FRONTIERS OF KNOWLEDGE IN SLEEP AND SLEEP DISORDERS:
OPPORTUNITIES FOR IMPROVING HEALTH AND QUALITY OF LIFE

MONDAY MARCH 29

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Carl E. Hunt, MD, Director, National Center on Sleep Disorders Research

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Barbara Alving, MD, Acting Director, National Heart, Lung, and Blood Institute

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VADM Richard H. Carmona, MD, MPH, FACS
United States Surgeon General - US Department of Health and Human Services

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Robinson Fulwood, PhD, MSPH, Office of Prevention, Education, and Control, NHLBI

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CHARLES A. CZEISLER, MD, PHD

DETERMINANTS AND CHARACTERISTICS OF HEALTHY SLEEP: MAINTAINING PHYSIOLOGIC HOMEOSTASIS (CIRCADIAN RHYTHM, SLEEP DEBT)

Abstract unavailable

THOMAS ROTH, PHD

PREVALENCE OF SLEEPINESS AND SLEEP DISORDERS

Until recently our understanding of the prevalence and risk factors associated with various sleep disorders was limited, as much of the data was clinic rather than population based. Also, many aspects of sleep and its disorders were not well defined. Thus terms like insomnia and sleepiness were used differently across various studies. With the development of diagnostic systems (e.g. ICSD, DSM-IV) standardized tests (e.g. MSLT, PSG), and questionnaires (e.g. ESS, PSQI) significant advances have been made in our understanding of variations in sleep and sleep disorders.

Insomnia is defined as difficulty initiating, maintaining or non-refreshing, despite adequate time in bed, associated with negative daytime consequences. Insomnia is viewed both as a symptom of a medical, psychiatric, circadian or sleep disorder as well as a primary disorder in and of itself. While the prevalence of a transient insomnia varies from study to study and from time to time, the prevalence of chronic insomnia is consistently reported to be between 9% and 13% of the adult population. The identified risk factors for insomnia include: age, sex, family history of insomnia, medical disease, psychiatric disease, and shift work. Aside from defining the prevalence of insomnia, research has found the prevalence of insomnia comorbid with psychiatric disorders to be 40% to 50%, Restless Legs Syndrome 10%, and shift work sleep disorder 5% (25% of shift workers.)

Daytime sleepiness is defined as an inability to maintain wakefulness when desired. This is considered excessive or pathological when the sleep episode interferes with activities of daily living. Sleepiness can be quantified by standardized questionnaires or by standardized tests. It can be reflective of a sleep disorder (e.g. narcolepsy, obstructive sleep apnea syndrome) or by voluntary restriction of time in bed relative to biological sleep need. The prevalence of sleepiness as defined be an Eppworth Sleepiness Scale score of >10 is 20%, and as defined by a mean Multiple Sleep Latency Test of < 10 min. is 36%. It is generally felt that the most of the sleepiness is attributable to voluntary or occupationally mandated restriction of sleep time. Populations at risk for this include: transportation workers, medical staff and trainees, shift workers, early risers, and 18-25 year old males. It is generally accepted that biological sleep need for adults is 8 hours per 24 hours, the effects sleep loss accumulate across time, and there are compensatory mechanism to attenuate the sleepiness mediated impairment. However, the risk associated with different levels of sleep loss as well as the duration of sleep loss is not well defined. The relative prevalence of various disorders leading to daytime sleepiness has, thus far, only been determined in clinic populations. However the prevalence and risk factors for sleep apnea have been systematically studied. The sleep apnea syndrome is thought to occur 3% to 5% of the population and risk factors include sex, age and obesity. The prevalence of narcolepsy in the U.S. is about 0.05% of the population. Finally it is important to recognize that disorders such as Restless Legs Syndrome and Shift Work Sleep Disorder previously discussed under insomnia also can lead to excessive sleepiness. The morbidity associated with sleep disorders as well as sleep restriction has profound effect on both patient and public health. Thus, gaining further insights into the epidemiology of sleep and its disorders can help in our identification and prevention of these conditions as well as enhance our understanding of the pathophysiology of these problems.

DANIEL BUYSSE, MD

INSOMNIA (WHAT IS IT; WHAT NEEDS TRANSLATION)

Insomnia is defined as a subjective complaint of difficulty falling asleep, difficulty staying asleep, poor quality sleep, or inadequate sleep duration. However, insomnia only occurs when the individual has an adequate opportunity for sleep. This distinguishes it from sleep deprivation, which has different causes and consequences. Although insomnia is usually considered to be a symptom, it may also be part of a disorder that includes, in addition to the complaint, daytime consequences such as impairments in mood, cognitive and psychomotor function, or alertness. Insomnia disorders generally occur in three groups: those that are secondary to other medical, psychiatric, neurologic, or medication conditions; those cases associated with other known sleep disorders such as sleep apnea, restless leg syndrome, or circadian rhythm disorder; and finally, a group of primary insomnia disorders such as psychophysiological and idiopathic insomnia. Although insomnia is most often considered to be a symptom, emerging evidence suggests that it may be appropriate to think of it as a clinical syndrome in its own right.

Insomnia is very prevalent. Most population surveys suggest a prevalence of approximately 30 to 40 percent in the adult population. A smaller number of these cases have chronic or severe insomnia, consistent with the above definition of an insomnia disorder. Approximately five to ten percent of the population would qualify for a diagnosis of such a disorder. The epidemiology of insomnia demonstrates consistent increases with age and in female sex. Psychiatric symptoms, particularly depression, are commonly associated with insomnia, as are all types of medical symptoms and disorders. However, the strongest single risk factor for current insomnia is a previous history. That is, insomnia is a chronic condition in 50 to 80 percent of cases. The morbidity of insomnia includes increased risk for psychiatric disorders, decreased quality of life, increased healthcare utilization and costs, and poor daytime function. A growing body of evidence suggests that insomnia may be considered to be a disorder of “hyper arousal.” This increased arousal can be considered from cognitive and physiological perspectives. Cognitively, patients with insomnia typically have increased ruminative thoughts at night. Physiologically, recent evidence has demonstrated increased cortisol in the evening hours, increased fast EEG activity (an indicator of arousal), and regional changes in brain metabolism suggesting a less “deep” transition into sleep.

Efficacious behavioral and pharmacologic treatments for insomnia have been well documented. A variety of behavioral treatments have been studied. These typically share some key elements, including restriction of time in bed, establishing regular sleep-wake hours, avoiding the bed and bedroom at times when the individual is awake, and avoiding practices that obviously help or hurt sleep. Pharmacologic agents approved for the treatment of insomnia are limited to benzodiazepine receptor agonists. These drugs are clearly efficacious over the short term, and recent evidence suggests that they may be useful over longer periods of time in certain patients. Other medications that have been used to treat insomnia include sedating antidepressants.

Opportunities for translation exist in the areas of education, recognition, and treatment. Both the general public and healthcare communities need to be educated regarding insomnia’s prevalence and consequences. Encouraging specific definitions of insomnia will help to distinguish this condition from other sleep problems, such as sleep deprivation. Improved recognition is important both in the general public and in the healthcare community as well. Specifically, physicians need to ask their patients about sleep in order to make appropriate treatment recommendations. There is a large need for translation of efficacious treatments for insomnia into routine care settings. That is, forms of behavioral treatment that are feasible for routine care settings, and clear guidelines regarding the use of medications, will help to promote the public health.

MARK W. MAHOWALD, MD

RESTLESS LEGS SYNDROME (WHAT IS IT; WHAT NEEDS TRANSLATION)

Although commonly thought of as a sleep disorder, restless legs syndrome (RLS) is actually a neurologic sensory-motor movement disorder that commonly presents as a sleep complaint – severe insomnia. RLS is one of the most important causes of insomnia - both because of its prevalence (5-15% of the general population), and because of the gratifying response to treatment. RLS may begin in childhood, but tends to be more prevalent with increasing age. A recent study found a prevalence of 3% in those 18-29 years, 10% of those 30-79 years, and 19% in those 80 years and older. It affects both men and women. Its association with menstruation, pregnancy and menopause may explain the possible female predominance.

Clinical Features

RLS is characterized primarily by a vague and difficult-to-describe unpleasant sensation involving the lower extremities. This discomfort appears primarily during periods of inactivity, particularly during the transition from wake to sleep. Patients often have difficulty in describing the unpleasant sensations, rarely using conventional terms of discomfort such as "numbness, tingling, or pain," but rather bizarre terms such as "pulling, searing, drawing, crawling, or boring," suggesting that the sensations are unlike any experienced by unaffected individuals. These unpleasant sensations are typically relieved only by movement or stimulation of the legs. Many patients resort to various techniques to alleviate these symptoms, such as walking about; stomping the feet; rubbing, squeezing or stroking the legs; taking hot showers or baths; or applying hot packs to the legs. Although these maneuvers may be effective while they are being performed, the discomfort usually returns as soon as the individual becomes inactive or returns to bed. Those more severely affected may be unable to sit for prolonged periods of time such as during long performances, car trips, or airplane rides. The motor restlessness often follows a striking circadian pattern, with symptoms maximal between midnight and 4 am.

Etiology

The majority of cases are idiopathic or familial. A positive family history may be obtained in up to 50% of cases. Hormonal influences are suggested by the history of exacerbation during menstruation, pregnancy, or menopause. Up to a quarter of pregnant women may experience RLS. Although RLS has been associated with a wide variety of other medical and neurological conditions such as iron deficiency anemia and various peripheral neuropathies, such cases appear to be uncommon. RLS affects 20-40% of patients with chronic renal failure on dialysis, and may be extraordinarily bothersome. The RLS symptoms disappear following successful renal transplantation.

