
ARTISS SYMPOSIUM 2013

Psychiatry and Sleep Disorders

SPONSORED BY

Department of Psychiatry, Walter Reed National Military Medical Center

Department of Medicine, Walter Reed National Military Medical Center

National Intrepid Center of Excellence
Sleep Laboratory Department

Center for the Study of Traumatic Stress
Department of Psychiatry, Uniformed Services University



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From the Conference Series:

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Editor's Note: This transcript has been edited, however, as in most transcripts some errors may have been missed. The editors are responsible for any errors of content or editing that remain.

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First Edition



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History of the Artiss Symposium

Kenneth L. Artiss (1913–2001), the namesake of this symposium, was an Army officer, a research psychiatrist and instructor at Walter Reed Army Medical Center. Dr. Artiss, who served for 21 years in the Army Medical Corps retired in 1964 as a Lieutenant Colonel. He was Chief of the Department of Psychiatry in the Division of Neuropsychiatry at Walter Reed's Institute of Research. His work included development of treatment methods for combatants with severe psychiatric disorders.

After his retirement from the Army, Dr. Artiss was a senior consultant for many years to Walter Reed's psychiatric residency training program. Dr. Artiss created an award in 1983 to spur military psychiatry residents to conduct high quality research. This award still exists today and was presented at the conclusion of this symposium.

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For their support the committee wishes to thank:

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- Mr. Vernon Woods
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- The Command at WRNMMC for providing a climate where we are allowed the space and creative license to think about complex issues.
- Dr. Robert Ursano for his support and encouragement to document this important symposium.
- All the patients that continue to inspire and teach us.

The Legacy of Kenneth L. Artiss

Rear Admiral Alton L. Stocks

Since Walter Reed and Bethesda have merged, we say that we have taken the best of two great medical centers and we have moved forward. As we move forward, we do not want to lose our historical traditions because they are important. They are not only important to the individual services but we recognize we have brought together two wonderful psychiatric services.

The Artiss Symposium is something near and dear to us at Walter Reed National Military Medical Center. As many of you know, Dr. Artiss worked for 21 years at the Department of Psychiatry at the Walter Reed Army Medical Center. After his retirement, he continued to serve as a consultant at Walter Reed which is the dream job for many who have committed so much to the military. They do not want to say goodbye. It is wonderful to meet someone with Dr. Artiss' talent and commitment to continue to contribute long after retirement. What he meant to us and what we meant to him was certainly a spectacular part of his career.

In 1983, Dr. Artiss created an award to spur military psychiatry residents to conduct high quality research. Since that time the award has been given every year. At the conclusion of today's symposium we will, once again, present the award. If you think back to 1983, Dr. Artiss was ahead of his time. Involving residents in research early in their careers was not common. It is certainly something we do today and we think it is natural but in 1983 it was forward thinking. But Dr. Artiss was a forward thinker and because of his insight patients, particularly military patients, are better off today. It is a great pleasure for me to see this tradition continue.

Enjoy today's conference on psychiatry and sleep disorders. Thank you for everything you do each and every day to promote a better life for our patients and their families.

Preface

“Sleep no More” — William Shakespeare
Harold J. Wain, PhD

Interestingly, issues regarding sleep have been a theme in place for centuries. One of my colleagues has his residents read Shakespeare’s plays to teach the psychopathology of sleep. Shakespeare highlights the problems with sleep going back to Macbeth. He describes how Macbeth and Lady Macbeth conspire to kill King Duncan. “Sleep robs the guilty of rest and condemns them,” Shakespeare states. Shakespeare uses the image of sleep and sleep deprivation in the play to express feelings of guilt. Both Lady Macbeth and Macbeth experience fitful nights of nightmares and sleepwalking because of a deep-rooted sense of guilt and conflict.

“Sleep no more.” Macbeth expresses that he is having trouble sleeping. He says, “In the affliction of these terrible dreams that shake us rightly. Better be with the dead whom we, to gain our peace, have sent to peace, than on the torture of the mind to lie in restless ecstasy.” Macbeth states he would rather be dead like King Duncan, rather than continue the conflict he has with regard to his nightmares and dreams.

Lady Macbeth feels guilty for her crimes as well. She helped plan and later participated in King Duncan’s death. She babbles and washes her hands while sleepwalking. Both Lady Macbeth and Macbeth feel remorse for their actions. And Shakespeare punishes them by not allowing them to rest or sleep.

Many of our patients describe feelings similar to our Shakespearean characters with regard to their sleeplessness. There are many other reasons, in addition to nightmares or sleepwalking, that contribute to sleep and waking disorders. More than 100 different disorders of sleeping and wak-

There are many other reasons, in addition to nightmares or sleepwalking that contribute to sleep and waking disorders. More than 100 different disorders of sleeping and waking have been identified.

ing have been identified. They can be grouped together in four categories: 1) problems with falling and staying asleep; 2) problems with staying awake; 3) problems maintaining a regular sleep schedule; and 4) unusual behaviors during sleep.

We have three leaders from The Academy of Sleep Medicine with us today. Papers presented at their recent meeting reflect the variety of biopsychosocial parameters associated with sleep disorders. They range from basic science, to clinical science, to instrumentation. These papers address many of the issues we see in our clinical and wounded population. The thoughts and discussions about psychiatry and sleep disorders are timely and significant. The following pages are a summary of this important topic.

INTRODUCTION

Sleep and DSM-5

Brett J. Schneider, MD

Why is sleep so important? At last year's Artiss Symposium we talked about evaluation and treatment of genital injuries, combat stress, post traumatic stress disorder (PTSD), and the psychological impact of amputation. You might ask how well does sleep fit into a symposium that typically talks about that? We think of sleep as a symptom. Is sleep worthy of a daylong symposium? I would argue that we are at a crossroads right now in the specialty of psychiatry. We are at a crossroads because of the new DSM-5. That is part of what I am going to talk about today.

We are at a crossroads because there are new treatments for sleep issues. For example, I have mentioned the cognitive behavior therapy (CBT) for insomnia and things like alpha stimulation and other therapies. There is more consideration of the underlying sleep disorders with the proliferation of polysomnograph and sleep specialists. Most of the people talking today will be sleep specialists. All clinicians, especially behavioral health clinicians, are at a point where we need to reassess how we approach sleep issues in our patients. Psychiatry needs to re-assess the role of sleep disorders in our patient population.

There a study framing the idea that the DSM-5 Task Force had when they established the new criteria for some of the sleep disorders. The study highlights sleep as a comorbid disorder, rather than merely a symptom of a great many other disorders.

Sleep disorders are now called sleep-wake disorders. The DSM-5 underscores the need for independent clinical attention of those disorders, regardless of the mental or other medical problems that may be present. I found

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an electronic copy of the DSM-I and searched it. Sleep is only mentioned 3 times in the DSM-I. In the DSM-IV sleep was listed as a criterion of at least 19 conditions. And the DSM-5 takes another progression forward with how we manage sleep.

There is an overview of the changes in the DSM-5 on the American Psychiatric Association's (APA) website. One of the important changes is how we look at insomnia. Insomnia used to be classified as primary and secondary. It is now classified as insomnia disorder with specific criteria. There are 3 breathing-related disorders which more appropriately line up with the diagnoses that sleep specialists would use. Circadian rhythm sleep-wake disorders were expanded to include advanced sleep phase syndrome, irregular sleep-wake type and non-24 hour sleep-wake syndrome. Jet lag is now gone. Rapid eye movement and restless leg syndrome are specific disorders, rather than merely as a dyssomnia, not otherwise specified.

Another innovation in the DSM-5 is the extensive use of dimensional assessments. Historically, the DSM has been a categorical type of book, which means you go through and you pick one of these, and two of these, and that sort of thing. The dimensional assessment aspect will help clinicians assess the extent to which disorders are affecting patients. We know that everybody wants us to have quantifiable data for our patients that we follow over time. That is the direction the DSM-5 is taking with sleep disorders. Severity, duration, and impact of a disorder are the kinds of measurements or assessments that fall under dimensional categories.

To facilitate measurement-based care DSM-5 would look at things like mood, anxiety, and cognition as related to sleep problems. And the idea that sleep disorders are a risk factor for the development of common mental disorders and, therefore, may be a risk factor for a prodromal expression is part of the DSM-5. Most clinicians educate their patients diagnosed with mania about not sleeping. We tell these patients that this is the first sign that you need to contact me. Do not wait. Do not wait more than a day or two. Perhaps this is something we need to be thinking about with the rest of our patients as well. When your sleep deteriorates talk to us earlier rather than later because that could be the harbinger of a comorbid disorder.

Here is an example of the old concept. You have a depressive disorder, SIGECAPS, the first S, typically sleep, is just a symptom. Now, with the DSM-5 we say you have a depressive disorder plus an insomnia disorder. They are comorbid. They are bidirectional. They are interactive. One is not merely a symptom of the other. It is a new paradigm for thinking.

Sleep disturbances affect 50 to 80% of all patients with mental disorders and it is currently a symptom of 19 axis one disorders. That may be different in the DSM-5. I have not tallied that yet.

It is a disorder in and of itself so keep track of that.

“The New DSM-5 Sleep-Wake Disorders,” is the name of the chapter in the volume. It lists ten conditions. Primary insomnia has been changed to insomnia disorder. The switch is intended to avoid the primary/secondary designation. There are some categorical requirements. The diagnosis of insomnia disorder requires an occurrence of at least 3 nights a week for a duration of at least 3 months,

We also have disorders of arousal, as Dr. Wain mentioned earlier. These are recurrent episodes of incomplete awakening from sleep usually occurring during your first third of the major sleep episode. The DSM-5 talks about different types of arousal disorders. There were similar ones in the DSM-IV.

The circadian rhythm sleep disorders are characterized by persistent and recurrent patterns of sleep disruption leading to excessive sleepiness, insomnia, or both primarily due to an alternation of the circadian system or to a misalignment between the endogenous circadian rhythm and the sleep-wake schedule. There are different subtypes now.

Obstructive sleep apnea hypopnea was previously known to us as breathing-related sleep disorder. Most people will call this snoring. If you are not asking your patients about snoring, you should be. Primary essential sleep apnea, previously known as breathing-related sleep disorder, also has specific criteria. There is primary alveolar hypoventilation, previously the breathing-related sleep disorder and this diagnosis requires a polysomnograph.

We now have rapid eye movement behavioral disorder and restless leg syndrome. There is the Kleine-Levin Syndrome that is also called the Sleeping Beauty Syndrome, although it occurs more often in males. This syndrome is defined by successive recurrent episodes of sleep, more than 11 hours a day, that go on for long periods of time.

In summary, the DSM-5 changed diagnoses. We have sleep medicine. We have 2 new techniques, a new paradigm that equals a need to spend time considering the role of sleep and the significant sleep issues in our patients. These facts help to answer the question, “Why are we devoting the Artiss Symposium this year to psychiatry and sleep?”

Overlap Between Sleep and Psychiatric Disorders: Bidirectional Relationship

Samuel A. Fleishman, MD

I am a psychiatrist and the recent past president of the Academy of Sleep Medicine. There are only 5 to 10 psychiatrists who are sleep medicine specialists. Psychiatry gave birth to sleep medicine and most of the research that was done on human beings was done at NIMH. We looked at psychiatric patients and the sleep that occurred in these patients. Polysomnography was born. I challenge all psychiatry residents to take sleep medicine seriously because almost 100% of our patients have sleep disorders. It is important that we invigorate sleep medicine. Sleep medicine needs our voice and needs our perspective.

I am going to talk about sleep disorders associated with psychiatric illness. I have 4 major objectives: 1) understand how insomnia is a risk factor for psychiatric illness; 2) understand the impact of insomnia over the course of a psychiatric illness; 3) discuss how sleep disorders and sleep disturbances are associated with post-traumatic stress disorder (PTSD); 4) discuss treatment options related to PTSD.

What is the most common type of chronic insomnia? How many of you think it is insomnia comorbid with a psychiatric illness? How many of you all think it is insomnia comorbid with a medical illness? How many of you think it is primary insomnia? Most people think the answer is primary insomnia. The correct answer is insomnia comorbid with a psychiatric illness.

You heard earlier from Dr. Schneider and Dr. Wain about the breakdown of the various different sleep disorders. Some people categorize sleep disorders as insomnias, hypersomnias, parasomnias, and circadian rhythm disorders. There are also sleep-related breathing disorders. When we look at the

What is the most common type of chronic insomnia?... Most people think the answer is primary insomnia. The correct answer is insomnia comorbid with a psychiatric illness.

prevalent studies on insomnia up to 30% to 50% of insomnia may be occurring at any one time across the year. Chronic insomnia can affect up to 15% to 30% of the population. And certainly chronic insomnia may be 10 to 15 percent. When you break down the 10% of chronic insomnia patients, about half that group will have some sort of psychiatric disorder.

There is a great deal more insomnia with medical illness than we appreciate. This is an underappreciated population. Data supports the most common insomnia is insomnia comorbid with a psychiatric disorder. Dr. Schneider talked about the fact that we do not want to talk about insomnia due to a psychiatric disorder or due to a medical problem. This paradigm shift has occurred in the last four to five years in sleep medicine. We want to focus on these entities as two separate entities because they interact with each other.

The definitions of insomnia in the DSM-5 and in the ICSD are very similar. The ICSD is our sleep medicine DSM-5. The most common diagnosis is insomnia comorbid with a psychiatric disorder. The most common diagnosis of comorbidities is major depressive disorder. Data supports insomnia due to other disorders but the biggest percentage is major depressive disorder.

The definition of insomnia in the DSM-5 has several criteria. One part of the definition is difficulty falling asleep or difficulty staying asleep, or early morning awakening, or poor quality of sleep. Any of these could meet part of the initial criteria for insomnia but they must always have next day consequences. Someone who sleeps poorly at night without next day sequelae like headaches, fatigue, tiredness, irritability, inattention, or concentration issues does not have the diagnosis of insomnia. In these instances, we would not necessarily initiate treatment. The absence of next day sequelae is very important. Tom Roth, who is one of the gurus of insomnia, recently talked about the fact that a great number of elderly people have difficulty sleeping at night without next day sequelae. They do not have a diagnosis of insomnia.

