed to isolate factors contributing to non-adherence during the first week of treatment. She is the principal investigator of an international multi-center randomized placebo-controlled clinical trial study designed to evaluate the efficacy of CPAP treatment for milder OSA on functional status, daytime sleepiness, and blood pressure.