Low ferritin levels may be associated with either the development or exacerbation of RLS. Importantly, serum ferritin levels may be low despite normal hemoglobin, hematocrit, and serum iron values. Patients with RLS have abnormally reduced CSF ferritin levels as compared with controls - despite normal serum ferritin levels. MRI studies revealing decreased iron concentrations in the substantia nigra and putamen support the concept of abnormal CNS iron metabolism in RLS. Recent PET studies suggest central dopaminergic dysfunction in RLS and functional neuroimaging studies have identified thalamic, red nucleus, and brainstem involvement in the generation of periodic limb movements in patients with RLS. Transcranial magnetic stimulation studies suggest that the entire motor cortex is disinhibited in RLS. A recent FDOPA PET study indicated mild nigrostriatal presynaptic dopaminergic hypofunction in PLMD-RLS. These studies support the concept that RLS is associated with a primary abnormality of CNS iron metabolism. There is absolutely no evidence that RLS is related to any psychological or psychiatric problems.

Treatment

RLS symptoms usually respond dramatically to the newer dopamine agents such as pramipexole or ropinirole. Other effective treatments include benzodiazepines, opiates, and some anticonvulsants.

Summary

- Restless legs syndrome (RLS) is one of the most common causes of severe insomnia.
- RLS is easily diagnosed by history alone. Formal sleep studies are rarely, if ever, indicated. The only routine laboratory study indicated is a serum ferritin level.
- The vast majority of patients with RLS obtain substantial relief with a variety of medications.

Translational Issues

The most health care practitioners have never heard of RLS, and therefore cannot be expected to even suspect the diagnosis. Introduction of Sleep Medicine on the curriculum of medical and nursing schools is mandatory. Web sites providing RLS patients with written materials that can be presented to their health care providers will serve to educate both patients and health care professionals.

References:

1. Allen RP, Barker PB, Wehrl F, Song HK, Earley CJ. MRI measurement of brain iron in patients wth restless legs syndrome. Neurology 2001;56:263-265.
2. Bucher SF, Seelos KC, Oertel WH, Reiser M, Trenkwalder C. Cerebral generators involved in the pathogenesis of the restless legs syndrome. Annals of Neurology 1997;41:639-645.
3. Earley CJ, Connor JR, Beard JL, Malecki EA, Epstein DK, Allen RP. Abnormalities in CSF concentrations of ferritin and transferritin in restless legs syndrome. Neurology 2000;54:1698-1700.
4. Hening WA, Walters AS, Wagner M, Rosen R, Chen V, Kim S, et al. Circadian rhythm of motor restlessness and sensory symptoms in the idiopathic restless legs syndrome. Sleep 1999;22:901-912.
5. O'Keefe ST. Restless legs syndrome: a review. Archives of Internal Medicine 1996;156:243-248.
6. Nichols DA, Allen RP, Grauke, JH. Brown JB, Rice ML, Hyde PR, Dement WC, Kushida CA. Restless legs syndrome symptoms in primary care. A prevalence study. Archives of Internal Medicine. 2003;163:2323-2329.
7. Phillips B, Young T, Finn L, Asher K, Hening WA, Purvis C. Epidemiology of restless legs symptoms in adults. Archives of Internal Medicine. 2000;160(14):2137-41.
8. Ruottinen HM, Partinen M, Hublin C, Bergman J, Haaparanta M, Solin O, et al. An FDOPA PET study in patients with periodic limb movement disorder and restless legs syndrome. Neurology 2000;54:502-504.
9. Silber MH. Restless legs syndrome. Mayo Clinic Proceedings 1997;72:261-264.
10. Tergau F, Wischer S, Paulus W. Motor system excitability in patients with restless legs syndrome. Neurology 1999;52:1060-1063.
11. Turjanski N, Lees AJ, Brooks DJ. Striatal dopaminergic function in restless legs syndrome. Neurology 1999;52:932-937.
12. Walters AS, Hickey K, Maltzman J, Verrico T, Joseph D, Hening W, et al. A questionnaire study of 138 patients with restless legs syndrome: the 'night-walkers' survey. Neurology 1996;46:92-95.

STUART QUAN, MD

SLEEP DISORDERED BREATHING (WHAT IS IT; WHAT NEEDS TRANSLATION)

Sleep disordered breathing (SDB) including its most conspicuous variant, obstructive sleep apnea (OSA) is caused by narrowing or obstruction of the upper airway. Hallmark symptoms are loud snoring and excessive daytime sleepiness. Patients frequently are overweight and have a large neck circumference. The diagnosis usually is confirmed with polysomnography which demonstrates frequent episodes of apnea or hypopnea associated with sleep fragmentation and oxygen desaturation. However, SDB presents within a broad range: from severe OSA with frequent apneic episodes to upper airway resistance syndrome with arousals but without overt apnea or hypopneas.

In middle aged men and women in the Wisconsin Sleep Cohort, the estimated prevalence of symptomatic SDB is a 4% and 2%, respectively.[1] These rates are comparable to those observed for coronary heart disease and cancer, and are much higher than that reported from stroke. Moreover, some populations appear to be at slightly greater risk. For example, SDB in the United States is more common in American Indians and African Americans than in Caucasians.[2] Despite the relatively high prevalence of SDB, there is general agreement that it is underdiagnosed resulting in many individuals not being treated. In the Sleep Heart Health Study, approximately 4% of the population had symptoms consistent with SDB, but only 1.6% reported a physician diagnosis of the condition and <1% had been treated.[3]

The impact of SDB on society and affected individuals is considerable. Patients with SDB have higher health care costs than non-affected persons. Excessive daytime sleepiness resulting from SDB leads to more motor vehicle accidents, especially those involving a single driver.[4] In addition to linkages with hypertension and cardiovascular disease,[5.6] SDB is associated with impairment in quality of life which is equivalent to that reported for other chronic illnesses such as diabetes and hypertension.[7]

Despite increasing medical research concerning the epidemiology and recognition of SDB, there remain substantial obstacles to recognition. These barriers to the translation of known methods of diagnosis are the following.

1. There is a failure to consider the diagnosis due to insufficient public awareness as well as inadequate recognition on the part of practitioners;
2. Accurate diagnostic testing is not always readily available. The number of proficient sleep laboratories does not meet the demand and consequently there are long waiting times for polysomnography in many locales. Portable diagnostic testing is not always accurate and frequently misinterpreted.
3. There are inadequate numbers of Sleep Medicine practitioners.

The principal treatment options for those with the diagnosis of SDB are use of continuous positive airway pressure (CPAP), oral appliances and various forms of surgery. Effectiveness ranges from high (CPAP) to modest (palatal surgery). Patient acceptance of these therapies is quite variable. Thus, despite the availability of treatment for SDB, many patients do not receive, do not comply or are undertreated.

Barriers to improving translation of proven methods of treatment to all patients are the following.

1. There are impediments to accessing treatment. Reimbursement guidelines by CMS do not recognize all forms of SDB such as upper airway resistance syndrome. Not all insurance carriers will cover CPAP or oral appliances. In addition, there is a shortage of Sleep Medicine and other practitioners who are well trained in the treatment of SDB. General internists and family practitioners do not have sufficient specific knowledge concerning the treatment of SDB to care for these patients.
2. Adherence to therapy is poor. CPAP and oral appliances can be uncomfortable and not well tolerated. Methods to improve compliance using behavioral techniques are not always available to patients.

3. There needs to be more treatment alternatives for patients. Some surgical approaches are only Y in a few select medical centers. Medical therapy is not generally effective.

In summary, SDB is common and is associated with considerable health care consequences, increased health care costs and impairment in quality of life. Despite increasing research in this area, it is still under-recognized and untreated. There remain substantial barriers to providing adequate diagnosis and treatment.

References:

1. Young, T., M. Palta, J. Dempsey, J. Skatrud, S. Weber, and S. Badr, The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med, 1993. 328(17): p. 1230-5.
2. Young, T., E. Shahar, F.J. Nieto, S. Redline, A.B. Newman, D.J. Gottlieb, J.A. Walsleben, L. Finn, P. Enright, and J.M. Samet, Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med, 2002. 162(8): p. 893-900.
3. Kapur, V., K.P. Strohl, S. Redline, C. Iber, G. O'Connor, and J. Nieto, Underdiagnosis of sleep apnea syndrome in U.S. communities. Sleep Breath, 2002. 6(2): p. 49-54.
4. Young, T., J. Blustein, L. Finn, and M. Palta, Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. Sleep, 1997. 20(8): p. 608-13.
5. Shahar, E., C.W. Whitney, S. Redline, E.T. Lee, A.B. Newman, F. Javier Nieto, G.T. O'Connor, L.L. Boland, J.E. Schwartz, and J.M. Samet, Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med, 2001. 163(1): p. 19-25.
6. Nieto, F.J., T.B. Young, B.K. Lind, E. Shahar, J.M. Samet, S. Redline, R.B. D'Agostino, A.B. Newman, M.D. Lebowitz, and T.G. Pickering, Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. Jama, 2000. 283(14): p. 1829-36.
7. Baldwin, C.M., K.A. Griffith, F.J. Nieto, G.T. O'Connor, J.A. Walsleben, and S. Redline, The association of sleep-disordered breathing and sleep symptoms with quality of life in the Sleep Heart Health Study. Sleep, 2001. 24(1): p. 96-105.

EMMANUEL MIGNOT, MD, PHD

NARCOLEPSY/HYPERSOMNIA (WHAT ARE THEY; WHAT NEEDS TRANSLATION)

Narcolepsy and hypersomnias are a group of disorders characterized by centrally mediated excessive daytime sleepiness. Diagnosis is usually performed using nocturnal polysomnography followed by the multiple sleep latency test (MSLT). This diagnostic test is well validated in the case of narcolepsy-cataplexy but may be difficult to interpret if the clinical picture is complex; for example, if associated sleep disorders or pharmacological treatments are present.