In the DSM-5, as Dr. Schneider mentioned earlier, the criteria have changed. Insomnia has to have a duration of at least 3 months instead of 1 month. The insomnia also has to occur at least 3 days out of every week. Poor quality of sleep is no longer part of the diagnosis. People who have poor quality of sleep and do not feel refreshed will not be part of the new insomnia diagnosis.

How does this correlate with psychiatric illness? What is the prevalence of comorbid insomnia with psychiatric disorders? A study done by the National Epidemiological Catchment Area Study looked at 10,000 people who had insomnia versus not having insomnia. The group with insomnia had a higher percentage of psychiatric illness. The 2 largest diagnoses were major depressive disorders and anxiety disorders, compared to the individu-

als who had no sleep complaint. The people with no sleep complaint were much less likely to suffer from a psychiatric illness. The other side of that is insomnia patients clearly have a much higher likelihood of suffering from psychiatric illness, primarily mood disorders, anxiety disorders or substance use disorders.

What is insomnia? And does insomnia suggest that people will develop a psychiatric illness? Is insomnia a harbinger for other illnesses? A study by Breslau et al looked at patients that had a prior history of insomnia to determine the likelihood of developing a mood or a psychiatric disorder. In a follow up 3.5 years later, the group that had insomnia was much more likely to develop a psychiatric illness. Major depressive disorders and anxiety disorders were the most common. There is some signal that says chronic insomnia may be a sign of more things to come.

What happens if the insomnia resolves? If someone has insomnia and it resolves, does that mean that the risk for major depression or a psychiatric illness goes away? Data adapted from Ford and Kamerow that showed that if your insomnia did not resolve you were 3 times more likely to develop a major depressive disorder and 15 times more likely to develop an anxiety disorder than those whose insomnia resolved. Clearly there is a signal that correlates well with unresolved chronic insomnia and developing a significant psychiatric illness.

What is the timing of a major depressive disorder and chronic insomnia? Does insomnia also predict the onset of a major depressive episode? A study looked at patients with first episodes of major depression and remitters or people who relapse. Most of these patients developed significant insomnia problems before the onset of the first episode as did the relapsers. If your patients with depression begin complaining about sleep issues maybe that is a sign that depression is coming. It begs the question; do we treat the insomnia more aggressively to abate the episode? If so, how do we go about that? There is an interrelationship between insomnia and an interaction with depression, other psychiatric illnesses, as well as other medical problems.

A recent paper from the *Journal of Clinical Sleep Medicine* looked at patients with obstructive sleep apnea to determine the likelihood of developing depression. In a follow-up study one year later, the patients with sleep apnea were twice as likely to develop a depressive episode versus patients that did not have sleep apnea. Perhaps this finding makes you think about the patients in your offices that are large and snore? Could snoring be exacerbating their illness? This kind of data overlaps sleep disruption and sleep disturbances with psychiatric illness.

What happens to sleep in patients with depression? This is one of the most well researched areas in sleep medicine. We know that patients with depression have difficulty falling asleep and staying asleep. They have early

morning awakening and daytime fatigue. What does a sleep study show in these patients? These patients typically take longer to fall asleep. They have many of arousals across the night and they have a reduction of slow wave or deep sleep and daytime fatigue. These patients also have reduced rapid eye movement (REM) sleep latency with a prolonged first REM period. REM sleep occurs earlier in the night and in the middle of the night, as opposed to early morning. We also see a change in the rotation of sleep stages which is fairly sensitive and specific to depression. We do a better job diagnosing depression by taking a clinical history but if you see rotations of sleep stages on a polysomnogram, it is sensitive and specific, especially for severe depression. If I see a change in the rotation of sleep stages on a polysomnogram, I ask if the patient has a depressive disorder. Ask the questions and confirm a diagnosis.

What you do see if you look at a hypnogram? What you see is that patients fall asleep. They fall into stages two, and then three, and four sleep and then they have their first REM period. The first full rotation is about 90 to 120 minutes. Later on, the deep sleep occurs less and less. As patients go across the night, the REM periods get longer in this 120 minute rotation of sleep stages. Patients have more REM sleep in the latter part of the early morning and more deep sleep in the first part of the night in these rotations.

When patients are depressed there is phase advance of REM sleep. REM sleep occurs earlier and the first REM period is much longer. And you see more REM sleep in the first half of the night than you would typically see in a normal patient. There is a phase advance of REM sleep and a reduction in deep sleep. There are many more fragmentations and more wakening across the night. This finding is typical of what we see in depression. The REM advance is so dramatic that we used to think that was one of the major ways that the antidepressants worked since they suppress REM sleep. There were sleep deprivation studies that showed if you kept people awake that were depressed, it had an antidepressant effect. Unfortunately, when we allowed these patients to sleep the depression came back. Today there are newer antidepressants that are effective that do not depress REM sleep.

Insomnia is an independent contributor towards poor quality of life in depressed patients. There are a number of studies that show insomnia is also predictive of suicide. Apart from depression, why would insomnia be related to suicide? Maybe it is embedded in the activation syndrome that can occur and certainly it may be related to the reduction in serotonin. We are all familiar with the fact that low cerebral spinal fluid (CSF) serotonin levels are linked to completers of suicide. Maybe it is linked to the hopelessness-related issue feature common to insomnia and suicidal ideation.

Question number two: The most common residual symptom in an otherwise successfully SSRI-treated case of depression is? A) sad mood; B) in-

somnia; or C) poor appetite. What else could it be but insomnia? We all know that serotonin medications can be sleep disruptive even though they can be very effective antidepressants. The most common residual symptom after successful treatment of major depressive episode (MDE) with SSRIs is insomnia. Fatigue is number two.

Question number three: Complications of residual insomnia after treatment of depression include A) metabolic syndrome; B) low cortisol; C) increased rate of depressive relapse. Increased rate of depressive relapse is the correct answer. It is the most common residual symptom after otherwise successful treatment of major depressive episodes. It can be predictive of relapse and it may be a residual symptom. It may be induced by an antidepressant, and/or it could be a conditioned response. The evaluation of persistent insomnia in a psychiatric disorder could be an incomplete response. Perhaps people need more antidepressant or perhaps they need sleep medication. Persistent insomnia may be secondary to a medical disorder. It could be secondary to a primary sleep disorder. Maybe they have sleep apnea or another sleep disorder like restless leg syndrome. They may have poor sleep habits or conditioned insomnia.

Treatment options for insomnia after a major depressive disorder are cognitive behavioral therapy for insomnia (CBTI) and pharmacotherapy. I am going to talk about pharmacotherapy since you will hear about CBTI from Dr. Wickwire. I will talk about the hypnotics that people have used for sleep and then try to give you some parting pearls from my 17 years of experience.

What are the pharmacologic therapies we can use to help to treat our patients with chronic insomnia or insomnia comorbid with psychiatric illness? Melatonin is an over-the-counter remedy that many patients take at bedtime. Patients think it is going to give them a hypnotic effect and some patients will swear by it. The data is very questionable about the hypnotic effect of melatonin. Melatonin is not a good hypnotic agent. Melatonin is better at affecting circadian rhythm patterns. It can help people that go to bed late and get up too late or have what is light sleep phase syndrome. It can help jet lag. Some people can have vivid dreams while taking melatonin. There are some concerns about vasoconstriction of coronary arteries. I do not prescribe melatonin on a regular basis unless a patient has circadian rhythm issues. Melatonin is not regulated by the Food and Drug Administration (FDA).

What about over the counter antihistamines? Most of your patients have tried antihistamines by the time you see them. No prescription is required for antihistamines and they are inexpensive. There is no long-term data to show that they are very helpful for chronic insomnia. They have the potential for residual effects because of their long half-life and there is a probable tolerance with repeated nightly use. In high doses they have anticholinergic

effects and in the elderly and in children we sometimes see paradoxical effects.

The next group of drugs is the prescribing medications. Amitriptyline, doxepin, and trazodone are the medications that have been classically used. Trazodone got its birth as a sleep agent. Trazodone is also approved as an antidepressant but to use it as an antidepressant has to be prescribed between 400 to 600 milligrams. Most of your patients could not stay awake at that dosage. When Prozac came on the market it was very activating and it was taken in the morning. The buzz was about serotonin and how we were going to augment the serotonin effects of Prozac with trazodone because it was serotonergic, too, and it was sedating. Trazodone accelerated and augmented the antidepressant effect of Prozac. That is how trazodone got its birth as an hypnotic agent. It can also be effective for sleep maintenance. Sometimes people have hangover effects the next day but it is certainly used a great deal. All these type of medicines have their side effects. With trazodone, the side effect I have seen most often is orthostasis the next morning. People talk a great deal about priapism and trazadone. Priapism is a dose-related response and easily adjusted if necessary.

What sedating antidepressants are commonly used? Amitriptyline or Elavil is used a great deal. The problem with amitriptyline and doxepin is that they have anticholinergic effects with dry mouth, constipation, and urinary retention. They also have quinidine-like effects so they can actually effect cardiac conduction. Doxepin now has an FDA indication as a sedative-hypnotic in a product called Silenor. In some patients doxepin can increase slow wave sleep. Doxepin is fairly sedating and it can be effective for some patients.

The drugs that have been used the most and get the most attention are the benzodiazepine receptor agonists (BzRAs). The benzodiazepines are much better than the barbiturates we had before. I am sure all of us have used klonopin or clonazepam, or lorazepam along with triazolam and temazepam. They are effective hypnotic agents.

The problem with benzodiazepines is that they have four major effects. They have anticonvulsant effects, anxiolytic effects, myorelaxant effects, and hypnotic effects. That is wonderful if you want all four of those effects but we usually only want a sleep effect unless you have a patient that is anxious and you want to get an anxiolytic effect. The problem with the myorelaxant effect is you can exacerbate snoring and sleep apnea in overweight patients. The other issue with all these medications is they are schedule four drugs, which means they are potentially habit-forming.

Many people are now using the non-benzodiazepine classification of medications such as ambien or zolpidem, zaleplon and zopiclone. These are fairly rapid-acting drugs with a short half-life. It is extremely important that

you talk to your patients on a regular basis about how they are using their medication. Patients change their behavior over time so it is very important that you ask them what time they take their medication relative to what time they go to bed. Patients may be taking their sleep medications at times that are not safe creating all sorts of side effects where patients do things they do not remember. They eat in the middle of the night. You even hear about sleep-related driving and other unusual behaviors. Some patients think they should take their sleep medication prior to driving to the sleep lab. This is very scary behavior. These medicines work quickly and patients do not realize what is happening to them until after it happens.

It is important that psychiatrists and primary care physicians take better sleep histories. When medicines do not work as expected it may be due to the patients' behaviors. I think you need to go back to basics. When caring for psychiatric inpatients we do not think to ask them how you slept last night. It is either good, bad, or it is better. We do not get quantifiable numbers about what time patients are going to bed and what time patients are getting up. When adjustments are needed it is often more about shifting patients' behaviors as opposed to shifting the medications.

It is extremely important to make sure patients take their sleeping medications and get in bed. Emergency department visits involving adverse reactions to zolpidem rose nearly 220% from 2005 to 2010. Most of this increase was seen in the elderly and in women. Women tend to metabolize these drugs a little bit slower and differently than men. The FDA has scaled back the recommended dosages for women. For zolpidem products, data shows the risk for next morning impairment is highest for patients taking the extended-release forms of these drugs (Ambien CR and generics). I am not a big fan of time release or controlled release hypnotic agents. These medications work on the omega-1 side of the GABA receptor which is specific for the hypnotic effect. If patients use them at the prescribed doses they have that unique effect and benefit. Zolpidem products are not habit-forming from a withdrawal syndrome although I have seen psychological dependence. Rozerem is another drug that is FDA approved for initial insomnia. It binds the melatonin 1 and 2 receptor with high affinity. It is not used a great deal because it has not shown to be very effective. It may shift circadian rhythms. Rozerem is non-scheduled and non narcotic.

There is another large group of medications that are used for sleep. The only group I would like to speak to very quickly are the atypical antipsychotics. I do not know why anyone would prescribe these drugs unless the patient has a psychiatric illness like major depression, recurrent major depression, or bipolar depression with a severe insomnia.

I want to spend a little time on post-traumatic stress disorder (PTSD). For sleep doctors, PTSD is the smorgasbord of sleep of a patient. Everything

we could ever think about treating in a patient for a sleep disorder is in post-traumatic stress disorder. Almost patients with PTSD have insomnia and almost all of them have obstructive sleep apnea. Almost all of them have nightmares, sleep terrors, nocturnal panic attacks, and complex motor behaviors. They do not necessarily have what is called REM behavior disorder but patients with PTSD certainly have a lot of REM like behaviors.

Patients with PTSD have a 24-hour syndrome, and it certainly is an overrun of the adrenergic and catecholaminergic systems. Patients with insomnia and chronic insomnia fall into the same category. They are a catecholamine activated group, too, but not as much as PTSD. Patients with PTSD not only have insomnia, they have avoidance of sleep at night. They want to avoid sleep because they do not want to re-experience the trauma that has occurred. Patients with PTSD have a double whammy.

What do we know about sleep and PTSD and how does it impact PTSD? We know that if people have sleep issues within one month of a trauma, they are more likely to develop PTSD. Sleep disturbances caused by PTSD clearly contribute to poor physical and mental health outcomes. Often sleep disturbances are resistant to traditional PTSD treatment. We know that sleep focused treatments will reduce daytime symptom severity and improve daytime functioning in PTSD.