The disorder narcolepsy-cataplexy is the most studied and understood of all hypersomnias. The population prevalence is approximately 1:2000 individuals. It is also tightly associated with HLA-DQB1*0602 and a deficiency in the neuropeptide system hypocretin (orexin). The most likely pathophysiological mechanism is an autoimmune process targeting the hypocretin-containing cells in the hypothalamus. Recent studies have shown that it is possible to diagnose the disorder with very high specificity and sensitivity, by measuring hypocretin-1 in the cerebrospinal fluid of patients suspected of narcolepsy. This test should be made more widely available to clinicians.

Another area of progress in need of translation has been the introduction of several new drugs that greatly improve treatment of narcolepsy. These include the FDA-approved stimulant modafinil, the FDA-approved sedative gammahydroxybutyric acid (GHB), and anticataplectic adrenergic reuptake inhibitors developed for depression or attention deficit hyperactivity disorders (ADHD). Unfortunately, however, the use of these drugs is still rare and often poorly managed due to a lack of education in the area.

In the areas of hypersomnias other than narcolepsy-cataplexy, the major difficulty is to ensure proper diagnosis. The population prevalence of these conditions is unknown but likely to be significant. More and more of these patients will be diagnosed as sleep medicine continues its developement. A possible etiological continuum with narcolepsy-cataplexy is likely in some cases while others are misdiagnosed patients or subjects with entirely different etiologies. Too many “narcoleptic” patients are diagnosed and treated when the true cause of their sleepiness is another sleep disorder, generally sleep apnea or insufficient sleep. The need for education is very significant in this area. Treatment for these entities is also challenging as many patients are drug resistant and may develop tolerance. Careful evaluation and slowly escalating drug regimen should be the rule, but too often, these patients are treated too aggressively with no result.

References:

Mignot E, Chen W, Black J (2003). On the value of measuring CSF hypocretin-1 in diagnosing narcolepsy. Sleep 26(6):646-9.

SESSION 2: NORMAL AND ABNORMAL SLEEP: WHAT PRICE DO WE PAY?

ROBERT STICKGOLD, PHD

NEUROCOGNITIVE (SLEEP, LEARNING AND MEMORY)

We are a sleep-deprived society. This chronic sleep restriction may lead to accidents, cardiovascular dysfunction, obesity and diabetes, mood disorders, cognitive deficits in attention and alertness, and the failure of sleep-dependent learning and memory consolidation I present here data on the importance of sleep-dependent learning, and how it can fail.

Sleep Consolidates Perceptual Learning: On a visual learning task, no improvement is seen following training until after subjects sleep. If no sleep is obtained within 30 hr after training, the potential benefits of the training are lost. Both deep, "slow wave sleep" (SWS) and REM sleep are needed for this improvement, and they can be obtained either across an 8 hour night, or with a nap of as little as one hour. Chronic cocaine users perform well on this task, showing normal overnight improvement. But during periods of extended abstinence, they show no overnight improvement at all, suggesting that they have lost the ability to support this sleep-dependent learning in the absence of their drugs.

Sleep Consolidates Motor Skill Learning: As with the visual perceptual task discussed above, motor skill learning also shows a sleep dependent component, now appearing to require light (Stage 2) non-REM sleep, rather than either SWS or REM sleep. On this finger tapping motor sequence task, subjects show a 20% improvement in speed, and up to a 50% reduction in error rates after a night of sleep, but not after an equivalent amount of waking time. Again, chronic cocaine users show a deterioration in overnight performance after two weeks of abstinence, suggesting a more general deterioration of sleep-dependent learning processes. Interestingly, chronic medicated schizophrenics show no overnight improvement either, despite a normal time course of improvement during training.

Sleep Consolidates Complex Learning, Leading to Insight: Sleep-dependent learning is not limited to simple tasks. In learning a complex technique for analyzing strings of digits, subjects develop insight into a simpler technique for completing the analysis as the result of a night of post-training sleep. In the absence of such sleep, either across several hours of normal daytime waking, or across a night of sleep deprivation, the number of subjects gaining insight into this simpler solution drops from 60% to less than 30%.

Failure of deterioration of sleep-dependent learning and memory consolidation represents just one of the deleterious consequences of chronic sleep restriction. In our culture, major sources of this restriction include (*i*) medical problems, including sleep apnea and chronic pain, (*ii*) psychophysiological insomnia, usually due to stress and anxiety, (*iii*) circadian phase delay in adolescents producing later bed times and a drive for later mornings, (*iv*) "sleep bulimia" in college and graduate students, characterized by shorter sleep during the week and "binge" sleeping on weekends, and (*v*) a culture of late-night TV & internet use.

Within the context of this conference, important opportunities for translation of research into improved health are found in our ability to *identify and treat* chronic sleep restriction. Identifying individuals suffering from chronic sleep restriction should be the responsibility of physicians, psychologists, and teachers. It can be achieved through simple patient interviews, asking questions such as, "Are you having trouble getting enough sleep?" Poor sleep can be identified with simple pencil and paper or internet based sleep logs, and provisionally confirmed with relatively simple home sleep monitors, such as wrist actigraphs or the Nightcap® home sleep monitor. Treatment can include CPAP or medication for such disorders as apnea and restless leg syndrome, and can use cognitive behavioral therapy for psychophysiological insomnia. But for the larger, cultural sleep restriction, education programs are needed, programs aimed at physicians, psychologists, teachers, and the public at large.

References: Maquet, P. (2001). The role of sleep in learning and memory. Science **294**, 1048-1052.
Wagner, U., Gais, S., Haider, H., Verleger, R., and Born, J. (2004). Sleep inspires insight. Nature *427*, 352-355.

SESSION 2: NORMAL AND ABNORMAL SLEEP: WHAT PRICE DO WE PAY?

DAVID F. DINGES, PHD

PERFORMANCE (ACCIDENTS, DROWSY DRIVING)

Millions of people are exposed to sleepiness and fatigue and the cognitive deficits and risks that they impose. Patients with excessive sleepiness due to sleep disorders and neurological/psychiatric disorders that have symptoms of hypersomnolence and excessive fatigue, as well as those experiencing sedation as a side effect of medication are subject to these risks. Adults, adolescents, and children with lifestyles that involve having limited sleep and sleep debt accumulation, night shift workers, aviation travelers crossing multiple time zones, as well as military personnel engaged in sustained operations are all examples of people who can be exposed to the performance risks posed by sleepiness and fatigue. Sleepiness and fatigue originate in neurobiology, eroding performance in systematic ways, and can have serious consequences for safety. Sleepiness and fatigue need to be prevented, detected, and treated and there are both opportunities and barriers for reducing risks posed by sleepiness and fatigue.

Sleep can be measured by polysomnography (PSG) consisting of recordings of brain waves (EEG); eye movements (EOG); muscle activity (EMG); cardiovascular activity (ECG); respiration and behavioral observation. Daytime sleepiness (sleep propensity) can be measured by recording the latency to sleep onset when attempting to sleep (MSLT), or when attempting to remain awake (MWT). Sleepiness involves the brain quickly falling asleep, hence latency to sleep onset can reflect sleep need. Microsleeps and sleep attacks are the expression of sleep propensity or incipient sleep initiation while a person is attempting to be awake and engage in activity. Microsleeps can result from inadequate sleep due to untreated sleep disorders and sleep deprivation in healthy persons. Microsleeps and elevated sleep propensity can lead to “state instability” over time, which refers to the waxing and waning of sleepiness/drowsiness; sleepiness intrudes into wakefulness causing moment-to-moment variability in attention and waking cognitive functions requiring executive attention processes. This can be especially problematic while operating a motor vehicle or other mode of transportation; while operating dangerous machinery; and while monitoring safety-sensitive processes.

Behavioral alertness is among the most fundamental cognitive functions eroded by sleepiness. One aspect of behavioral alertness—sustained attention performance as measured by reaction times (RTs)—has proven to be particularly sensitive to sleepiness and fatigue, showing admixtures of normal RTs, lapses (prolonged RTs) and errors of commission during sleep deprivation. For example, lapses of attention (and other cognitive performance deficits) increase after 18h awake in healthy individuals following a normal night of sleep. At approximately 22 hours of wakefulness (i.e., around 5AM) psychomotor performance is equivalent to a 0.08 blood alcohol concentration. Two recent studies showed that when nightly time in bed for sleep was less than 7 hours, performance lapses got progressively worse each day (i.e., performance deficits accumulated with chronic sleep restriction). Such psychomotor vigilance performance deficits also have been observed in patients with excessive sleepiness and people working the night shift. In addition to an erosion of behavioral alertness, sleepiness and fatigue are associated with other neurobehavioral and cognitive effects including but not limited to the following: cognitive slowing; increased working memory errors; reduction in learning and acquisition; loss of situational awareness; preservation on ineffective solutions, and related executive function deficits.

Sleepiness and fatigue make operating motor vehicles and other modes of transportation, as well as safety-sensitive equipment, particularly dangerous. Drowsy driving represents perhaps the single greatest risk to people who have had inadequate sleep due to medical disorders, work schedules or life styles. Drowsy driving crashes have a daily distribution consistent with the neurobiology regulating sleepiness and fatigue—having a peak incidence in the early morning hours between 3-8 AM. They have a fatality rate and injury severity level similar to alcohol-related crashes. Groups at risk for such crashes include patients with untreated sleepiness; people who sleep less than 6 hours per day; young adult males (ages

16 to 24); commercial drivers; night shift workers; and those transiting home after with prolonged work hours (e.g., medical / surgical residents post-call).

There are opportunities for preventing performance risks posed by sleepiness from medical disorders. There is a need to identify and treat people with excessive sleepiness from such disorders. Primary care physicians and nurses must be trained to detection sleepiness as a symptom. However, there is currently a lack of objective, valid, reliable, practical measures of sleepiness for medical use. There is also a need to increase physician, pharmacist, nurse and public awareness of synergy between sleepiness and sedating medications, but to achieve this will likely require development of a standard system for rating the sedating risks of medications relative, to guide health care professions.

There are also opportunities for preventing performance risks posed by sleepiness and fatigue from work hours. The management of fatigue risks in safety-sensitive occupations by federal and non-federal regulatory limits on work hours and off-duty hours is the oldest approach, but still controversial. Opportunities exist to update regulations based on science and scientifically proven countermeasures for sleepiness and fatigue from work schedules and to develop and validate “fatigue prevention,” “fatigue-detection” and “fatigue-management” systems within a regulatory framework. A lack of valid, reliable, practical measures of sleepiness and fatigue, as well as a lack of lack of public knowledge about how to use valid countermeasures and a lack of awareness of when risks escalate to unacceptable levels, serve as barriers to these opportunities.

Finally, there are opportunities for preventing performance risks posed by sleepiness and fatigue induced by life style. This is an area that has had perhaps the lowest public awareness and received the least attention until recently. There is a need for greater public education on the risks posed by acute and chronic sleep loss; drowsy driving; etc., especially in vulnerable populations. Passage of legislation inspired by Maggie’s Law in New Jersey for example, has prompted Congress to move forward on legislature that would grant incentives to states that develop safety traffic programs related to driver fatigue and sleep deprivation. States legislators and law enforcement agencies must enact the law, enforce the law, and educate the public.

VIREND SOMERS, MD

CIRCULATORY CONTROL DURING NORMAL AND DISTURBED SLEEP– IMPLICATIONS FOR UNDERSTANDING THE RELATIONSHIPS BETWEEN SLEEP, DEATH AND THE HEART

Sleep is generally perceived as a state of somatic and circulatory rest. However, cardiovascular disease pathophysiology may be closely linked to state changes related to sleep. Autonomic and hemodynamic measures are strikingly affected by normal sleep, by arousal, and by disordered sleep. The evidence linking sleep to cardiovascular events will be reviewed, with special attention to several hypothesized mechanisms that may be implicated. Data from several laboratories, and from our own, will be presented.

Normal sleep constitutes a remarkably heterogenous autonomic and hemodynamic profile, with blood pressure, heart rate and sympathetic activity closely dependent on sleep stage. During non-REM sleep, there is a gradual decrease in blood pressure, heart rate and sympathetic activity, with deepening stages of sleep. By contrast, REM is accompanied by marked increases in sympathetic drive and intermittent surges in blood pressure and heart rate, more frequent during phasic REM. REM is most prevalent later during sleep, closet to the time of waking. Cardiac and vascular events manifest clear circadian rhythms, with peak occurrences at between 6am and 11am. The relationship between these events and sleep itself, or with arousal from sleep, is not well understood. Autonomic excitation and hemodynamic responses during REM or arousal may conceivably contribute to early morning cardiovascular presentations and to cardiac ischemia during sleep.

An overall reduction in blood pressure during sleep is part of the normal sleep profile. Disturbances in blood pressure control, such as the absence of an appropriate blood pressure reduction during sleep (the “non-dipping” phenomenon), may be associated with increased cardiovascular risk. However, excessive hypotension during sleep may also imply increased risks for cardiac and vascular events.

The most compelling data linking sleep to heart disease is in the area of sleep apnea. Obstructive sleep apnea induces profound derangements in arterial blood chemistry. Chemoreflex activation by hypoxemia and hypercapnia is a potent mechanism for sympathetic activation and surges in blood pressure. Cardiovascular diseases linked to OSA include hypertension, heart failure and atrial fibrillation. Untreated OSA in these disease conditions may blunt the effectiveness of standard therapy.

This discussion will evaluate potential mechanisms activated during normal and disordered sleep, which may contribute to the relationship between sleep and cardiovascular death and disease.

EVE VAN CAUTER, PHD

OBESITY AND DIABETES

Sleep exerts important modulatory effects on most components of the endocrine system. The secretion of growth hormone (GH) and prolactin (PRL) is markedly increased during sleep, whereas the release of cortisol and thyrotropin (TSH) is inhibited. Conversely, awakenings interrupting sleep inhibit GH and PRL secretions and are associated with increased TSH and cortisol concentrations. The modulatory effects of sleep on endocrine release are not limited to the hormones of the hypothalamo-pituitary axes; these effects are also observed for the hormones controlling water and electrolyte balance, and glucose regulation. There are also important interactions between immune function and sleep.

Sleep curtailment is a hallmark of modern society. In the United States, "normal" sleep duration has decreased from approximately 9 hours in 1910 to an average of 7 hours in 2002. Today, many individuals are in bed 5 - 6 hours per night on a chronic basis. Although well-controlled animal studies have demonstrated that total sleep deprivation for extended periods of time leads to death, until a few years ago, the consensus was that sleep is for the brain, not for the rest of the body. It was thought that sleep loss results in increased sleepiness and decreased cognitive performance but has little or no effect on peripheral function.

In this presentation, we will discuss evidence indicating that sleep curtailment in young adults is associated with a constellation of metabolic and endocrine alterations, including decreased glucose tolerance, decreased insulin sensitivity, elevated sympatho-vagal balance, increased concentrations of evening cortisol, abnormal profiles of leptin and growth hormone secretion, reduced response to influenza vaccination and increases in markers of metabolic and cardiovascular risk. We will also review epidemiologic evidence associating short sleep with increased body mass index and diabetes risk. Finally, we will review studies that have examined markers of the metabolic syndrome in patients with sleep-disordered breathing. Altogether, the evidence points at a possible role of decreased sleep duration and quality in the current epidemic of obesity and diabetes.

References:

Meier-Ewert, H., Ridker, P.M., Rifai, N., Regan, M.M.., Price, N., Dinges, D.F., Mullington, J.M.: Effects of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. Journal of the American College of Cardiology (in press).

Mullington JM, Chan JL, Van Dongen HP, et al. Sleep loss reduces diurnal rhythm amplitude of leptin in healthy men. J Neuroendocrinol 2003;15(9):851-4.

Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry 2002;59(2):131-6.

Vioque J, Torres A, Quiles J. Time spent watching television, sleep duration and obesity in adults living in Valencia, Spain. Int J Obes Relat Metab Disord 2000;24(12):1683-8.

Shields M. Long working hours and health. Health Rep 1999;11(2):33-48(Eng); 37-55(Fre).

Ayas, N.T., et al., A prospective study of self-reported sleep duration and incident diabetes in women. Diabetes Care, 2003. 26(2): p. 380-4.

Vgontzas, A.N., et al., Sleep apnea and daytime sleepiness and fatigue: relation to visceral obesity, insulin resistance, and hypercytokinemia [see comments]. J Clin Endocrinol Metab, 2000. 85(3): p. 1151-8.

Ip, M.S., et al., Obstructive sleep apnea is independently associated with insulin resistance. Am J Respir Crit Care Med, 2002. 165(5): p. 670-6.

Punjabi, N.M., et al., Sleep-disordered breathing and insulin resistance in middle-aged and overweight men. Am J Respir Crit Care Med, 2002. 165(5): p. 677-82.

SESSION 2: NORMAL AND ABNORMAL SLEEP: WHAT PRICE DO WE PAY?

RUTH BENCA, MD, PHD

MOOD/QUALITY OF LIFE AND PSYCHIATRIC SEQUELAE

A. Sleep disturbances associated with decrements in quality of life and psychiatric sequelae include
    1. Insomnia
    2. Hypersomnia
    3. Primary sleep disorders
    4. Sleep deprivation

B. Insomnia associated with
    1. Poorer quality of life
    2. Increased rates of psychological distress
    3. Decreased ability to handle stress
    4. Increased rates of psychiatric disorders, particularly depression and anxiety

C. Insomnia precedes the onset of new or recurrent depressive episodes
    1. Insomnia or difficulty sleeping under stress increased risk for depression later in life
    2. Odds of developing depression increase during episodes of persistent insomnia
    3. Associated with increased risk of suicidality in depression
    4. Insomnia frequently precedes episodes of mania

D. Insomnia-depression links
    1. Insomnia precedes depression
    2. Acute depression worsens insomnia
    3. Both may result from similar neurobiological abnormalities?

E. Hypersomnia correlated with
    1. Increased risk of accidents
    2. Decreased productivity
    3. Increased rates of psychiatric illness

F. Primary sleep disorders and mood/QOL
    1. Narcolepsy, Restless Legs Syndrome
        a Reduced quality of life
        b Increased rates of depression, other psychiatric disorders
    2. Obstructive Sleep Apnea
        a Reduced quality of life
        b High rates of comorbidity with depression

G. Sleep deprivation
    1. Associated with mood impairment in normal subjects
    2. Has antidepressant effects in severely depressed subjects
    3. Can exacerbate or precipitate mania in bipolar patients

H. Translation: Research questions
    1. Does treatment of insomnia, sleep disorders decrease risk of psychiatric illness?
    2. Are insomnia and depression caused by similar mechanisms?

I. Translation: Clinical practice
    1. Given the high comorbidity between sleep and psychiatric disorders, patients with sleep problems or primary sleep disorders should be screened for depression, anxiety and other disorders.

References:

Benca, R. M., Obermeyer, W. H., Thisted, R. A., & Gillin, J. C. (1992). Sleep and psychiatric disorders: a meta-analysis. *Archives of General Psychiatry, 49*, 651-668.

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biological Psychiatry, 39*(6), 411-418.