What are the possible treatments? A study done by researchers from Walter Reed looked at active duty soldiers and their sleep issues prior to exposure to combat. The study showed that people who had sleep issues before they went into theater were more likely to develop PTSD than those who had normal sleep. We see a revolving circle between sleep and other psychiatric illness.

What are the best practice guidelines for post-traumatic stress disorder? We typically treat PTSD symptomatically. At least that has been my experience. We tend to treat whatever is the biggest symptom and to use pharmacology appropriate for the symptoms. There are some good drugs for nightmare disorder that have come out in the last year that block adrenergic output. There is good data that shows prazosin can be very helpful in reducing nightmares in patients with post-traumatic stress disorder.

The other therapies for treatment of PTSD associated nightmares are behavioral strategies. In rehearsal therapy, patients who have been traumatized rehearse their dream during the day and change the content and then they rehearse the change in content. When patients do this on a regular basis they can actually change their dreams over time. There are other strategies and other papers that look at behavioral strategies.

I would be remiss without talking about sleep apnea and PTSD. A paper by Dr. Collen, Dr. Lettieri, and Dr. Hoffman at Walter Reed looked at the adherence rate of continuous positive airway pressure (CPAP) in patients

who had PTSD. The study included 90 patients who were age and match controlled for apnea hypopnea indices (AHIs). The patients with PTSD had many more insomnia issues and they were using many more medications. The AHIs were relatively matched. Patients with PTSD regularly used CPAP 25% of the time while the control group used CPAP 58% of the time.

In summary, sleep disorders and psychiatric disorders commonly coexist. Sleep disorders and psychiatric disorders appear to exacerbate and perpetuate each other. Optimal outcomes require treatment of both disorders.

Healthy Nights and Better Days: Cognitive-Behavioral Treatments for Insomnia

Emerson Wickwire, PhD

I would like to step back to ten thousand feet and provide a little bit of context. The fact that the Artiss Symposium is dedicated to the relationship between sleep and psychiatric disorders, the fact that you cannot read the paper, or a magazine, or even turn on the television and not see a sleep-related headline in any given week speaks to two facts that are abundantly clear. The first is we are facing an epidemic of disordered sleep with significant costs and consequences that warrants urgent attention. And secondly, we are in the middle of a data-driven, needs-based paradigm shift where the way we think about sleep and sleep disorders, and how best to recognize and manage these conditions is undergoing significant change. With an eye toward that future, I would like to delve into these topics in more detail. Specifically, we are going to talk about the cognitive behavioral treatment of chronic insomnia but we will touch on a number of other areas as well.

We are going to talk about three topics. The first is what is CBT (Cognitive Behavioral Treatment)? Why is this so important? And in some ways most importantly, how can you include CBT into your practice?

What is cognitive behavioral treatment for insomnia? We will examine three things. First, what is insomnia? Second, how does insomnia take on a life of its own? And third, what are some of the consequences of insomnia?

We typically think of insomnia simply as trouble falling asleep, trouble staying asleep, waking up too early, or previously in the DSM-IV, this somewhat amorphous symptom called non-restorative or poor quality sleep. As you have heard this morning, that has changed or will change shortly when the DSM-5 goes live. All of these complaints must be associated with a day-

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time consequence. It is a gross disservice to psychiatrists, psychologists, and anyone who works in the “mental health” domain that we do not receive more training on the impact that disturbed sleep can have on daytime function.

If you live to average life expectancy in the United States, you will spend 24.8 years of your life asleep. It is your job, not your patient’s job, to identify possible connections between sleep disturbance and next-day function. The majority of your patients will be unaware of this. Here is a simple example. Thirty eight percent of children identified and treated for attention deficit hyperactivity actually have occult sleep disorder breathing. The significance of sleep and next day function is huge. If you are not asking your patients about their sleep, you are doing your patients a disservice. Next day consequences can range from cognitive dysfunction to poor workplace performance, irritability, mood disturbance, fatigue, and sleepiness. Regardless of what your patient’s presenting complaint is, when you are thinking about possible causes, think about sleep.

As Dr. Fleishman mentioned, 10 to 15% of the general population reports symptoms consistent with chronic insomnia. In clinical practice, across medicine and psychiatry, but in the military in particular, we see statistics where these numbers are much higher. Insomnia, in general, is the second most common complaint. It is the second most common reason patients go to their primary care providers. It is second only to pain. Insomnia is a real problem and one that your patients are experiencing.

Insomnia is highly comorbid with medical conditions. The data for older adults, has been replicated repeatedly. All of the data that I will cite has been replicated or I will specifically point out that it has not been replicated. What the data shows is that the more medical problems you have, the more likely you are to have sleep complaints. The relationship between sleep and psychiatry is more established but the relationship between sleep and medical problems will become increasingly well-established. Not only do we see increased insomnia complaints concurrent with increased medical problems, but we also see increased medical problems in patients with insomnia.

Insomnia is a reliable predictor of major depressive onset and of major depressive relapse. Treating insomnia will reduce major depressive relapse. There are both pharmacologic and behavioral studies suggesting this. When patients have insomnia, we need to be on the lookout for major depression. For that reason alone, we should be sensitive and treat insomnia. Conversely, insomnia tends to emerge concurrently or can follow anxiety disorders. Insomnia comes before depression and insomnia emerges at the same time as anxiety.

I want to present a model of insomnia as a disease of physiological hyperarousal. We know that patients with insomnia demonstrate increased metabolic activity, increased core body temperature, increased catecholamine ac-

tivity, and increased high-frequency EEG. In good sleepers, high frequency EEG activity stays very low. This is what we want. We see this because they are asleep. In patients with insomnia high frequency EEG activity remains prominent throughout the night. Literally, the brains of patients with insomnia do not settle down as well during sleep as we would like.

The same thing happens when we look at HPA activity. In a study design between patients with primary insomnia and masked healthy controls we see elevations in adrenocorticotrophic hormone as well as cortisol in the patients with insomnia. This is a 24-hour condition.

There is a similar study design showing increased brain metabolism. What we see are regions of the brain that do not cool down as well in patients with primary insomnia. Data from the University of Pittsburgh shows there are regions of the brain that remain more active during sleep.

When we think about our warriors we are treating, the regions of the brain that remain active are those that assess alertness, sensory processing, novelty detection, emotional excitability, and disgust and pain. Imagine being in theater and scanning for danger at night, looking at pain reactions and having disgusted emotional responses. Hypervigilant states are the biological antecedents of chronic insomnia.

As a biobehaviorally-trained psychologist, I want to shift gears very slightly. On the one hand, I have talked about insomnia as a disease of physiologic hyper arousal. We are talking about organic components and physiological components of the disease. The history of western medicine is founded on the assumption that biology drives behavior. Physiologic hyper arousal creates biological problems. Therefore, patients are going to behave differently downstream. One of the areas of greatest scientific discovery and clinical merit in the past 20 to 50 years has been a much better understanding of the bi-directional relationship. Biology influences behavior and behavior also influences biology. It is a two-way street.

How does insomnia take on a life of its own? There is a model called the behavioral model of insomnia. It tells a pretty useful story that is going to apply for approximately eight to nine out of ten of the patients that you see in your practice who have sleep complaints. Where we begin is simply an arbitrary threshold for trouble sleeping versus no trouble sleeping. I tell my patients that we start with you. Each of us brings a unique predisposing risk for the development of chronic insomnia. Typically, this is associated with biological factors like genetic risk. How am I hardwired? What is my cellular composition, my personality, and my psychological factors? How do I manage stress? Am I a worrier? Do I internalize things? It is the combination of what I bring to the table biologically and psychologically that places me at a higher or lower risk, the same way that we all have a risk for developing cardiovascular disease or diabetes.

An external or environmental stressor can occur. This can be an acute stressor, a trauma for example, or an acute medical illness or hospitalization, or a period of acute financial distress, dissolution of a romantic relationship, or loss of a loved one. The beginning of insomnia does not have to have acute onset. Most of the time, patients cannot identify exactly what “caused” their insomnia. They will say, “Doc, I am not sure. It has just gotten worse over time.” Or they might say their sleep has been bad for years. The important thing is that the stress and subsequent insomnia is caused by the interaction of patients’ stuff with life.

What do patients do? They try to do things that in the short run make them feel better. They sleep in on Saturdays. They increase caffeine consumption. They use over the counter or even prescription sleep aids in a chronic fashion. They become over-focused on sleep, so the first thing when they wake up, they wonder is tonight going to be the night when I finally get that good night’s sleep this week. Or perhaps they have already decided how the rest of their day is going to be based on the way they slept the night before. Patients become less active because they do not have enough energy. They stay in bed and try harder to sleep. On the one hand, these behaviors make sense. If you do not feel well during the day, you are going to do something to protect yourself. The problem is, that even when that initial stressor dies down or goes away over time, compensatory behaviors become a bigger and bigger part of the problem and contribute to insomnia.

This is where the transition from acute to chronic sleep disturbance in the DSM-5 takes place and how insomnia takes on a life of its own. This is one of the most important things that cognitive behavioral interventions do for patients. CBT interventions eliminate the compensatory behaviors. When people use generic expressions like cognitive behavioral treatment or behavior modification, this is what they are talking about. I tell patients that they have had a great deal of practice at being lousy sleepers. They have become very good at it. What we need to do is retrain the body how to sleep. When you see patients in your practice more than 90% of them will resonate with this description.

Insomnia is associated with a number of negative health consequences. A very interesting study looking at insomnia and quality of life shows that in every single domain of quality of life patients with mild insomnia report lower quality of life than good sleepers. Patients with severe insomnia report worse quality of life than patients with mild insomnia. There is a striking linear relationship between trouble sleeping and overall quality of life. These studies have been replicated.

I would be remiss not to point out data from Johns Hopkins that looked at complaints of insomnia during medical school. It was a questionnaire-based complaint of all male medical students since the data was gathered in the

1950s — “Do you have trouble falling asleep or staying asleep?” The average follow-up was 38 years. If you were a medical student your risk for future development of major depression was 4 times higher than males in the general population. Interestingly, insomnia is the most common symptom of post-traumatic stress disorder reported during the first 30 days post-deployment and it predicts onset of future post-traumatic stress.

In 1983, the NIH released a consensus statement talking about insomnia as a symptom. That is the way that most folks in the room were trained. Insomnia is a symptom. Treat the depression or the primary disorder and the sleep will get better. In 2005, NIH revised its consensus statement, as Dr. Fleishman mentioned earlier, to say we have an independent co-occurring condition that warrants independent treatment.

I am very interested in the comorbidity of insomnia and sleep-related breathing disorders, which have become increasingly popular in the literature and of great importance in the military. Dr. Fleishman reported that 94% of patients with post-traumatic stress disorder have insomnia and 50 to 80% of patients with post-traumatic stress disorder also have obstructive sleep apnea. How can we manage these patients in a more thoughtful way? Often, we ask a patient who cannot fall asleep to use CPAP or we give a patient with insomnia an hypnotic that may be masking an underlying occult sleep-related breathing disorder.

A review that we published several years ago evaluated 42 patients referred for overnight polysomnography to evaluate obstructive sleep apnea. These patients are stereotypical. They are obese and have a high likelihood of obstructive sleep apnea. Send them to the sleep lab and let them take care of the problem; however, it is not one problem. There are several problems taking place. Even when we use very strict diagnostic criteria for insomnia that are far more restrictive than the research diagnostic criteria for insomnia, 40% of these patients still meet diagnostic criteria for chronic insomnia.

We know that insomnia plus obstructive sleep apnea (OSA) is worse than insomnia or OSA alone. These are patients like our warriors and like the patients that we see. These are not 55-year-old lean, anxious women who cannot relax at night. These are not 400-pound truckers who cannot stay awake during the day. Dr. Lettieri refers to this as diagnostic profiling and it does not work. We need to ask more sensitive questions and be thinking about the full range of sleep complaints that may be impacting our patients. The take-home message is that you should treat both insomnia and obstructive sleep apnea.

The most important thing I can tell you today is to ask your patients about their sleep. Do you have trouble falling asleep? Do you have trouble staying asleep? Do you snore? How do you feel during the day? How do you feel when you wake up? What caused your sleep problem? How long has it been

bothering you? And what have you done to try and solve the problem? You can screen for chronic insomnia using a validated questionnaire called the insomnia severity index. We use it in our practice to assess which patients should be co-managed by an MD and a PhD.

I want to talk about cognitive behavioral treatments (CBT). According to the clinical guideline of the American Academy of Sleep Medicine, CBT is a recommended first line treatment. I am also going to talk about combined therapies. CBT works in so-called primary, as well as in comorbid, or as previously known, secondary insomnias. What does CBT look like? There are multiple components of cognitive behavioral treatments. You have heard of “sleep hygiene”. The reason I put the phrase in quotes is because there is not a single published study that supports the use of sleep hygiene in the treatment of chronic insomnia. We have things like stimulus control, sleep restriction therapy, or restriction of time in bed, and relaxation. You have heard of these. I will return to at least one of them later, but we cannot cover all of them.

What happens when a patient comes to see me? If it is a relatively straightforward patient, the average number of treatment encounters that I have in a private practice setting is just over five. I tell patients that they should commit to 6 treatment visits. This does not look like what I would call traditional psychotherapy. I see patients every other week and my follow-up encounters are 20 to 25 minutes in duration. I have the luxury of pulling the sleep piece out and I work with a number of psychiatry colleagues who are delighted that, when the patient is sleeping better, the treatment for their primary mental health problem becomes much more effective. How many treatment visits are enough? An interesting study reported that 60% of patients who undergo biweekly treatment with a total of 4 treatment visits have the best outcomes.

Why is CBT so important? We know that CBT is effective. There are 6 meta-analyses of randomized controlled trials looking at cognitive behavioral treatments for insomnia. We know that CBT works in multiple patient populations, including patients with medical disorders, as well as patients with psychiatric disorders. Sleep efficiency is a common outcome measure in insomnia research. It is the ratio of total time slept to time in bed. If I am in bed 10 hours but only sleep 5, my sleep efficiency is 50 percent. We are looking at pulmonary disease, osteoarthritis, and coronary artery disease relative to a relaxation/stress management/wellness control group. In all three chronic medical conditions, CBT out-performs an active placebo. This is not a wait list placebo.

A meta-analysis, looking at primarily older benzodiazepine receptor agonists, shows that in the first 28 days, CBT and pharmacotherapy are relatively equally effective in terms of helping patients fall asleep faster, staying

asleep, improving sleep quality, and improving duration of sleep. Statistically, behavioral interventions help patients fall asleep faster. That is a bit of an artifact because one of our recommendations is do not get in bed until you are ready to fall asleep; however, the data clearly suggests that these treatments are relatively efficacious over the first 28 days.

Four head to head trials have compared behavioral interventions to pharmacotherapies for chronic insomnia. The first is published in the *Journal of the American Medical Association* in 1999. I do not need to remind you that this is the most sophisticated and competitive scientific medical journal in the world. What we see in terms of sleep efficiency on the graphs is that over 24 months, which is an astounding follow-up period for a randomized controlled trial, patients who underwent behavioral interventions demonstrated greater improvements in sleep efficiency that were maintained over time. They also spent less time awake in the middle of the night. This improvement was maintained over time. Their total sleep time increased more gradually, which is not surprising, because of pharmacokinetic effects of Restoril, but also because in the acute phase of insomnia treatments we may recommend that patients spend less time in bed. In the initial treatment phase pharmacotherapies will increase total sleep time more rapidly than behavioral interventions. Over a two year period, the total sleep time of patients who undergo behavioral interventions continues to increase. Remember, the goal is to retrain your body how to sleep. The more practice you get at sleeping well, the better you will sleep. Conversely, patients who took Restoril were almost at baseline two years later. A sleep impairment index looks at daytime impairment based on past night's sleep. You see greater reductions in impairment from behavioral interventions that are maintained over two years.

The next study published in *Archives of Internal Medicine* looked at Ambien in a similar study design. We see that patients who underwent behavioral intervention fell asleep faster. This is 12-month follow-up data. Again, total sleep time here favors medication. This is not one-year data. It is only eight-week data.

How do we assess sleep efficiency? We see greater improvements through behavioral interventions that are maintained at 12 months. A study, published in *JAMA* looked at zopiclone, which is the precursor of Lunesta. We see that patients who undergo behavioral intervention with six month follow-up data spend less time awake during the night. Total sleep time improves with behavioral intervention. Sleep efficiency is increased and maintained relative to pharmacotherapy. Polysomnography shows an increase in delta sleep or slow wave sleep, with behavioral intervention.

We know conclusively that pharmacologic agents and behavioral agents improve sleep. What happens when we combine these approaches? Three

of these four randomized controlled trials were published in the Journal of the American Medical Association. The take-home message is that there is a slight advantage for combined therapy in the acute treatment phase. In the first six weeks, the group receiving combined therapy does slightly better. But at 12 months, the group that has CBT alone has a 68% remission rate of insomnia. The group that started out with combined therapy has a 40% remission rate of chronic insomnia. No pill can teach your body how to sleep.

Many patients prefer behavioral interventions and given the option for a non-drug approach will opt for it. I am sure that industry has its own unpublished data, but the only two studies to look at this question both suggest that patients prefer non-drug treatments if they are available.

Since the release of Ambien, the use of non-benzodiazepine hypnotic agents has skyrocketed. The problem is they are disproportionately prescribed in patients who are obese and elderly. Patients who are elderly have an increased risk for falls using hypnotic agents. Patients who are obese have an increased risk for obstructive sleep apnea.

What does CBTI look like in a busy academic medical center or a busy military medical center? What does CBTI look like for a psychiatrist who may or may not have time, interest, or training in administering behavioral interventions? Too often we forget our job is to improve our patient's condition. That means we need to understand where our patients' starting points are in terms of their diseases, their attitudes, and their beliefs. What does the patient want and what are their goals? Our job is to move patients from point A to point B. Whether you use a behavioral intervention, a combined intervention, or a pharmacologic intervention, the point is not to give someone an antidepressant as an end. The point is to give someone an antidepressant as a means to an end so they have an improved quality of life.

The problem is what patients see. You may recall Ernest Shackleton, the legendary Antarctic explorer. "Men wanted for hazardous journey. Small wages. Bitter cold. Long months of complete darkness. Constant danger. Safe return doubtful. Honor and recognition in case of success." We are asking our patients to do something in a different way. We need to remember that we are walking our patients through a clearly defined sequential series of steps to change their sleep behaviors. Changing behavior is not a surgical procedure.

When I was a psychology fellow I wanted to watch brain surgery. I introduced myself to Dr. Alleva, the Chairman of Neurosurgery, and said I am a sleep guy and I want to watch a brain surgery. And he said, "Great." We washed up, scrubbed in, and cut through the skull and cut through the dura to remove a cancer. I am holding the skull of a patient and it is pretty cool stuff. All I could think about was, wow, this is the opposite end of the spectrum from what I do. Changing behavior is not a surgical procedure.

When we administer CBT, we attend all the biologic factors and we manipulate the biologic factors that influence sleep to improve sleep quality. We do not have time to discuss the physiology of sleep, but what CBT is doing is leveraging innate biological processes. Again we see the bidirectional relationship between biology and behavior. For example, by increasing a patient's natural drive to sleep, we can help them fall asleep faster, sleep more deeply, sleep through the night, and improve daytime functioning. This is especially effective with patients who are hyperaroused, which is present in the majority of patients who have difficulty with sleep. We are also going to target that arousal more directly when we discuss circadian rhythm disorders and circadian issues. These are also things that we attend to in the course of CBT.

I want to conclude about how to talk to your patients about changing behaviors. If you recall earlier, I said that patients have a lot of practice at being a poor sleepers. The solution is to retrain the body how to sleep. There is a very clearly defined problem and solution. There is no one in the audience who does not understand this simple concept. Too often what we do as healthcare providers is give our patients a list of 14 things. Go change these 14 things about your life. I know you have been operating this way for 20 years, but I want these 14 things to be different the next time I see you. People do not work that way. We can only deal with one issue at a time. I want to give you quick example of how I manage this issue with patients.

One of the most common interventions and one of the most effective interventions for you to include in your practice is what is called stimulus control therapy. I am not going to discuss the science. I am going to tell you how to implement the therapy using this formula. First, I frame the issue for the patient. Next, I provide guiding principles so the patient understands exactly what we are going to do. I always conclude with specific behavioral recommendations.

Through repetition of behaviors your body has learned that bed is a place to be awake. Patients tell you that they feel sleepy but when they get in bed all of a sudden they feel wide awake. This behavior occurs in more than half of your patients with insomnia. I tell my patients that through repetition your body has learned that bed is a place to be awake. The solution is to retrain your body to feel that bed is a place for sleep. Any questions? I have never had a single question because the concept is so simple and to the point. The intellectual function of your patient does not matter. Patients understand this explanation.

The next step is to give patients a few guiding principles. The first is, you need to do less of the bad stuff. You need to avoid time awake in bed. When you are texting, or reading, or watching TV, or listening to music, or talking on the phone, you are practicing insomnia. You have to stop these behaviors

when you are in bed. The second thing we need to do is re-pair the act of getting in bed with falling asleep quickly and staying asleep. So Mr. or Mrs. or Doctor Patient, does that make sense? Do you have any questions?

I am going to give you a few specific behavioral instructions that I want you to work on between now and next time I see you. This is how we are going to make this happen. First, I only want you to get in bed when you are highly confident that you are ready to fall asleep. Do not go to bed because your spouse goes to bed. Do not go to bed because it is 10:15 pm and that is your usual bedtime. Do not go to bed because you are bored or because you need to rest and reflect on the day. Only go to bed when you are highly confident that you are ready to fall asleep.

And the second thing is if you cannot fall asleep or if you wake up and cannot fall back asleep, I want you to get out of bed and refer back to rule number one. Only return to bed when you are highly confident that you are ready to fall asleep.

The team of psychology and psychiatry has to share a vision for our patients. We need to agree when to refer to a behavioral sleep specialist and we need to make it easier to refer, especially between psychology and psychiatry. I think we have so much to offer each other and our patients.

Sleep Issues in the Military Population

Christopher Lettieri, MD

Going back to the Civil War we have had problems with sleep in our military. It is part of our culture. We do more by 9:00 a.m. than most people do all day. Medicine is the same way. We start our day too early and we work too late. In the military we start our day too early and work all night. We are embracing and enhancing sleep deprivation. When you do not need sleep, it is a sign of toughness. In doctrine, in the United States Army, you get four hours, not of continuous sleep but in a 24-hour period. That is all being changed as a certain general for the Army's performance triad is emphasizing sleep and the importance of sleep. As you improve health, you decrease the need for healthcare. Sleep is the most important thing. Army doctrine is changing to say you need at least seven hours of sleep. You need seven hours of continuous sleep period.

Sleep Patterns in the Military

We are not sleeping enough. Compared to civilian cohorts, we are getting about 45 minutes less sleep per night. The average American is getting insufficient sleep and we, in the military, are even worse. In one study examining the sleep patterns of service members, two-thirds were not getting sufficient sleep meaning on average, they were getting 6.4 hours of sleep per night. The human body needs 7.5 to 8 hours of sleep per night. A similar study showed that almost half of service members are severely sleep-restricted meaning they got 5 hours of sleep or less per night. If you get 6 hours of sleep per night that is the same as missing 2 nights of sleep per week. If you are getting 5 hours of sleep per night, you might as well stay awake from Friday morning to Monday. You cannot catch up on the sleep debt.

We are not sleeping enough. Compared to civilian cohorts, we are getting about 45 minutes less sleep per night. The average American is getting insufficient sleep and we, in the military, are even worse.

When Does Sleep Debt Start?

Sleep debt starts when you come into the military. One study done by the U.S. TRADOC Command looked at sleep duration and basic trainee recruits. Sleep dropped from a baseline of 8.2 hours per night to 6.7 hours per night. From day one in the military you lose about 1.5–2 hours of sleep. At West Point, cadets got about 8.4 hours of sleep per night prior to matriculation which is about right for a teenager. As soon as the cadets entered West Point their sleep was restricted to 5.5 hours of sleep per night. The sleep pattern did not change throughout the course of time. This pattern ingrains behaviors and habits into cadets from day one. What does this mean? It means we are sleepy. We are very, very sleepy. Twelve percent of our service members are using medications to help them go to sleep. Coffee is used to try to overcome sleepiness in over 80% of service members. Almost 50% of people are using some form of energy drink, other than coffee, to maintain wakefulness. Of those who are using medications to go to sleep, almost two-thirds are also using some over the counter substance to stay awake. We are using things to keep us asleep and using things to keep us awake. This behavior describes a large proportion of our soldiers in a deployed setting. The number one product sold at a deployed AAFES is Monster or Red Bull.

Acute Sleep Deprivation

When you do not get enough sleep, you become a little slow. Your attention span narrows. You become irritable. You have an increased drive to sleep. You become a dangerous driver. You develop decreased moral reasoning and decreased problem solving. This is what happens with acute sleep debt. These are not behaviors you want to have in a deployed soldier.

Chronic Sleep Restriction

Chronic sleep restriction deactivates the prefrontal cortex. You experience less metabolic activity in the prefrontal cortex resulting in impaired cognitive function. The prefrontal cortex is our attention area. That is why chronic sleep debt or chronic sleep disorders lead to attention deficit disorders (ADD) or what I call the brain fog of sleep.

If you have an adult diagnosed with ADD, you need to look for abnormal sleep patterns. As Dr. Wickwire pointed out earlier, if you have a child diagnosed with ADD or ADHD, you have to look at the quality of their sleep. Sleep apnea is very common in both adults and children with ADD and ADHD. But any form of disruption of quality and quantity of sleep can lead to poor attention span.

The prefrontal cortex overlaps a bit with our personality. This is why chronic sleep debt or even acute sleep debt leads to irritability and moodiness. It impacts who we are and how we function. Chronic sleep restriction

decreases your ability to perform complex mental operations leading to a decreased quality of life. Sleep deprivation impacts both mood and health. It has been shown to be a risk factor for combat stress reaction. In every armed conflict going back to World War I, there has been literature to support the association of chronic sleep debt and combat stress.

Health Consequences of Sleep Deprivation

Inadequate sleep increases mortality. Inadequate sleep increases cardiovascular disease, causes weight gain, and increases the incidence of diabetes. Inadequate sleep is associated with an increased risk of psychiatric disorders especially depression, irritability, anxiety, and alcohol disorders. Reduced hours of sleep can be a predictor of long-term sickness, absence, and work disability. Poor sleep is also associated with impaired neurocognitive function. In our military population inadequate sleep is associated with more suicidality, more anxiety, more depression, more post traumatic stress disorder (PTSD), and more alcohol abuse.

Metabolic Effects of Sleep Deprivation

Chronic low-level sleep debt increases insulin production and changes our balance of leptin and ghrelin. These are the hormones that regulate hunger and satiety. Basically, you develop a carbohydrate craving. You become more efficient at storing fat than utilizing fat. The Wisconsin Sleep Cohort Study showed that if you slept less than 6 hours per night, that was an independent predictor of becoming obese and developing diabetes. If you slept a normal amount, 7.7 hours, you had the lowest body mass index (BMI).

The Nurses Heart Health Study (83,000 subjects) showed the longer you are sleep deprived, the more likely you are to gain weight. If you are sleeping less than 6.5 hours of sleep per night, you should expect to gain an additional three to five pounds per year. That same study, along with the Japanese Collaborative Cohort (104,000 subjects) and the NHANES NIH Cancer Registry (1.1 million subjects), followed subjects for 50 years. These studies showed truncated sleep duration associated with increased all-cause mortality. There is a u-shaped association between those who are not getting enough sleep and those who are getting too much sleep. Both create an independent risk for mortality.