Buysse, D. J., Reynolds, C. F., 3rd, Hauri, P. J., Roth, T., Stepanski, E. J., Thorpy, M. J., Bixler, E. O., Kales, A., Manfredi, R. L., Vgontzas, A. N., & et al. (1994). Diagnostic concordance for DSM-IV sleep disorders: a report from the APA/NIMH DSM-IV field trial. *Am J Psychiatry, 151*(9), 1351-1360.

Chang, P. P., Ford, D. E., Mead, L. A., Cooper-Patrick, L., & Klag, M. J. (1997). Insomnia in young men and subsequent depression. The Johns Hopkins Precursors Study. *Am J Epidemiol, 146*(2), 105-114.

Ford, D. E., & Kamerow, D. B. (1989). Epidemiologic study of sleep disturbance and psychiatric disorders: An opportunity for prevention? *Journal of the American Medical Association, 262*(11), 1479-1484.

Fredriksen, K., Rhodes, J., Reddy, R., & Way, N. (2004). Sleepless in Chicago: Tracking the effects of adolescent sleep loss during the middle school years. *Child Development, 75*(1), 84-95.

Katz, D. A., & McHorney, C. A. (1998). Clinical correlates of insomnia in patients with chronic illness. *Arch Intern Med, 158*(10), 1099-1107.

Mellinger, G. D., Balter, M. B., & Uhlenhuth, E. H. (1985). Insomnia and its treatment. Prevalence and correlates. *Archives of General Psychiatry, 42*(3), 225-232.

Ohayon, M. M., & Roth, T. (2003). Place of chronic insomnia in the course of depressive and anxiety disorders. *J Psychiatr Res, 37*(1), 9-15.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK
(INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

MARY A. CARSKADON, PHD

ADOLESCENTS/CHILDREN

Childhood and adolescence may be a time of significant risk because of the rapid changes in brain growth and development, cognitive/emotional development, maturation of the sleep/wake regulatory processes, and development of life-long behavior patterns. Much is known about sleep in children and adolescents; however, a great deal of information is also inferred from the larger set of investigations in adults.

What do we know?

The knowledge base is derived from studies that include observational, parental and self report, as well as experimental approaches using cross-sectional and longitudinal designs. Mechanistic studies are rare, and studies of clinical samples play an important role in terms of what is known.

Sleep need in children and adolescents comes in large measure from clinical "best guesses." Yet longitudinal parental report and laboratory evaluations that include measured outcomes have also been important in determining the range of "normal" sleep need in youngsters. Conclusions, such as those published by the National Sleep Foundation, are reasonably well accepted, particularly in the context of individual differences. Given this context, many youngsters appear to have reduced or insufficient sleep.

Reduced sleep is associated with a number of factors, and one of the most difficult issues is to determine the direction of the associations. For example, televisions in the bedroom and/or extended time spent watching television are associated with delayed and reduced sleep in young children as well as adolescents. This important association may point to a third factor, e.g., dysregulated family life, that is at the root of both television watching and sleep disruption. Nevertheless, the association is important because—even if the third factor is operative—it points to an opportunity for intervention. Other media, including computer game playing and Internet use, have also been associated with reduced sleep in children and adolescents.

Caffeine use and other substance use are associated with reduced and disrupted sleep, as well as daytime sleepiness in youngsters, particularly adolescents. Adolescents who are employed 20 hours a week or more also sleep less, go to bed later, and oversleep more on school days than those who do not. Early school start time is also associated with reduced sleep.

Looking at outcomes associated with reduced sleep, the evidence grows strong that many children with disturbed daytime behavior even including attention deficit disorder and attention deficit hyperactivity disorder (ADD/ADHD) may suffer from reduced or disordered sleep, particularly sleep disordered breathing disorders (e.g., obstructive sleep apnea) or restless legs syndrome (RLS). Experimental studies have also shown disrupted daytime behavior associated with reduced sleep.

Adolescence adds another layer of vulnerability as the pressure for a delay of the timing of sleep, stemming from psychological development (e.g., autonomy seeking) as well as changes in the sleep regulatory processes, clash with early starting times for school. The combination contributes to a large number of youngsters with reduced sleep.

Outcomes in which a directional association with reduced or disrupted sleep in children and adolescents has been shown with reasonable confidence include poor school performance, increased substance use, depressed mood, decreased self-esteem, poor mood regulation, excessive classroom sleepiness. Other outcomes are less well supported by definitive data or may be inferred from data collected in adults,

including learning problems, disrupted immune function, difficulty with weight regulation and obesity, initiation of substance use, disrupted family life.

What can be done?

Several possibilities exist for translating this knowledge into action. At the level of parents and families, public education can be marshaled to support a more reasoned approach to the sleep of youngsters. In addition, efforts need to be increased to assist schools in becoming part of the solution to insufficient sleep, particularly for middle school and high school students. Operational solutions need to be developed and distributed. The American Academy of Pediatrics has made some strides, and their efforts to education and mold the behavior of pediatricians should be supported and expanded. Finally, public education at a broader societal level can emphasize sleep as a positive priority, emphasize the importance of preparing children for optimal learning by enhancing optimal sleep, and creating educational curricula about the science of sleep for teachers to use in instructional settings.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK
(INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

PHYLLIS ZEE, MD, PHD

OLDER ADULTS

Sleep disturbance is one of the major health complaints in the elderly, with an estimated prevalence of over 50% in community dwelling older adults. Sleep disturbances are even more prevalent among older demented patients when compared to "cognitively normal" age-matched controls. Frequent sleep complaints in older adults include sleep maintenance insomnia, characterized by early morning awakening and frequent nocturnal awakenings and daytime sleepiness. Disordered sleep in aging is associated with excessive daytime sleepiness, impaired cognition, depressed mood, increased risk of injury (nighttime falls), overuse of hypnotic and over the counter sleep aids, and adverse interactions with medical, psychiatric and primary sleep disorders, any of which can decrease an individual's quality of life, or create social and economic burdens for caregivers.

Reduced sleep efficiency, long and frequent awakenings, increased amounts of light sleep, and decreased amount of slow wave sleep are probably the most consistent and prominent findings noted in this population. In addition to alteration in sleep architecture, there is evidence that aging is associated with alterations in the amplitude and phase of circadian rhythms, which may in part explain the early morning awakening and daytime napping that is common among older people.
Although there are clear age-related changes in sleep and circadian rhythm regulation, the etiology of sleep disturbances in the older population is often multi-factorial. In older adults, when sleep is poor, medical and mental illnesses, nocturia and primary sleep disorders, such as obstructive sleep apnea, periodic limb movements of sleep, or restless leg syndrome are the most likely contributors. In fact, sleep complaints are an excellent predictor of poor mental and physical health related quality of life.

Although there is substantial evidence that poor sleep quality has a negative impact on health, and that poor health itself is a common contributor to sleep disturbances in late life, the relationship between sleep and health is vastly under recognized by health professionals who care for the elderly. Not recognizing and appropriately treating sleep disorders in later life may result in deterioration in quality of life, the development of affective disorders, worsening of cognitive impairment and increased risk of morbidity and mortality. Therefore, improved knowledge and treatment strategies for sleep disorders in this population have significant clinical, social and economic value.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK (INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

KATHRYN LEE, RN, PhD, FAAN

WOMEN'S HEALTH

The purpose of this presentation is to review current knowledge related to sleep and sleep disturbances in women during key time points across their lifespan. These key time points include onset of menstruation, pregnancy and childbearing, and menopausal transition. Sleep changes associated with phases of the menstrual cycle, polycystic ovary syndrome, and shiftwork schedules will be discussed. Alterations in sleep during pregnancy and postpartum will be discussed in relation to risk for postpartum depression. Sleep during menopausal transition will be discussed in relation to hot flashes, night sweats, hormone replacement therapy, and ethnic differences. Finally, implications for clinical practice will be discussed.

References:

Moline ML, Broch L, Zak R, Gross V: Sleep in women across the life cycle from adulthood through menopause. Sleep Medicine Reviews. 2003;7:155-177.

Menstrual Cycle:

Baker FC, Driver HA, Rogers GG, et al: High nocturnal body temperatures and disturbed sleep in women with primary dysmenorrhea. Am J Physiol.1999;(Endocrinol Metab 40):E1013-E1021.

Gopal M, Duntley S, Uhles M, Attarian H: The role of obesity inthe increased prevalence of obstructive sleep apnea syndrome in patients with polycystic ovarian syndrome. Sleep Medicine. 2002:3;401-404.

Labyak SE, Turek FW, Nelson J, Zee PC. Effects of shiftwork on sleep and menstrual function in nurses. Health Care for Women International. 2002;23:703-714.

Lee KA: Self-reported sleep disturbances in employed women. Sleep. 1992;15:493-498.

Mauri M: Sleep and the reproductive cycle: A review. Health Care for Women International. 1990;11:409-421.

Parry BL, Mendelson WB, Duncan WC, et al: Longitudinal sleep EEG, temperature and activity measurements across the menstrual cycle in patients with premenstrual depression and in age-matched controls. Psychiatry Research. 1989;30:285-303.

Schindler AE: Differential effects of progestins. Maturitas. 2003;46(suppl1):S3-S5.

Vgontzas AN, Legro RS, Bixler EO, et al: Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. J Clin Endocrinol Metab. 2001:86;517-520.

Pregnancy and Postpartum:

Coble P, Reynolds CF, Kupfer DJ, et al: Childbearing in women with and without a history of affective disorder.II. Electroencephalographic sleep. Comprehensive Psychiatry.1994;35:215-24.

Corral M, Kuan A, Kostarus D: Bright light therapy's effect on postpartum depression. Am J Psychiatry, 2000;157;2-3 (Letters to the editor).