Sleep Deprivation and Attention Span

Low level sleep debt or even acute sleep debt impairs or increases attention lapses and decreases our vigilance. It takes about 26 hours before we have complete sleep deprivation creating a substantial decrease in attention. Most of us in this room are getting 6 hours of sleep per night so only after a week, we are cognitively impaired. Many of you, like me, have probably been

sleeping like this not for 6 days, but 6 years or more. A graph showing people who have normal sleep at baseline was explained. For one week subjects were sleep restricted to different degrees and in the recovery phase they were allowed as much sleep as they wanted. Afterwards psychomotor vigilance and reaction times, and vigilance were measured. When you truncate 1 hour of sleep per night you see more attention lapses. If you truncate down to 5 hours of sleep per night there are substantial decreases in performance. If you look at the recovery phase, subjects do not return to baseline. We do not make up sleep debt. Even trying to sleep in on the weekend and getting more sleep on the weekends, is not going to make up for the sleep debt during the week and is only going to impair sleep quality on successive nights. The best approach is not to develop sleep debt.

An interesting study looked at U.S Army soldiers who were deployed for at least 9 months. They all got 1 hour of sleep less compared to the baseline. What they found was that enlisted men had an increase in the number of reported errors. The officer group seemed to do better when sleep deprived. In another study in Scandinavian military, soldiers were evaluated who were deprived 6.0 hours per night versus 7.5 to 8.0 hours per night. The study looked at numerous things but largely leadership reaction courses. Even with the sleep debt, soldiers were able to perform and get through a combat reaction course with no difference between those who slept well and those who slept less well. When they looked at leadership reaction course, there was a significant difference. What they concluded was, complex thought processes become blunted and impaired with sleep debt; more automatic task oriented functions were not so impaired. At 19 hours of continued wakefulness, we have as much memory lapse and attention span deficit as we would have if we had enough alcohol to make us illegal to drive. At 19 hours of continued wakefulness, you are an impaired driver. Being sleep-deprived causes impairment.

Deployment and its Affect on Sleep

We know we are not getting enough sleep in the military. We know that sleep debt is bad. We decided to throw in an 11-year war. That did not help sleep. Lots of things disrupt sleep during deployment. It is noisy. We are co-sleeping. I slept with 7 or 8 of my best friends for 8 months right next to a flight line and we all had radios that went off constantly. You throw in the occasional camel spider and it was not good environment. We worked all night and we worked all day. Many of us were eight and a half time zones in the future. I was fortunate since I was coming from the east coast. Soldiers from the west coast and Hawaii were completely inverting their sleep-wake cycle. In Afghanistan, the sun came up at 3:30 in the morning. If you went one country to the north, you went ahead an hour and a half in time zones. It made no sense.

What Do We Want to Have Good Sleep?

We want enough time in bed and we want to have a sleep environment conducive for good sleep. Both of these are impaired when we deploy. We are getting less sleep and the quality of that sleep is worse. When we look at sleep studies that evaluate duration of sleep when soldiers are deployed we see that sleep duration is always less, but the studies do not assess quality of sleep. Different studies have looked at overlapping findings. Studies look at stress at home, stress in the deployed state, the physical environment, workload, and work schedules, all of which can lead to bad sleep. Soldiers are deployed for six, nine, or twelve months. Soldiers actually phase shift their circadian rhythms in that much time. When a soldier comes home, all those life stressors do not go away. Their circadian rhythms and sleep patterns have changed. This is when we see sleep complaints or sleep disorders that are persisting or developing following deployments. Seventy-eight percent of people deployed are sleepy during the day. Now here is an amazing thing. Only half of them felt that they were sleep-deprived. The mean sleep duration in this study was 5.6 hours per night and only half felt they were sleep deprived. It tells you that we do not understand and we do not value what normal sleep is.

In another study of almost 2,800 soldiers who had deployed, only 16% reported impairment due to sleepiness. Their mean sleep duration was 5.8 hours per night. I think this is important. One out of every six soldiers downrange feels impaired because of sleepiness. That is a great many people. Yet the sleepiness is largely under reported or underappreciated. There was a study done on pediatric residents post-call. None of them felt impaired, yet every one of them failed the simulated driving test. This is the same type of problem we are having with our soldiers. The Air Force is also sleep-deprived and sleepy. They get an extra hour of sleep a night compared to the Army but the amount is still insufficient. Three-quarters of them felt that their sleep was worse during deployment and the majority of them had difficulty initiating or maintaining sleep.

The Millennium Sleep Cohort Study that started in 2001 studied 42,000 people who had deployed from all branches of the service, both active duty and reserve components. They were asked how much sleep they had in a 24-hour period, allowing for naps. They were asked about some quality of life measures and sleep-specific quality of life indices. Being deployed or post-deployment increased their risk of having sleep disorders. Those who had direct combat experience were at increased risk. Almost 75% of the study participants developed a sleep disorder.

Does Deployment Affect Insomnia?

All branches of service reported an increase in insomnia during deploy-

ment except the Coast Guard. Deployment does not improve sleep quality with the most profound differences found in the Army and the Marines. When the Millennium Cohort Study came out, the thought was the length of deployment and the amount of combat exposure for the Army accounted for the differences.

What do we see when we compare different units? In general, there is a great deal of poor sleep and a large number of people using sleep aids in units during deployments. Ten percent of deployed troops are using some prescription substance to induce sleep. There is more sleep medication use in sustainment units. Why is that? It could be that sustainment units have easier access to care or because they are working less at night. It is hard to take a sleeping aid when you have a nighttime patrol. That might be why maneuver units use less sleeping medications. The bottom line is 10% of deployed personnel are using a prescribed substance to put themselves to sleep at night.

Sleep post-deployment may not improve even though soldiers change their sleep environment. They are home having changed eight and a half time zones or eleven and a half time zones. Life stressors do not always go away when a soldier comes back from deployment or new stressors develop. Soldiers developed poor sleep habits and circadian rhythm misalignments when they were deployed. Those habits do not go away. Mood disorders and PTSD impact sleep. We have traumatic brain injury (TBI). TBI and PTSD are the signature injuries of the current war. All these things play a part in disrupting our sleep and developing or propagating more sleep disorders post deployment.

Post-deployment Sleep

We see more anxiety, more panic disorders, more depression, and more PTSD in those who have deployed and who have had a concomitant sleep complaint. If a soldier is very sleep restricted, we see a profound increased risk in all of those things and, interestingly enough, more traumatic brain injury. Many people consider TBI to be a sleep disorder or a cause of a sleep disorder.

Sleep Disorders in the Military

Sleep disorders in the military are on the rise. People with chronic pain have more insufficient sleep, more sleep apnea, and more insomnia. People with depression have more insufficient sleep, more sleep apnea, more insomnia, increased anxiety, PTSD, and TBI. These are the conditions that we see in our patients. We also see the overlap of sleep deprivation or insufficient quality or quantity of sleep and the development of behavioral health issues.

The diagnosis of obstructive sleep apnea (OSA) is skyrocketing. Ten years

ago, OSA was a rare diagnosis. Now everybody has OSA. It is no different in the civilian community. Yet sleep apnea has been around forever. It is described in ancient Egypt. It is described throughout European 18th century literature. We did not have a treatment for it. If you do not have a treatment for it, why look for it?

CPAP was introduced and CPAP got better and better. CPAP machines are now quiet and they are comfortable. We are getting older and we are getting heavier which increases OSA. We have more comorbid conditions and we are more sleep-deprived as a society. All these conditions, in combination, lead to more sleep apnea.

Sleep Apnea in the Army

The Army is a population of young, healthy adults who are pre-screened for health and forced to maintain height and weight standards. Why are we seeing so much sleep apnea in the Army? We see sleep apnea largely because we have a lot of low level sleep deprivation in the military. Compared to our civilian cohorts, we are younger and thinner and yet, in the military, we have a great deal of sleep apnea.

The diagnosis of insomnia is also skyrocketing in the military and also in the civilian community. There are some very interesting studies looking at the gross national product, the way the stock market goes, and unemployment rates. All correlate well to the incidence of insomnia, not just in America, but in all westernized nations. In the military we have added the stress of fighting a war which increases the diagnosis of insomnia.

Seven years ago, the *Army Times* reported that, "One in six deployed soldiers is on a psychoactive medication." The use of psychiatric drugs has spiked creating concerns about suicide and other dangers. This is a population of young and healthy adults. How much of this increase is overuse of medications and how much of it is an unfortunate need for medications?

Sleep and PTSD

Current literature reports that 30 to 70% of people with post traumatic stress disorder (PTSD) will have a sleep complaint. We looked back in the *New England Journal of Medicine*, 1946. The authors said with great accuracy they could predict who was going to develop PTSD. Soldiers with pre-existing behavioral health issues or poor sleep going into the combat were at risk. Those were the only two things they found. We jumped — we forgot those lessons.

In Israel there are many different studies looking at PTSD in both the military and civilian community. One study following scud attacks in the first Gulf War showed 60% of those attacked developed insomnia and 30% developed chronic sleep disturbances. We see the same pattern after the

bombings in Oklahoma City. Of those affected, the majority developed insomnia and 50% developed nightmares. In the short term we see insomnia and nightmares. In the long term we see a predominance of sleep complaints that includes difficulty initiating sleep, waking after a sleep onset, nonrestorative sleep, daytime sleepiness, and increased incidence of nightmares.

Study after study shows that if you have PTSD and a concomitant sleep complaint you have a much worse outcome with more relapse, increased use of psychoactive meds, more work days missed, more disability, and lower quality of life scales than if you have PTSD without a substantial sleep complaint.

PTSD and Comorbid Insomnia

What is most commonly reported in large cohorts is insomnia and nightmares likely due to a hyper vigilant state that is part of PTSD. This is potentiated by psychoactive medication. As Dr. Fleishman pointed out, SSRIs and SNRIs increase sleep fragmentation. A concomitant sleep disorder portends a worse outcome. Patients whose sleep complaints go unresolved have more major depression, more suicidality, decreased therapeutic response to antidepressants, and then, increased risk of relapse compared to patients whose sleep complaints resolved.

PTSD and our Soldiers

The burden of PTSD is largely unknown. As many as one in six to seven deployed soldiers has PTSD. We looked at 165 consecutive people with PTSD who were admitted to the Warrior Transition Unit (WTU). Sleep complaints were almost universal with sleep fragmentation in two-thirds of patients and difficulty initiating sleep in over half of patients. On average, the majority were on 6 psychoactive medications. Six psychoactive agents per patient is what our patients with PTSD are on. There are meds to put them to sleep, more meds to put them to sleep, meds to keep them awake, meds to make them happier. All these medications fragment sleep.

PTSD patients with a sleep complaint were hospitalized almost 50% longer than those who did not have a sleep complaint. If you had insomnia and PTSD, you were hospitalized an additional five months.

PTSD and Obstructive Sleep Apnea

We looked at 156 people with PTSD and did sleep evaluations on them. Half of them had sleep apnea. That is pretty profound. We asked why? Why are so many young healthy people diagnosed with sleep apnea? And we looked at those who were injured versus those who were not injured and it made sense. You suffer an improvised explosive device (IED) injury and you lose two arms and a leg. You have PTSD and it makes sense. What about

those who are not injured? They have not experienced the same emotionally traumatic event. Why do they develop PTSD? Perhaps it comes down to resiliency. What will impair your physical and emotional resiliency better than poor sleep? We go back to the *New England Journal of Medicine* in 1946. They said it. We look at what Israeli literature is saying. If you had pre-existing sleep issues, you are more likely to develop PTSD and the PTSD has a worse outcome than those with PTSD who did not have pre-existing sleep issues.

Sleep Disorders and Traumatic Brain Injury (TBI)

Sleep disorder breathing is significantly more common in those following a TBI. What is about the connection between sleep disorder breathing and TBI? If you had untreated sleep apnea and you fall asleep driving, you hit your head. We all relate to that association. But there is nothing about having sleep apnea that is going to increase your risk of TBI. Is there something about TBI that increases your risk of developing sleep apnea? The answer is yes, there is. What happens? In all cases of TBI, orexin producing cells in your brain are damaged. Orexin is one of the main wake-promoting substances and damage leads to hypersomnia. If you get hit in the head hard enough and you have a closed head injury, sleepiness is very common. If you remember back in the old days if you had a head injury, you were told to stay awake. Do not go to sleep and perhaps lapse into a coma. Now we have gone 180 degrees and if you suffer a head injury inducing sleep improves outcomes.

What the connection between sleepiness and getting hit in the head? If you suffer mild head injuries or concussions, you are going to have more somnolence. In the vast majority of people that will resolve within a few days. Objectively, it gets better within a few months. In some people the sleepiness will extend past 6 months. After 6 months, it is called post-traumatic hypersomnia. You can also develop post-traumatic narcolepsy.

Looking at studies of veterans show us that sleep disorder breathing is very common following a traumatic brain injury. We know TBI combined with OSA causes more cognitive dysfunction, increased psychiatric illnesses, behavioral health diagnoses, and more neuromuscular sequelae. We know that having concomitant sleep apnea and TBI hinders recovery.

We looked at a study of 175 soldiers with sleep disturbances with combat related traumatic brain injury. The vast majority had subjective sleep complaints and 68% reported insomnia. Two-thirds of those studied could not fall asleep, half could not stay asleep, and the majority were sleepy during the day. We found sleep apnea in 34% of soldiers post deployment. Those studied were young, active duty, thin, and mostly men.

We found PTSD, TBI, depression, and anxiety. Almost all subjects in the

study group were on psychoactive medications. Patients with TBI were, on average, on five psychoactive medications. The medications contribute to sleep disruption.

If we look at a comparison by mechanism of injury, blunt force trauma to the head caused more sleep disorder injury and blast injuries to the head caused more insomnia.

Sleep and Chronic Pain

Sleep and chronic pain is another important topic for our military population and also for clinicians in psychiatry and psychology. More than 50% of people with chronic pain have a sleep disturbance. I was part of the task force that is coming out with a new statement on sleep and pain. I will tell you what we learned. Three-quarters of people with chronic pain have sleep disturbance. The Surgeon General reported on a position paper saying 28 million Americans have sleep complaints due to chronic pain issues. We know that chronic pain is associated with insomnia. If a patient has both conditions, they have decreased quality of life than either condition independently and they have increased healthcare utilization. We also know that with the sleep disturbance there is a linear and independent association with pain severity after controlling for health and sleep habits.

What about sleep and pain and depression? There is a multidirectional reciprocal relationship. Poor sleep leads to depression. Depression fragments sleep. Insufficient sleep increases the pain response. Having pain fragments sleep. Having chronic pain causes depression. You cannot separate these conditions.

We know that pain fragments sleep architecture. It causes increased EEG arousals, at least with alpha-delta sleep. Delta sleep is our best quality slow wave coma-like sleep, where we rest our body. Alpha-delta sleep is common with chronic pain where a wake rhythm (alpha) intrudes into deep sleep. We see this pattern with people with chronic pain syndromes.

We know that pain medications fragment sleep by disturbing breathing in normal individuals. Opioids, benzos, even tricyclics, all decrease slow wave sleep and decrease REM sleep. We need slow wave sleep and REM sleep to restore our body and mind. Numerous studies have shown that opioids precipitate sleep disorder breathing. Opioids decrease central respiratory patterns causing apneustic breathing. Apneustic breathing is a very bizarre respiratory pattern with decreased tidal volume, decreased respiratory rate, decreased respiratory depth, increased airway resistance, and more collapsibility of the upper airways. All this happens in normal people. Those susceptible to sleep apnea develop more sleep apnea. In a study of acute oral narcotics, OSA was observed in more than a 33% of patients and CSA was observed in 14% of patients. One third to one half of all patients in long term

pain clinics have obstructive sleep apnea. Their OSA is more refractory to PAP therapy and residual sleepiness is common.

In a study of young, non-obese women who were chronic opioid users we found that many of them had severe sleep apnea. Not only did they have more obstructive events but the pauses in breathing were longer and they had more nocturnal hypoxia. Because this type of disorder is more refractory to therapy with regular CPAP they often need nocturnal ventilator support and BiPAP with a backup route.

Another study looked at long term young, non obese opioid users with a mean age of 32 years and a mean body mass index (BMI) of twenty five. Sixty percent of the patients were women. These are not profiles of patients you would expect to have sleep apnea. Mild sleep apnea was present in 63% of patients. Sixteen percent had moderate sleep apnea and 17% had severe sleep apnea.

Narcotics are clearly needed for pain management. Opioids are clearly needed to treat chronic pain but everything has a cost. The consequence of narcotic use is more sleep disruption. We know that more sleep disruption with pain is going to lead to worse outcomes and an increased pain response. It becomes a self-fulfilling prophecy. Pain medications can actually increase the need for more pain medications because of what happens to your sleep and, subsequently, what sleep disruption does to your pain response.

Cognitive behavioral therapy works. Cognitive behavioral therapy (CBT) specific for insomnia and pain is new. Studies show that it works. CBT plus analgesics versus only analgesics, as you would suspect, is substantially better at improving quality of life and depression. It also results in less pain.

In summary, we have talked about several concepts. We do not get enough sleep in the military. We do not get enough sleep in America. The military is even worse. It has a direct, unfortunate, and negative consequence on health and mood outcomes. We know that the war is making it worse. We are seeing more life stressors with war. We are seeing more suicidality. We are seeing more PTSD and more TBI and greater divorce rates. I am not saying all are related to sleep but all clearly can be exacerbated by poor sleep. If we ignore the sleep, all the medications in the world are not going to work if we do not address the basic principles.

All the insulin in the world will not fix diabetes if you eat birthday cake four times a day. All the psychoactive medications in the world will not fix our patients' behavioral health issues if we ignore our patients' sleep.

Traumatic Brain Injury and Sleep Disorders

Michael R. Yochelson, MD, MBA

I am going to discuss disorders of sleep after traumatic brain injury. There is not necessarily anything that is different from managing someone who has a brain injury with sleep problems compared to someone who has not had a brain injury with sleep problems. I am going to talk about recognizing sleep problems, as well as some of the more common types of sleep problems that we see. I will also discuss excessive fatigue after brain injury, the types of problems we see, and their management. Excessive daytime somnolence is a sleep disorder although fatigue in and of itself may or may not be a sleep disorder. I think they go hand in hand and you cannot discuss one completely without the other.

As the father of a 14-month-old, I am very familiar with sleep disorders and particularly external factors that affect one's sleep. I was fortunate to have a child who, at 2 months of age, decided she was going to begin sleeping through the night. I thought this was wonderful. About 3 weeks ago, she decided that, about once an hour, she was going to wake up and scream all through the night. If you have interrupted sleep every hour throughout your entire night, you do not get a good night's sleep. This affects your ability to function and it affects how you feel during the day. You feel tired and your cognitive function is impaired. Twice in the last 3 weeks, I forgot to wear a belt to work. I have never, ever forgotten to wear a belt to work. I have never had a brain injury either. When you recognize the impact of sleep on multiple areas of function, and particularly cognitive function, you can only imagine how that magnifies in someone who may have some of these impairments by virtue of having had a brain injury.

Other external factors affect one's ability to get a good night's sleep. Traveling to different time zones, particularly if you go beyond one or two time

Excessive daytime somnolence is a sleep disorder although fatigue in and of itself may or may not be a sleep disorder. I think they go hand in hand and you cannot discuss one completely without the other.

zones and working nighttime shifts are two examples that our military personnel may experience on a regular basis. Other environmental factors, such as being deployed and having rockets and grenades exploding when you are trying to sleep, can create sleep problems. The fear one might feel in a deployed situation can create sleep disturbances.

An alteration in neurotransmitters is something that occurs after a traumatic brain injury. Psychological disorders, psychological stressors and medical and physiologic disorders, not the least of which includes pain, are other internal factors to consider.

How do you know that someone who has had a brain injury is having problems with sleep? In my clinical practice, patients usually do not tell me they have problems sleeping. Patients may describe sleep issues in a number of other ways. They might say they have trouble falling asleep. That is the phrase I hear most commonly in terms of an actual sleep complaint. Sometimes patients will talk about waking up. Sometimes it is a caregiver, a partner, or spouse who tells me about confusion at night, wandering around in the middle of the night, or other sleep related behaviors. Sometimes patients may complain of hallucinations and I might hear about snoring or sleep apnea. I would encourage you to ask about snoring and sleep apnea because those are very important.

Inefficient sleep can lead to a number of other factors like fatigue, agitation, depression, pain, and cognitive problems. I already talked about my cognitive problem like forgetting to wear a belt. I can also tell you that someone who is sleep deprived will have a much lower threshold for pain. If take any one of you and sleep deprive you for 3 or 4 days or a week, your threshold for pain will be much different. We know in the military population there are many pain factors. In fact, in a traumatic brain injury population, by definition, there was a trauma. There could be other injuries besides the brain injury that could lead to pain. The lack of sleep exacerbates pain issues.

Do patients have problems because they are sleep deprived or are do they have problems because they have a brain injury? Often it is difficult to tease out the two. For that reason, when a patient complains about increasing pain or cognitive problems it is important to recognize the nature of the complaint and to make an assessment of sleep habits.

Insomnia is very prevalent in patients with traumatic brain injury (TBI). In the general population, insomnia affects 10 to 17% of people. In the population with brain injury insomnia affects up to 87 percent. There is a wide variability from about 17 to 87 percent. That is because studies and reports in the literature are done in a variety of ways. Some studies might look at patients with mild brain injuries and other studies might be looking at patients with more severe injuries. Where are they looking in the time line of

the brain injury and the recovery? How was the study done? Was the study a symptomatic survey of patients or did the study design use polysomnograms and other more objective data? That is why we see so much variability. Nonetheless, if you look mid-range, insomnia is still significantly higher in patients with TBI than in the general population.

We did a short study in our in-patient unit, keeping in mind our inpatient brain injury unit has more moderately to severely injured patients. We looked at about 1200 hours of sleep data. Nurses checked on patients every hour and documented whether or not they were asleep. Clearly, there were many limitations to the study because patients could be asleep for a large part of the hour and then awake when the nurse came in or vice versa. We found that 25% of the time patients were not sleeping when they should have been sleeping. Furthermore, we also found a smaller subset of the group that was having sleep problems and they were having problems more than 25% of the time. In other words, if you have 100 patients, it is not 25% of them who have a problem. It might be 10% of the patients who have a problem but they are not sleeping for 50% of the time.

This distribution tended to occur in association with the more agitated patients. Those patients with a Rancho Los Amigos score of 4 had the worst sleep problems, which is not particularly surprising. Their sleep problems generally occurred earlier in their hospitalization. There were some factors that seemed to make their sleep worse. One was transitioning into a new environment. Moving from an acute hospital into our rehab hospital was difficult. The first few days were the most difficult. The level of Rancho Los Amigos at admission also correlated with their degree of sleep disturbance.

There are some positive factors to consider in a rehab hospital. In a rehab hospital patients are not awakened quite as much as they are in an acute hospital because they are not having vital signs measured every few hours during the night. Rehab hospitals tend to be quieter at night creating a better environment for sleeping. Patients slept better, at least subjectively, than they did in an acute care hospital setting. We also do a better job of managing sleep because we actually pay attention to it, while in the acute hospital setting physicians are more interested in the acute medical problems. In an acute care setting physicians are not checking sleep behavior or asking patients questions about how they are sleeping. The three main sleep disorders we see in traumatic brain injury are insomnia, circadian rhythm sleep disorders, and sleep apnea.

Insomnia is any nightly or near nightly complaint of insufficient amount of sleep or not feeling rested when you get up from sleep. More importantly, it has to be associated with some degree of impairment of social or occupational functioning, feelings of restlessness, irritability, anxiety, daytime fatigue, or tiredness. If someone sleeps 5 hours a night and they feel rest-

ed without impaired social or occupational functioning they do not have insomnia. We counsel these patients by saying that some people need less sleep than others.

The definition of circadian rhythm sleep disorders is a persistent or a recurrent sleep disturbance due to alterations in the circadian cycle. In other words, you have misalignments between your endogenous cycle to sleep and external factors. You might be sleeping in the middle of the day and awake at night or vice versa. This can lead to insomnia, excessive daytime somnolence, or both. Again, the insomnia must be associated with some impairment of function, social function, or quality of life.

There are four types of circadian rhythm disorders that I will touch on briefly. They are delayed sleep phase, advanced sleep phase, free running, and irregular sleep-wake cycles. Delayed sleep phase and irregular sleep-wake cycle are the most common in patients with brain injury.

There are external factors that affect our circadian rhythm like jet lag and shift work that were mentioned earlier. The delayed sleep phase circadian rhythm cycle creates problems falling asleep. Patients tend to fall asleep later than they should and they have problems waking up. The difficulty waking up is generally because patients work and live in a society that forces them to wake up at a certain time. If you allow patients to sleep as long as they want they have fewer problems but waking up when they are supposed to wake up is difficult for them. As a result, they tend to sleep for shorter periods of time and have excessive daytime somnolence which interferes with their function.

The advanced sleep phase is less common in patients with brain injury. These patients have late day sleepiness and they tend to take naps. They wake up early in the morning and then have trouble falling back asleep. If you force this group to stay awake late, they can do that but they still will tend to wake up at their usual time, thus shortening their sleep cycle even more.

There is no good pattern in the free-running sleep wake cycle. Some days may be fine. Other days, patients may not sleep very much. Free-running cycle can advance forward day, after day, after day. This is what you tend to see in patients who are blind because they do not experience the light and dark stimulation of a 24 hour day.

The irregular sleep-wake cycle is the second most common sleep disturbance in patients with traumatic brain injury. There is no clear pattern. Patients often have sleep cycles that last one to four hours. Usually the longest cycle tends to be very late in the night from 2:00 a.m. to 6:00 a.m. This pattern is not uncommon in other neurologic disorders but is very common in patients with traumatic brain injury.

We see both central sleep apnea and obstructive sleep apnea in patients with traumatic brain injury. Central and obstructive sleep apnea combined

is seen in about one-third of patients who have traumatic brain injury. What are some of the sequelae for someone with sleep apnea? In any form of sleep apnea we see excessive daytime somnolence. Sleep apnea can also impact general health. Cardiac problems are not uncommon among patients with sleep apnea. Problems with sustained attention and memory are affected by sleep apnea. This is very important to remember in patients who have traumatic brain injury since they may also have cognitive impairment due to their injury. Patients may also have other conditions such as depression and agitation.

What are some of the treatments for sleep disorders in patients with TBI? Pharmacotherapy is not very effective in the circadian rhythm disorders. Also patients with TBI typically are already on many other medications and many of the medications that we would use for sleep are going to have a negative impact on cognitive functioning. If possible, we use chronotherapy to control the patient's bed time and wake time. This can be very difficult. With a delayed sleep phase, we want to advance the patient's sleep and wake cycles on a regular basis every couple of days. If the patient is going to sleep at 2:00 a.m. instead of at 11:00 p.m., we want to shift the sleep phase all the way through the day. This is the ideal way to do it. Clearly, this takes a great deal of time, a great deal of effort, and diligence on the part of the patient. In my experience, most of the time, this ideal model is ineffective because it is a very difficult process.

Light therapy can be very effective when early morning light is used to help advance the delayed sleep phase. Some people use melatonin. It is important not to give melatonin at bedtime. Typically, melatonin is administered about 6 hours prior to bedtime.