Gay C, Lee KA, Lee SY: Sleep patterns and fatigue in new mothers and fathers. Biological Research for Nursing. 2004; (in press).

Lee K, Zaffke M: Parity and sleep patterns during and after pregnancy. Obstet Gynecol 2000;95:14-18.

Lee, K, McEnany G, Zaffke ME: REM sleep and mood state in childbearing women: sleepy or weepy? Sleep. 2000;23:877-885.

Lee, K, Zaffke, M, & Barette-Beebe, K: Restless legs syndrome and sleep disturbance during pregnancy: the role of folate and iron. J Women's Health & Gender-Based Medicine. 2001;10:335-341.

Oren DA, Wisner KL, Spinelli M, et al: An open trial of morning light therapy for treatment of antepartum depression. Am J Psychiatry. 2002;159:666-669.
Parry BL, Curran ML, Stuenkel CA, et al: Can critically timed sleep deprivation be useful in pregnancy and postpartum depressions? J Affective Disorders. 2000;60:201-212.

Menopause:

Baker A, Simpson S, Dawson D: Sleep disruption and mood changes associated with menopause. J Psychosom Res. 1997;43:359-369.
Carskadon MA, Dement WC, Mitler MM, et al: Self-reports versus sleep laboratory findings in 122 drug-free subjects with complaints of chronic insomnia. Am J Psychiatry. 1976;133:1382-1388.
Erlik Y, Tataryn IV, Meldrum DR, et al: Association of waking episodes with menopausal flushes. JAMA. 1981;245:1741-1744.
Freedman RR: Physiology of hot flashes. Am J Hum Biol. 2001;13:453-464.
Freedman RR, Roehrs TA: Menopausal sleep disturbance. Sleep. 2003;26(suppl):A161.
Guttuso T, Kurlan R, McDermott MP, et al: Gabapentin's effects on hot flashes in postmenopausal women: a randomized controlled trial. Obstet Gynecol. 2003;101;337-345.
Lee K, Taylor DL: Is there a generic midlife woman? The health and symptom experience of midlife women. Menopause. 1996;3:154-164.
Lock M, Kaufert P: Menopause, local biologies, and cultures of aging. Am J Biol. 2001;13:494-504.
Montplaisir J, Lorrain J, Denesle R, Petit D: Sleep in menopause: differential effects of two forms of hormone replacement therapy. Menopause: J North Amer Menopause Society. 2001;8:10-16.
Newton KM, Buist DSM, Keenan NL, et al: Use of alternative therapies for menopause symptoms: results of a population-based survey. Obstet Gynecol. 2002;100:18-25.
Owens JF, Matthews KA: Sleep disturbance in healthy middle-aged women. Maturitas.1998;30:41-50.
Purdie DW, Empson JAC, Crichton C, et al: Hormone replacement therapy, sleep quality and psychological well-being. Br J Obstet Gynaecol. 1995;102:735-739.
Sharkey KM, Bearpark HM, Acebo C, et al: Effects of menopausal status on sleep in midlife women. Behav Sleep Med. 2003;1:69-80.
Shaver J, Giblin E, Lentz M, Lee, KA: Sleep patterns and stability in perimenopausal women. Sleep. 1988;11:556-561.
Shaver JLF, Giblin E, Paulsen V: Sleep quality subtypes in midlife women. Sleep. 1991;14:18-23.
Stearns V, Beebe KL, Iyengar M, et al: Paroxetine controlled release in the treatment of menopausal hot flashes; a randomized controlled trial. JAMA. 2003;289;2827-2834.
Woodward S, Freedman RR: The thermoregulatory effects of menopausal hot flashes on sleep. Sleep. 1994;17:497-501.
Young T, Rabago D, Zgierska A, et al: Objective and subjective sleep quality in premenopausal, perimenopausal, and postmenopausal women in the Wisconsin Sleep Cohort Study. Sleep. 2003;26:667-672.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK (INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

W. VAUGHN MCCALL, MD, MS

PSYCHIATRIC DISORDERS

Psychiatric disorders account for the largest single portion of persons with chronic insomnia. Correspondingly, physician/patient encounters that end with the prescription of a hypnotic medication are more likely to involve a psychiatric diagnosis than a sleep or medical diagnosis. The total number of persons with insomnia secondary to depression is approximately the same as the number of persons with obstructive sleep apnea. Insomnia is a diagnostic criterion for several important psychiatric disorders including depression, dysthymia, mania and generalized anxiety disorder. Indeed, insomnia is such a common concomitant of depression (>60-80% of cases) that physicians must resist the temptation to assume that all chronic insomnia is indicative of depression.

The medical literature on sleep and psychiatric disorders is overwhelmingly focused on depression and anxiety. The character of the insomnia complaint during a major depressive episode (MDE) is changeable, making the specific nature of the insomnia complaint an unreliable diagnostic indicator. Insomnia can precede, accompany, or follow a MDE. As a preceding symptom, insomnia carries great prognostic risk for a new MDE. During MDE, insomnia may signify greater risk of suicide, and may add to an already-poor quality of life in depressed persons.

The use of tricyclic antidepressants (TCAs) as mainstay treatment of MDE in the 1970's and 1980's was reliably associated with improvement in the insomnia complaint. The shift away from TCAs to selective serotonin reuptake inhibitors (SSRIs) in the 1990s has lead to the realization that, as a class, SSRIs do not have a reliable beneficial effect on insomnia, and instead may be associated with treatment-emergent insomnia in about 10% of cases. Further, SSRIs may disrupt polysomnographic (PSG) sleep even when the depressed patient reports clinical improvement in their insomnia complaint. As a result, insomnia is among the most common residua symptoms in otherwise successfully treated MDEs.

There is no clear guidance on whether insomnia should be symptomatically treated during MDE, or when the intervention should occur, or what the intervention should be. The PSG has revealed abnormalities in REM sleep in about 70% of cases of MDE, with shortening of REM latency as the most robust finding. A short REM latency may have predictive value in treatment choice of MDE, may partially correct with treatment of MDE, and may be a trait marker in first-degree unaffected relatives. Short REM latencies are sometimes seen in mania and schizophrenia, thus limiting the usefulness of PSG in discriminating among different psychiatric disorders.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK
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TIMOTHY ROEHRS, PHD

SUBSTANCE ABUSE, ALCOHOLISM AND SLEEP/WAKE STATE

Most central nervous system (CNS)-active drugs have profound effects on sleep and alertness. The possibility that the sleep-wake altering effects of CNS-active drugs might contribute to their use and abuse has received sporadic scientific attention. The effects of a drug or its discontinuation on the sleep-wake system may serve as the basis for the initiation or the maintenance of substance abuse.

Substance abuse is characterized by physiological and behavioral dependence. Physiological dependence is a state induced by repeated drug use that results in a withdrawal syndrome when the drug is discontinued or an antagonist is administered. Many CNS-active drugs produce physical dependence, although the syndrome intensity, relation to dose, and necessary duration of use for development of physiological dependence varies among drugs. In the sleep field REM disturbances and sleep maintenance disturbances are observed during the initial and the protracted drug abstinence period and are predictive of relapse. Physiological dependence may be a component of, but it is not a necessary nor sufficient condition, for behavioral dependence. Behavioral dependence is a pattern of behavior characterized by repetitive and compulsive drug seeking and consumption. Drug taking, whether in a therapeutic and socially accepted recreational form or in an excessive, socially unacceptable, and physically hazardous form, is a behavior that can be analyzed to determine those factors important to the initiation and maintenance of drug taking. A drug can be viewed as a reinforcer that promotes and maintains drug-seeking and drug self-administration behaviors as a function of the drug's consequences. Both disturbed sleep and disturbed alertness can have been shown to enhance the likelihood of drug self-administration.

The clinical challenge is to differentiate therapy seeking vs drug seeking behavior in making diagnoses and treating patients. Some of the potentially differentiating and defining characteristics of drug seeking versus therapy seeking will be discussed The defining characteristic of drug seeking is evidence that the drug is chosen more frequently than placebo. To the degree that the drug is chosen over other drugs or commodities is evidence for the extent of its risk for abuse. Supportive of its reinforcing capacity is evidence that the drug is readily discriminated from placebo by behavioral and subjective assessment. Then, to the degree that the dose is escalated over time, one has evidence of the development of tolerance and possible physical dependence.

On the other hand, therapy seeking is evident if the drug has demonstrated efficacy for the disorder or condition being treated. As well, the patient has the signs and symptoms and the appropriate diagnosis for the indicated use of the drug. The pattern of drug taking, its dose and duration of use, ought to be consistent with its therapeutic effects. Finally, the patient believes that the drug is effective and readily experiences its therapeutic effects. But, the drug seeking versus therapy seeking distinction becomes difficult in situations where therapy seeking shifts to drug seeking behavior. For example, one is concerned regarding the use of ethanol as a hypnotic by an insomniac. While pre-sleep ethanol use may initially be effective in improving the sleep of the insomnia, rapid tolerance development is likely, which then leads to dose escalation.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK
(INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

DAVID RYE, MD, PHD

NEUROLOGICAL DISORDERS

One-in-five individuals will develop one or more primary disorders affecting the central or peripheral nervous systems at some stage in life. In a substantial, additional number, the brain, peripheral nerves or muscle will be affected secondarily by a common medical illness. While advances have been made in the prevention, diagnosis, and pathophysiology of these disorders, many treatments remain symptomatic. Until only very recently, the "default" medium through which clinicians have viewed the behavioral consequences of nervous system dysfunction playing out, has been the waking state. Increasing attention, however, is being paid to how nervous system dysfunction or its treatment affects the broader wake/sleep continuum, and by extension, health and quality of life. This realization derives from four sources: 1) patients and their caregivers; 2) an increasing number of clinician scientists versed in sleep medicine; 3) advances in understanding of the brain substrates mediating normal and pathological sleep; and 4) the availability of pharmacologic and non-pharmacologic treatments.