For the irregular sleep/wake cycle problems, you want to consolidate sleep. Patients are getting blocks of sleep, anywhere from about one to four hours throughout the day, often taking multiple naps. Counsel patients to use light therapy during the day, avoid naps, and darken the room at night to help to consolidate their sleep.

What are some of the drugs used in the pharmacologic management of sleep disorders in patients with traumatic brain injury? We talked about melatonin briefly. Ramelteon is the melatonin analogue. We use ramelteon in some of our patients with brain injury with variable success. When patients do not respond or are not appropriately using the light therapy or the chronotherapy, we can use other drugs. I do not recommend the "Z" drugs like zolpidem and zaleplon as first line use, although for inpatients we probably use them more often than I would like. There are some studies that suggest benzodiazepines are helpful. Be alert to the potential side effects of benzodiazepines, particularly in this patient population because of the CNS depressant effects and the cognitive side effects. Your ability to do a

neurological exam may be impaired if a patient is on benzodiazepines. There are a number of studies that suggest that benzodiazepines administered to patients during the acute inpatient rehab period actually slows down overall recovery. Under most circumstances, I do not recommend this classification of drugs.

Central sleep apnea is more common among patients with traumatic brain injury than in the general population. Obstructive sleep apnea, of course, is the most common sleep apnea that we see in the general population. The treatment, however, is very similar. We treat both conditions with airway support, CPAP, or other noninvasive positive pressure forms of ventilations.

There are no medications that have been clearly demonstrated to improve central sleep apnea, particularly in patients with brain injuries. There are some small studies and anecdotal evidence that theophylline or acetazolamide might be helpful. These were small studies with cardiac patients where central ventilation was stimulated by the drugs.

Obstructive sleep apnea is more common in the general population but is also commonly seen in patients with traumatic brain injury. Obstructive sleep apnea is seen a great deal with other comorbidities such as obesity. Fortunately, we do not see as much obesity in the military population.

We use the same treatments for obstructive sleep apnea whether patients are brain injured or not. Mechanical treatments include CPAP and BiPAP. Provent is now available for people with mild obstructive sleep apnea who cannot tolerate a CPAP device. We use medications like modafinil and R-modafinil, not to help with sleep, but to help with the side effects of sleep apnea. Other stimulants can also be used to help with side effects of having sleep apnea like fatigue.

The third large category of sleep disorders in patients with traumatic brain injury is insomnia. Cognitive behavioral therapy is the best place to begin in terms of treatment for this patient population. In patients with severe traumatic brain injury CBT is not possible. In patients with mild traumatic brain injury, CBT is an important place to start, especially if there is an overlap with PTSD.

As part of the CBT treatment patient education is very important. Patient education includes talking to your patients about caffeine use, alcohol use, exercise, and stimulus control. Stimulus control addresses what you can and cannot do in a bedroom, the timing of going to sleep, and waking up.

Oral hypnotics are the “Z” drugs that we discussed. They are also effective for insomnia and are appropriately used for insomnia, particularly when there are significant functional problems during the day. We try to use them for short durations but if drugs are necessary these are appropriate. Other drugs may be used depending on symptoms. If you have a patient with insomnia who is also depressed, we would commonly use trazodone. We com-

monly use trazodone in patients who have more severe brain injuries when CBT is not an option.

SSRIs are used to treat patients who have severe depression. When you control the depression, you may also help to treat the insomnia. Tricyclic antidepressants such as amitriptyline used in fairly low doses are used to treat insomnia. In the low doses we are taking advantage of the cholinergic side effects of the drugs because that makes patients drowsy. To effectively treat depression patients would have to take higher doses. In the patient population that has both insomnia and depression, it is a reasonable drug regimen.

We see a great deal of agitation and psychosis in patients with mild to severe brain injuries. The newer generation of antipsychotics, particularly ziprasidone and quetiapine can be helpful in helping these patients get through the night and sleep. We use these drugs often on our inpatient unit because we have more severely impaired patients who have a great deal of agitation. In the mild TBI population, we do not tend to see agitation and psychosis to the same extent. Nonetheless, this is a group of drugs that could be considered in the right population.

We hear about nightmares in PTSD. There are some studies that suggest that prazosin is effective in the treatment for nightmares specifically in patients with PTSD. I am not familiar with any literature suggesting that prazosin helps specifically with nightmares in TBI, nor do we see that nearly as much. Obviously, there is a significant overlap between mild TBI and PTSD.

Anecdotally, I want to share the story of a patient who had a severe anoxic brain injury. When I first met her she was 30+-year-old woman, post-partum, who had a cardiac arrest resulting in significant cognitive impairment. She developed severe nightmares that were waking her daily. I started her on a low dose of prazosin, and the nightmares decreased to one or two times a week, which is a significant improvement for her.

I want discuss fatigue. Fatigue may or may not be related specifically to sleep disorders but we see fatigue in patients with sleep disorders. We see fatigue frequently in traumatic brain injury and it is important to link the two together. We see fatigue very often in the early post-traumatic period. Among my more severe patients, fatigue is the number one complaint. Among more mild patients, headaches are the number one complaint but fatigue ranks right up there among outpatients. Fatigue is the number two complaint among outpatients with the mild brain injuries. For my patients, I always have to distinguish the difference between fatigue and somnolence or drowsiness. Fatigue is a level of energy or endurance versus the feeling of sleepiness like you have to take a nap. We all experience fatigue at times, particularly mental fatigue, especially if we are working long hours. Physical fatigue is what we feel when we have worked out at the gym. After exercise we feel physical fatigue. It is important to recognize the interplay between

the two. Many people recognize physical fatigue but they do not appreciate how their physical activities impact their mental or their cognitive reserves.

Endocrine dysfunction is not uncommon in patients with severe brain injuries. About 5 to 20% of patients will have hypothyroidism. There are also a number of other neuroendocrine dysfunctions. I test patients with brain injury who have significant fatigue, especially if I do not have another explanation for their fatigue. I check their thyroid function and treat with hormone replacement if it is low.

More recently we have come to recognize that there is a loss of hypocretin neurons due to hypothalamic dysfunction creating low hypocretin-1 levels in the CSF. There is a new drug called Suvorexant currently under review by the FDA. Suvorexant is a drug that works at the orexin or the hypocretin receptor as an antagonist and it is showing some promise.

What do we do first? First, if a patient is complaining of issues related to fatigue, find out if they have sleep dysfunction. Treat the sleep dysfunction first because then you are treating fatigue and sleep dysfunction at the same time. We also encourage increased physical activity but again with caution because of the interplay with cognitive function discussed earlier. I would like to share this example. TC was 19 years old when he came to my clinic. He was a football player in his sophomore year of college. He became my patient after 2 concussions in the same game. TC had never had a diagnosis of concussion prior to that, although as I took his history, it sounds like he had multiple concussions throughout his football career. He was having many cognitive problems, many headaches, many problems with sleep and with fatigue. Over a number of months we gradually increased his workload. We gradually increased the number of hours that he was in school. We had kept him fairly low level physically. But we got to the point that I had released him to go back to full physical activity, except for contact sports. He was going to the gym. He was working out and lifting weights. He did that and then the next day he had exams and he failed some of them. He recognized at that point how much the physical activity had an impact on his cognitive functioning. His school, whom I had been working with closely, was gracious enough to let him retake the exams. We took him off of all physical activity, other than just sort of routine walking around. Basically we reduced his physical activity substantially, had him retake the exams within about a week and he got Bs on his exam. There was a very direct impact between physical and cognitive functioning.

We may have soldiers who have brain injuries while they are deployed or who come home but can they go right back to work? How much can they do physically? How much can they do cognitively? Can they pull 24-hour shifts? Can they take watch, stand watch? And generally speaking, there is no perfect formula. You have to look case by case and assess how patients

are functioning. You also have to look at their job duties. But I would say as a general rule of thumb, patients should not be going immediately back into full work and full physical activities.

Just as we have very clear return to sports guidelines in the sports literature where there is a graded return to play, we should have this same sort of guidance in terms of patient's return to work. We do that with students. They may go back to school half days and then maybe full days but with no homework and then we extend their test time. We need to be working with the military commanders and other folks to make sure that they appreciate this as well.

What about caffeine? Having recently had my sleep disturbed by my child, I have been drinking more of it and lo and behold, it actually works. We talk about stimulants and we put patients on things like methylphenidate or dextroamphetamine and they work, too but caffeine does as well. And I think with appropriate education, so patients are not drinking a giant triple espresso at 8:00 at night, the use of stimulants such as caffeine is appropriate for dealing with fatigue after traumatic brain injury. Aside from the caffeine, what other things do we do? In terms of pharmacologic management the goal is to try to reduce the fatigue. Reducing fatigue improves alertness. We use stimulants, as I mentioned. And we do use these fairly often in this patient population in the early periods, just to try to get them over the hurdles, especially if they have a lot of cognitive tasks that they need to attend to. You cannot keep somebody out of school for months on end or out of work for months on end. That is just not practical.

Modafinil and R-modafinil have been looked at in a number of studies in traumatic brain injury but modafinil has been shown to be effective, particularly in the more acute periods within the first six to twelve months, certainly. I have patients that I have had on modafinil a couple of years out from their brain injury. One patient who comes to mind had a mild brain injury. Every time I tried to take her off of modafinil or every time the insurance company made me take her off of it, she got significantly worse. She has a very high stress job, a lot of multi-tasking, and long hours. She functions well on this medication. Now, is this due completely to her brain injury? I do not know. But she was functioning very, very well in the same job prior to the brain injury so I can only assume, temporally, that it probably is.

SSRIs can also be helpful. Some of them are more activating than others. Sertraline is one that I use more commonly if I have a patient with depressive features. As you know, the depression itself may be contributing to the fatigue and you will see all of these factors together with the brain injury.

In summary, sleep dysfunction, problems with arousal, with attention, decreased alertness, and fatigue are all significant sequelae of TBI. They affect the patient's ability to function in day to day life. They affect their quality

of life. They affect their ability to get back and go on deployments or perform all of their duties.

There is a significant interplay between all of issues and a lot of diagnoses between brain injury, between PTSD, depression, or obstructive sleep apnea that they may have had before their TBI. There are a number of different factors. You want to address each of them or think of each of them independently. Do not assume that everything is a TBI or a sleep problem. Think about how can you manage them holistically. And again, in certain areas where you have an option of several different drugs to use or different modalities to use, if you have one that will help with several different areas, that is the best way to go.

Many questions still persist as far as the underlying etiology and the best treatment practices. We certainly need more research in this area. It is difficult because of the overlap in the different diagnoses that I mentioned. But in the interim, I think it is imperative that clinicians recognize all the different features and that they ask the appropriate questions in their history. They need to recognize that some patients may not come in complaining of sleep but if they hear some of the other problems, they will think about sleep, assess sleep appropriately, and manage sleep if it looks like that is part of the problem.

Melatonin, Light Therapy and Circadian Rhythm Disorders

Greg W. Morgan, MD

My goal is to discuss some pragmatic approaches to using light therapy and melatonin therapy in your practice to manage patients with circadian rhythm disorders. I will begin with a discussion of circadian rhythm anatomy and pathophysiology or physiology. I will also discuss endogenous and exogenous melatonin, review bright light therapy, and then discuss a brief review of circadian rhythm disorders. We will specifically review delayed sleep phase disorder and the utilization of melatonin, and bright light therapy because these disorders are seen a great deal in psychiatry among the spectrum of circadian rhythm disorders.

What drives sleep and what drives wakefulness? What makes up the envelope of our sleep period and our wake period? There are two modular processes that are at play. One is the homeostatic drive for sleep that is often called Process S. And the S comes from slow wave sleep, which is the primary marker historically for your homeostatic drive for sleep. The primary drive for wakefulness is your circadian rhythm. When we are getting very sleepy, we are experiencing a withdrawal of an arousal stimulus from our suprachiasmatic nucleus and then the homeostatic drive takes over because you have been awake longer. That is the balance that exists.

Your drive for sleep will begin to increase the longer you have been awake. Generally, after 14 to 16 hours of wakefulness, we have sufficient homeostatic drive for sleep and our circadian rhythm withdraws inducing sleep. Our homeostatic drive for sleep increases over the course of our wake period. At a certain point, though, our circadian rhythm is still fairly active in promoting wakefulness. When the circadian rhythm withdraws, we are

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able to induce a sleep period. As we are sleeping, our homeostatic drive for sleep is diminishing and at the same time our circadian drive is diminishing, so sleep continues. The low point or the nadir of your circadian rhythm is also correlated with what we call the core temperature nadir, which is a good marker of periodicity of the individual circadian rhythm. After the nadir, we begin to increase our circadian drive for wakefulness and because our homeostatic drive is low, we wake up. And the whole process repeats itself.

The circadian rhythm is generated from the suprachiasmatic nucleus in the hypothalamus, and it regulates a variety of rhythms in the body. It regulates the hormonal release of cortisol and melatonin. It also regulates immune function, digestive activity, and core body temperature.

What is the basic neuroanatomy of the circadian system? The retinohypothalamic tract runs from the retina to the suprachiasmatic nucleus. Generally, the influence of the suprachiasmatic nucleus on the pineal gland occurs through a multiple array of neurons that includes the superior cervical ganglion finally impacting on the pineal gland. When light is withdrawn from the environment, the pineal gland facilitates to release melatonin. The neurotransmitter that is active at the final post-ganglionic synapse is norepinephrine. Consequently, certain drugs, like beta blockers have an influence on your release of melatonin and can disturb sleep.

A very potent inhibitor of this process is light. At any time if you impose light, you stimulate the ganglion cells in the retina which have a pigment called melanopsin. The melanopsin will create an activity level in the suprachiasmatic nucleus that blocks the release of norepinephrine. When you apply a light force, you see an immediate drop in melatonin even if this occurs at night. This is a fairly rapidly titrateable process which makes light an effective means of controlling or shifting melatonin.