An in depth presentation of the specific abnormalities of the sleep/wake continuum unique to each individual disorder of the central or peripheral nervous system is beyond the scope of this presentation. Most attention has been focused upon, and the most advances realized from, studies of the most common of neurologic disorders: 1) Alzheimer's disease (AD); 2) Parkinson's disease (PD); 3) epilepsy; 4) stroke; 5) traumatic brain injury (TBI); and 6) neuromuscular disorders (NMD). While each of these disorders has its own unique clinical phenotype, three broad categories of problems in the sleep/wake continuum have been recognized and include: 1) sleep loss including displacement of sleep (e.g., 'sundowning' in AD and insomnia in TBI); 2) primary disorders of sleep such as central and obstructive sleep apnea (PD, stroke and NMD); and 3) disorders of arousal (viz., sleepiness in PD, epilepsy, TBI and NMD). While the construct of sleepiness and what determines 'pathologic' sleepiness has been the subject of much debate, the sleepiness observed in many patients with neurologic dysfunction is common, undeniably real, verifiable, and as severe as that seen in the prototypical disorder of sudden sleep attacks, namely, narcolepsy. Moreover, it cannot be explained as a side-effect of medication, or simply a consequence of poor or short sleep during the prior night. Rather, in many instances sleepiness in neurologic illness appears to be an integral part of the disease process and a symptom that by adversely affecting quality of life is a deserving target of a complete treatment regimen. This being said, the most commonly encountered cause of sleepiness is likely that the accompanies diffuse brain dysfunction in metabolic encephalopathies. Although mental status in such conditions passes through fairly predictable stages terminating in coma, that operationally defined sleepiness, distinct from coma, is part of this continuum, is often overlooked and its pathophysiological basis poorly understood.

The discipline of Neurology, more than any other, has its foundations firmly seated in 'structure-function' correlations. It is from these origins that neurologists will continue to be at the forefront of advances in deciphering the contributions of specific brain regions to normal and pathological sleep. Increasing interest is also being directed at the inverse relationship; i.e., how insufficient or poor quality sleep and sleep apnea impact the course of neurologic illness. Intermittent hypoxia, for example, may play a causative role in stroke and neurodegenerative processes and effect clinical outcomes.
There remain challenges to further expansion of knowledge and realization of a translational component to sleep research in the field of neurology. This will not be a simple task, as "sleep" is essentially a symptom based complaint such that the discipline of sleep medicine transcends many traditional medical disciplines (e.g., psychiatry, pulmonology, neurology, medicine). The practical implication is that the discipline of sleep medicine is not readily identifiable, nor does it reach the administrative stature afforded to departments within US Medical Schools. A tremendous advance with broad implications would be any directive(s) that advance recognition of Sleep Programs, collectively, within Medical School campuses. The pace could also be quickened with more focused directives that together get neurologists to simply

think about disorders of the sleep/wake continuum in their patients. Exposure to the basic neurobiology of sleep and sleep medicine will need to be established and/or broadened, if not required, within the medical school curriculum, residency, and general neurophysiological training programs. This educational effort must occur hand-in-hand with increasing availability of subjective and objective tools for assessment of disordered sleep. This will necessitate the development of novel methodologies or measures that are more routine, practical, less labor intensive and expensive than those currently available. Finally, the development of new therapies and their introduction into the clinic will continue to require funding mechanisms that reward novel basic (e.g., development of animal models of disease; genetic epidemiology) and clinical (e.g., outcomes based) research that transcend disciplines and in many instances the artificial silos inherent in Medical School administrations.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK (INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

CONRAD IBER, MD

CHRONIC MEDICAL DISORDERS

Many medical disorders are associated with an increased risk of sleep complaints including insomnia, sleep fragmentation and daytime sleepiness. Pain and arthritis may be associated with sleep fragmentation, difficulty initiating sleep, and daytime sleepiness. Sleep abnormalities do not always reflect the intensity of a disease process. Sleep complaints in arthritis are associated with an increased utilization of physicians, use of over the counter medications, and physical treatments. The worsening of sleep symptoms and breathing impairment in chronic lung disease varies with the nature of the breathing disorder and severity of the lung impairment.

In some conditions, sleep complaints are due to an increased prevalence of primary sleep disorders. Patients with end-stage renal disease are more likely to have the restless legs syndrome while patients with congestive heart failure are more likely to sleep complaints related to sleep-disordered breathing.

Fatigue may have different descriptors and clinical signs as compared to daytime sleepiness. In fatigue syndromes, perception of poor sleep quality may not be associated with comparable objective changes in sleep duration or structure.

SESSION 3: NORMAL AND ABNORMAL SLEEP: POPULATIONS AT RISK
(INCLUDING UNDER-SERVED, UNDER-REPRESENTED POPULATIONS)

MARK R. ROSEKIND, PHD

OCCUPATIONAL GROUPS (SHIFTWORK, TRANSPORTATION, HEALTH CARE, MILITARY)

Occupational challenges to health, alertness, and safety have been traditionally focused on the disruptive effects of shift work and altered schedules. However, modern work demands have evolved to 24/7 global activities and involve both safety critical operations such as healthcare, public safety, and transportation as well as access to convenience activities like shopping and gas stations. This work evolution into an around-the-clock society includes a transition to occupational demands that extend far beyond historical views of shift and night work.

The industrial revolution created an opportunity for the development of shift schedules to provide personnel that would maximize manufacturing and other machine-based output. Technological advancements in communication and computer-based capabilities have now expanded the opportunity for 24/7 productivity far beyond traditional “shift work” settings. Modern work demands can include early start times, long days, night work, unpredictable schedules, on-call requirements, crossing time zones, many consecutive work days, insufficient recovery opportunities, changing daily work times and other factors that can disrupt sleep and circadian rhythms. This requires an expanded view and definition of how 24/7 work requirements create physiological challenges that affect health, alertness, and safety. The number of individuals affected by sleep and circadian disruption associated with modern occupational demands far exceeds the traditional view of “shift work.”

Health outcomes have been a traditional focus of shift work research, especially by sleep and circadian scientists, and working altered schedules has been associated with increased risk for stomach problems, cardiovascular disorders, and other negative health outcomes. However, in most occupational settings, it is the effect of shift work on safety and productivity that equally important. Fatigue-related risks engendered by sleep and circadian disruption created by work demands can include increased errors, incidents, and accidents. These risks can affect both the occupational environment itself, as well as the individuals at the core of providing safe and productive operations.

The physiological disruption associated with modern work demands can include acute sleep loss and cumulative sleep debt, extended periods of continuous wakefulness, operating at periods of circadian low, and circadian disturbances related to crossing time zones, changing work times or day/night transitions. These physiological factors create sleepiness and degrade performance that underlies the fatigue-related risks associated with occupational demands. Beyond these physiological factors, work demands also can affect family, quality of life, and income.

Addressing the physiological challenges posed by modern work schedules can be a complex and contentious endeavor. Even in one occupational setting there are many diverse operational demands, individual differences among personnel, and sleep and circadian physiology interact in a complicated though predictable manner. These issues are further exacerbated by historical and cultural factors in the occupational setting and by economics. Given these challenges, a single or simple solution to managing sleep and circadian disruption in occupational settings is not possible. Instead, using a comprehensive alertness management approach offers the best opportunity to address the diverse challenges outlined.

A comprehensive Alertness Management Program would include education and training, alertness strategies, scheduling, healthy sleep, and scientific and policy elements. Introducing these programmatic components into occupational settings raises many questions. For example, what should the core educational activities involve and are they required or voluntary, how are alertness strategies such as napping supported in the environment, what process is used to examine and potentially change schedules, are personnel informed of sleep disorders such as apnea and have access to diagnostic and treatment services, and are organizational activities scientifically based and supported by policy?

The health, safety, and alertness issues posed by modern work schedules will be presented and the opportunity to translate available scientific knowledge into practical approaches that address these concerns will be identified. The challenges to successfully improving health, alertness, and safety related to sleep and circadian rhythm factors in occupational settings will be outlined as a basis for discussion and the development of translational activities that will address these issues in work environments.

References:

Rosekind, M.R., Gander, P.H., Gregory, K.B., Smith, R.M., Miller, D.L., Oyung, R.L., Webbon, L.L., and Johnson, J.M. Managing Fatigue in Operational Settings 2: An Integrated Approach. *Journal of Behavioral Medicine,* 1996, 21:166-170.

Rosekind, M.R., Boyd, J.N., Gregory, K.B., Glotzbach, S.F., and Blank, R.C. Alertness Management in 24/7 Settings: Lessons from Aviation. In K. Green (Ed.), *Occupational Medicine: State of the Art Reviews*, Hanley and Belfus, Inc., 2002.

Howard, S.K., Rosekind, M.R., Katz, J.D., and Berry, A.J. Fatigue in Anesthesia: Implications and Strategies for Patient and Provider Safety*, Anesthesiology* 2002; 97:1281-94.

Rosekind M.R., Flower D.J.C., Gregory, K.B., and Jung W.E. General Occupational Implications of Round-the-Clock Operations. In Kushida C.A. (Ed.), *Sleep Deprivation.*
New York: Marcel Dekker, (in press).

HECTOR BALCAZAR, PHD

TRANSLATIONAL OPPORTUNITIES & LESSONS LEARNED: PUBLIC HEALTH

Improving public health and quality of life must be the ultimate goal of the consequences of adequately diagnosing, treating and managing sleep disorders (SD) in the US population. The conversion of current scientific knowledge regarding SD diagnosis and treatment into an improved awareness of what SD are, how they are diagnosed, treated and ultimately prevented, requires incorporating medical interventions in addition to population-based strategies of enhanced dissemination and utilization.

In this presentation several concepts and specific guidelines will be described relative to translation opportunities and lessons learned from the public health perspective. Using a systematic approach of public health for the elimination of health disparities research and practice the following topics will be addressed as part of this presentation. These are:

- **Identification** of the core functions of public health: assessment, assurance and policy development that can guide translation opportunities in the SD field
- **Identification** of slow and rapid impact approaches in public health which can be used to translate opportunities of current knowledge about SD, its prevalence, burden, and management into effective educational messages and strategies that work
- **Differentiation** of public health strategies that consider the identification of vulnerable and/or high risk populations using social marketing and targeting approaches
- **Translation** opportunities for the community based on empowerment outreach models of health promotion/ disease prevention that reach vulnerable, high risk and culturally diverse minority populations
- **Examples** of dissemination strategies that work for the patient, the consumer and the community using a case approach of the NHLBI Cardiovascular Disease North Texas EDUC (Enhanced Dissemination and Utilization Center) Lay Health Worker (Promotores de Salud) Model

Final Remarks

SD have not entered the realm of public health and, as such, limited information exists on how translation opportunities of research and clinical practice can make a difference in assessing the burden of SD and their profound health implications afflicting millions of Americans. Carrying a public health message into the SD research and clinical practice arenas requires definition of what public health can do to move forward translation opportunities that can work in people from different socioeconomic, social, cultural and racial/ethnic backgrounds.

Key Recommendations/Messages

1. Translation of SD from the medical model of clinical services to the population-based model using public health requires a multidimensional approach.
2. No “one size fits all” approach can be used to address the complexity of SD, from awareness to behavioral change. Tailoring messages and/or interventions (clinical, population–based) to meet the needs of diverse audiences (with different socioeconomic, social, cultural, racial/ethnic profiles) requires a cost-effective plan of action.

Referenced:

Health Education Quarterly, Vol 23 (Supplement) (December 1996). The entire supplement is recommended.

SESSION 4 - WHAT IS TRANSLATION AND WHAT IS ITS OBJECTIVE?

JUDITH SANGL, SCD

TRANSLATIONAL OPPORTUNITIES & LESSONS LEARNED: HEATH CARE

AHRQ's Change in Mission to Translating Research into Practice and Policy (TRIPP)

- Reasons for Change
- Differences in Methods

Evolution of TRIP Research at AHRQ

- TRIP initiatives
- Partnerships for Implementation initiatives

Lessons from TRIP Research

- TRIP Barriers and Resolutions
- Theoretical Models and Steps for Change
- TRIP Process Overview
- Translation Reflections
- Partnership Action Model

AHRQ Patient Safety & Working Conditions Research Relevant to Sleep/Fatigue Problems

- Sleep Policy Translation Example

TRIP Resources

PHILIP RENNER, MBA

TRANSLATIONAL OUTCOMES (HOW TO DEVELOP PERFORMANCE MODELS; HEDIS)

Over the last decade there has been growing interest among a variety of stakeholders in assessing the quality of medical care. Much of this interest has been stimulated by a series of reports sponsored by the Institute of Medicine that have documented major gaps in safety, effectiveness and other domains of quality[1] [2]. Other driving forces include a growing awareness of clinical practice variation and the increased recognition of the patient's role in decision making, continued pressure for cost containment; and concern among the public, providers and policymakers that efforts to control spending may result in decreases in quality of care[3] (Clancy and Lawrence, 2002). More recently large employers (often as coalitions), state and federal legislatures, and consumers (through special interest/patient advocacy groups) have begun putting pressure on the health care system to improve quality and become more transparent in reporting quality information[4].

The National Committee for Quality Assurance has developed a performance measurement system to provide quality information to various stakeholders. Using the Health Plan Employer Data and Information Set (HEDIS®), NCQA reports on the quality of health care delivered to over 80 million Americans. There is a rigorous development and testing process, where measures being considered for inclusion in the set are assessed against the criteria of importance, scientific soundness, and feasibility. As measures have been implemented, there has been an incentive for health care organizations to improve quality. However, there is more work to be done in new areas of quality measurement.

References:

[1] Kohn, Corrigan, and Donaldson. To Err is Human: Building a Safer Health System. National Academy
[2] Crossing the Quality Chasm: A New Health System for the 21st Century. Committee on the Quality of Health Care in America, National Academy Press 2001
[3] Clancy CM, Lawrence W. 2002. Is outcomes research on cancer ready for prime time? Medical Care 40 (6 Suppl): III-92 – III-100.
[4] Shaller D, Sofaer S, Findlay SD, Hibbard JH, Lansky D, Delbanco S. Consumers and quality-driven health care: a call to action. Health Aff 2003 Mar-Apr;22(2):95-101

RICHARD J. SCHUSTER, MD, MMM

A DISSEMINATION AND IMPLEMENTATION MODEL

Translation is needed

Translation is the process of effecting change in health care practice by implementing new research findings into the active care of patients. Translational research is the process of developing new mechanisms to perform successful translation. The Institute of Medicine (IOM) in its sentinel report, *Crossing the Quality Chasm*, reported in 2001 that it often takes 15 to 20 years for a successful research discovery to be put into practice.[1] For example, the BHAT study of the early 1980's demonstrated the value of beta blockers post acute MI. That practice became the standard of care in the 1990's, but only in the past few years have more than 75% of post-MI patients been treated with beta blockers. Why did it take 20 years? Why aren't the additional 25% of post MI patients treated?

Why have we failed in translating knowledge into practice? It is highly unlikely that practitioner knowledge is the rate limiting step. Physicians remain well educated and, are also well informed. In fact, physicians actually believe they are much more successful than they actually are. Oliveria studied this recently. [2] Physicians were quite aware of national hypertension guidelines (JNC) and believed they followed them regularly; they reported that 62% of their patients were treated to JNC goals. Likewise they believed that 50 – 60% of their patients had blood pressure that was controlled. When their clinical records were studied, it was discovered that actually only 25% of their hypertensives were controlled.

Why are we so unsuccessful in actually implementing national guidelines and achieving more success in providing modern appropriate care? Doctors blame their patients for inadequate compliance; patients blame their doctors for failing to keep them in control. The problem is really a systems failure. The organization and delivery of health care is antiquated. In spite of the modern equipment, highly educated workforce, and effective diagnostic and therapeutic options, the system itself is virtually frozen in a late 19th Century structure. Our clinical information systems are essential "Victorian." Providers are generally required to hand write on paper the essential clinical information in the care of a patient. There is typically no automated mechanism to recall that clinical data. Likewise physicians and other health care providers are expected to remember what to do instead of having helpful automatic reminder systems. Doctors don't work for hospitals, labs are separate enterprises, and doctors themselves don't work together as an organization. This organizational anarchy makes it exceptionally difficult to implement any systematic approach to implementing consistent new practices quickly and efficiently.

Physician Oriented Translation

Changing physician behavior can be seen as a critical mechanism for changing clinical outcomes and implementing new mechanisms of care. John Eisenberg, the founding Director of the Agency for Health Research and Quality, focused his career on these efforts. [3] Although it is commonly believed that simple **educational programs** (e.g. Grand Rounds) are an effective mechanism to educate physicians, the knowledge retention is modest and the behavior changes that result are minimal. The managed care industry has learned that **"administrative changes"** (know to physicians as "hassles") will change behavior quite effectively. [If you want to prevent a physician from ordering a PET scan, make her fill out a 3 page form describing the findings and indications – then make her wait for 5 days for permission.] **Participation** is an effective way to change outcomes. If a group of physician peers meet and decide how calf vein DVT should be managed and they will likely conclude that outpatient treatment with fractionated heparin is preferred to inpatient admission and treatment with standard heparin. They'll change their practices accordingly. **Financial incentives** can be highly effective. Again, the insurance industry has taught the health care profession this behavioral change very clearly. Withhold full payment

for services for physicians who order “too many” MRI’s and fewer MRI’s will be ordered. The most powerful mechanism to change physician behavior is simply to show them their **clinical outcomes**. When physicians are presented with outcomes from a trustworthy source (generally not insurance companies) and are pertinent to their practices, they will almost automatically change their practices. If given a different standard of expectation they will come close to achieving it. Likewise if systems changes – particularly automated ones - are put into place they will improve outcomes. An automatic reminder at the time of discharge for a post MI patient will increase the likelihood they will be discharged on a beta blocker.

Population Oriented Translation

Translation can likewise be effective when executed on a population based level. Some aspects of best practices in health care can be communicated directly from the research establishment to the population; they don’t require digestion, education, and implementation through a health care provider. Dramatic examples of this type of translational approach can be seen by the successes of the National High Blood Pressure Education Program and the National Cholesterol Education Program. Led by NHLBI, these efforts have increased awareness, changed attitude, and behavior in the public. In the 1960’s patients never presented to their physicians reporting they had discovered they were hypertensive and requesting treatment, aware that untreated hypertension could lead to stroke. Now, an educated consumer will commonly present to a physician with the knowledge and eagerness for intervention. Population based approaches to translation and dissemination are effective.

Key Points

- *Measure physician outcomes – Give them their results*
- *Take a population based approach to translation of research*

References

1. Oliveria, et. al., Physician-Related Barriers to the Effective Management of Uncontrolled Hypertension*,* *Arch Intern Med*. 2002 Feb 25; 162(4):413-20.
2. Institute of Medicine, *Crossing the Quality Chasm: A New Health System for the 21st Century*, National Academy Press, Washington, 2001.
3. Schneider EC, Eisenberg JM, “Strategies and Methods for Aligning Current and Best Medical Practices. The Role of Information Technology”, *West J Med*. 1998 May; 168(5):311-8.