What is a normal circadian rhythm? You may have learned that it is 24.5 hours but that is actually because this number was acquired in relatively uncontrolled environments. When the environment is controlled the measurement is 24 hours and 11 minutes which is just beyond the typical earth day. What is important about this number is that it is not exactly 24 hours, meaning we have to reset our circadian clock every day to remain in alignment with our environment. If we did not maintain alignment, over the course of a week, we would drift about an hour later. This is a process that we do every day. If you let yourself drift on the weekend by staying up late or by sleeping in, it is much harder to get up and get going on Monday because you are having to shift closer to 20 or 30 minutes; whereas, on a daily basis we may only be shifting ten minutes. That is the basis of Monday morning blues and we can appreciate that it is real. This is an important principle when we are thinking about the exposure that patients have to light. Patients need to have

the right balance of dim light in the evening and bright light in the daytime in order to have this process realigned appropriately.

Currently, there are two biological markers that help us measure the circadian rhythm. Core body temperature is one and the minimum correlates with the minimum output of the circadian rhythm for wake drive. The other marker that is used more clinically is the dim light melatonin onset. And as you withdraw light from the environment there will be a point at which melatonin will start to be released by the pineal gland and it can be unique in every individual, especially if they have a circadian rhythm disorder. Dim light melatonin onset dictates the whole pattern of when our sleep period begins and our wake period begins. The dim light melatonin onset reflects the beginning of the individual's biological night. It is a signal to your body night is coming, and you need to prepare yourself for sleep.

Precise identification of the circadian markers requires measurement under controlled conditions that may be impractical. For instance, when you are trying to measure core body temperature accurately, you need to really do it in a very controlled environment in terms of a patient's activity level because you can imagine, exercise generates heat. You need to control the environmental room temperature. You need to control the food intake and typically this will be done in a fairly sophisticated circadian rhythm lab over the course of 3 to 5 days. Additionally, core body temperature is generally measured with a thermistor that patients are not too excited about wearing for 3–5 days.

Melatonin can be measured more easily but it still has some effort involved. Typically values can be obtained from saliva or plasma. The easiest method is via saliva. To collect from saliva you simply collect saliva on a cotton ball and label the collections serially. In the United States we do not have a commercial assay so you have to be linked to a research laboratory to measure melatonin from saliva. The timing of the collection depends on the condition you are looking for. For advanced sleep phase problems, you are going to need to do it earlier in the day. If you are looking for delayed sleep phase problems, you may wait. Generally, we begin at 6 pm and collect specimens at 30-minute intervals for 5 hours and plot out the melatonin level. There is certain threshold that the laboratory will say is evidence of the rise of the melatonin or the dim light melatonin onset. This is the most precise way to measure melatonin.

Since most of us do not have the capability to measure melatonin this way in our practice, how can we get around this? There are some estimations that can be made based on actigraphy data or sleep log data. It is best if you obtain 2 weeks of data in a free schedule. Free schedule means when a person does not have an imposed work schedule or school schedule. A vacation period is ideal. What do I do in circumstances when I cannot get that kind

of data? I generally obtain a patient's actigraphy for 2 weeks and I look at the weekends or the nights before they do not to go to work the following day. This method will be the best estimation of what their free schedule is. When you use this kind of estimate what you typically find that is the dim light melatonin onset occurs approximately 2 hours before sleep onset in a free running period, not an imposed schedule. For example, if you are seeing a patient who consistently goes to bed at 1:00 a.m. that would suggest their dim light melatonin onset is 11:00 p.m. There are also correlations that have been made between dim light melatonin onset and core body temperature with a difference of 7 hours. If you are having more difficulty estimating sleep onset because of variability but you see a fixed wake time in an unimposed schedule, you can also apply 14 hours beyond the wake time. For instance, if the patient's wake time is 11:00 a.m., their dim light melatonin onset would be 1:00 a.m.

Some very ambitious researchers have taken this process a step further in adolescents between the ages of nine and seventeen. This does not apply to adults. They monitored 150 children on a fixed schedule in the school year and 50 children on a free schedule during the summer. All subjects kept a sleep diary for 5 days and their dim light melatonin onset was measured on the sixth day in the laboratory. Researchers derived regression equations where you can plug in the bedtime using specific calculations for a dim light melatonin onset in time.

Estimating the minimum core temperature is not as precise but it typically occurs about 2 hours before spontaneous wake time. If you have a patient with delayed sleep phase and they are waking up at noon, their core temperature minimum is going to occur at 10:00 a.m. This timing is important to take into consideration when you are applying light therapy that we will talk about after we discuss melatonin.

I want you to think about melatonin as a darkness hormone. Melatonin is a signal of darkness to the body. That is its function. Melatonin prepares our body for sleep by affecting our body temperature, our pulse rate, and the chemistry of our body in the physiology that is receptive to sleep. Melatonin is produced by the pineal gland in response to the withdrawal of ambient light and it is a naturally occurring hormone. It is synthesized in a cascade from tryptophan and serotonin and the neural input to the pineal gland is noradrenergic. Stimulation with noradrenergic input results in release of melatonin. Anything that blocks this cascade could reduce the secretion of melatonin and that is the reason why beta blockers probably have their impact on quality of sleep. Once melatonin is synthesized, it freely diffuses into the bloodstream and crosses the blood brain barrier and it is ubiquitous. Melatonin can be measured in saliva and in serum.

Melatonin was first identified in 1958 and the first reported human ad-

ministration was in 1960, when a dose of 200 milligrams was given intravenously. This is an enormous dose but not a great deal was known about melatonin at that time. The dose led to mild sedation but not severe impairment. Subsequently, doses as high as 2 grams have been administered. There are a variety of uses of melatonin outside the realm of sleep. The point I am trying to make is that melatonin is not a very toxic substance.

The oral doses of melatonin range from 0.1 to 50 milligrams. There is no right or wrong dose of melatonin. It is important to learn that when you give the melatonin determines the dosage. We have to think about it that way. In my opinion, we are better off giving a lower dose because we can target the action of melatonin on the melatonin phase response curve more specifically. If a larger dose is given, the melatonin will be in the body longer and impact on various phases within the circadian rhythm.

We begin making melatonin about 3 or 4 months of age and that is typically when night time sleep consolidates. There is a correlation. The peak levels in your life are in the first 3 years and then we begin the decline through adulthood. By the time we are 70 years old, we make about a quarter of the levels of melatonin compared to young adults.

In the United States, the FDA considers melatonin a dietary supplement. And because it is a dietary supplement there is poor regulation of dosing and preparations. Some preparations may have additives that affect the bioavailability and the consistency of how the drug works. No prescription is required for melatonin. If you encourage your patients to take melatonin, they should purchase pharmaceutical grade or synthetic grade melatonin. The pharmaceutical grade production is not as controlled as a prescription drug production but it will have less additives. When you administer exogenous melatonin at doses of 1 to 10 milligrams, at the low end of the scale, you may raise levels as much as 60-fold of normal nighttime levels. It does not take a great deal of melatonin to adjust circadian rhythms. Doses as low as 0.1 and 0.3 milligrams have an impact on sleep. Low doses of melatonin cause sleepiness when administered in the daytime and can shift the circadian phase, which is the goal of treatment.

It is interesting that melatonin is very sensitive to light exposure. When a patient is administering melatonin to themselves, we have to make sure that they are taking it in a dim environment. Light in the home at night will completely negate the effect of melatonin. When patients accept the need to have their circadian rhythm disorder treated and they have accepted the idea of taking melatonin, we must impress upon them that they also need to have dim light when they take it. Once patients have taken their melatonin, recumbency seems to improve the efficacy versus being up and moving around.

When administering melatonin, the appropriate timing relative to the

circadian rhythm of the individual is paramount. For this reason it is important for you to do estimates of at least the dim light melatonin onset. You will induce the opposite effect if you give melatonin at the wrong time. Lower doses are preferable so that you can target phase shifting more specifically. Higher doses of melatonin given in the afternoon can actually be sedating or soporific. If you dose melatonin in the afternoon, you may actually induce a nap period, which is counterproductive to your goals.

Melatonin can have hypnotic effects but they are weak. Our goal is to try to shift a patient's circadian phase. That is exactly why hypnotic medication does not work very well in circadian rhythm disorders. In that circumstance you are forcing patients to sleep at an hour when the body really does not want to sleep. It is good for patients to have some recovery sleep but that is not optimal sleep. We want to be sleeping in sync with the phase of our body being in the physiologic state for sleep. That is what alignment is about. It is not about inducing sleep or inducing an hypnotic effect.

If you try to give melatonin at bedtime it has a zero effect. Melatonin at bedtime does nothing for shifting circadian phase. In the circumstances of the 3 milligram dose you have to administer the melatonin 5 hours before the dim light melatonin onset, which is 7 hours before the habitual bedtime. And the 0.5 milligram dose you need to administer it 5 hours before habitual bedtime. It is counterintuitive. If the goal is for a person to go to bed at 10:00 p.m. we want to give the 0.5 milligram dose at 5:00 p.m., and we want to give the 3 milligram dose at 3:00 p.m. To summarize, the peak phase occurs about 2 hours later relative to the dim light melatonin onset with the 0.5 milligram dose. Maximum advances occurred when 0.5 milligram was taken about 3 hours before dim light melatonin onset or 5 hours before habitual sleep onset. The maximum advance for the 3 milligram dose occurred 5 hours before dim light melatonin onset or 7 hours before habitual onset. Both doses produce similar sizes and advances. It is important to understand how to dose melatonin to get the desired effect.

An interesting study looked at the concept of melatonin as a hypnotic medication. Patients were put on a forced dysynchronous schedule where they were sleeping for 6.7 hours and awake for 13 hours creating a 20-hour day. This allowed participants to take melatonin at times when their endogenous levels of melatonin were low, high or normal. When you give melatonin exogenously in periods when endogenous levels are high, it has no impact on sleep induction because your endogenous melatonin is already creating the maximum effect. However, in periods of the circadian rhythm when you have a low endogenous melatonin level, even low doses of melatonin have a hypnotic effect. The bottom line is that melatonin is a very good drug to induce a nap but it is not a very good drug as a hypnotic medication at bedtime because your endogenous melatonin is going to take care of that.

There have been limitations to the development of melatonin as a prescription drug in the United States. Why is that? It is because similar doses of melatonin can produce different hypnotic effects, depending on the time that it is administered. It is really time-sensitive. The time sensitivity issue is very hard in terms of patient compliance and study design. Subjects often report that they can fight off the sleepiness that they feel with melatonin in a way that you do not see with typical hypnotic medications. I do not recommend melatonin as a hypnotic medication. It does not have an impact on sleep architecture in any stage of sleep.

Ramelteon (Rozerem) is the only FDA approved drug for sleep that has action at melatonin receptors. Ramelteon was approved by the FDA but only for insomnia. It has not been approved for circadian rhythm disorders. The only dose that is currently available is 8 milligrams. An abstract published in 2006 described that 1, 2 and 4 milligram doses of rozerem had a better response in phase shifting than an 8 milligram dose. This action might be similar to what we see with standard melatonin when high doses will spill over into phases of the circadian rhythm that we do not want to target. That is nearly all the information that exists. I do not recommend that you use rozerem for patients with circadian rhythm disorder. It is much more effective to use melatonin at the appropriate dosing time.

In Europe, there is a drug called Circadin made by an Israeli pharmaceutical company. Circadin is 2 milligrams of prolonged-released melatonin. It is approved by the European regulatory agency and is also approved for use in New Zealand. It is only indicated in patients over 55 years of age. Because levels of melatonin decline so much in old age, it was thought that a replacement concept may be an effective strategy. Clinical trials were based on that presumption. The drug had some modest benefit, enough to meet the criteria for European approval but Circadin is not approved for use in the U.S. If you are curious about clinical trials, visit clinicaltrials.gov. Some trials are recruiting patients.

In summary, taking exogenous melatonin at bedtime will have minor effect on circadian phase. If you take exogenous melatonin near the end of your sleep period it will delay your sleep phase and make you want to go to sleep later on future nights. The largest advance of phase shifting with exogenous melatonin occurs when there are low levels of endogenous melatonin. That is why we administer melatonin relatively early in the evening or late afternoon. The smaller dose should be taken about 2 hours before the 3 milligram dose which means 5 hours prior to typical sleep onset and 7 hours prior to typical sleep onset if using the 3 milligram dose. We do not have dose response curve to answer more specific questions relating to dosages of 5, 6, and 10 milligrams.

What is bright light therapy? Bright light therapy refers to the daily expo-

sure to bright, full, or limited spectrum artificial light. And the term bright light therapy is distinguished from phototherapy. Phototherapy is used in dermatology and in the NICU for newborns to reduce hyperbilirubinemia. The initial use of bright light therapy was in the field of psychiatry in 1981 and arose from circadian rhythm hypotheses for seasonal and nonseasonal depression. The most potent frequency of light that will impact on the release of melatonin and the shifting of melatonin is green light at 509 nanometers. When we talk about limited spectrum light, what we should target is green light. Blue light is effective in some ranges but it is not as potent as green light. Broad spectrum light is also effective and more available but it is not going to have the impact of green light.

A general principle with light therapy, which is the most potent mover of your circadian rhythm, is that it is going to be easier to phase delay. We can phase delay an individual by about 2 hours per day with appropriately timed light therapy. We can only advance a sleep phase by an hour to an hour and a half. When we fly west we are delaying our sleep phase rather than advancing it. This is one of the reasons why it is easier for us to fly west. When we fly east, we are advancing our sleep phase and we cannot do that as quickly. We recover from our jet lag more quickly when we go west for a few time zones. When we advance many time zones in either direction, that creates an extreme scenario but, in general, it is going to be easier for us to adjust when we fly east to west.

If you have a very large phase advance it might be more effective for you to actually phase delay around the clock. This is the principle behind chronotherapy. Chronotherapy is actually progressively delaying your sleep phase. For example, if a patient is going to sleep at 3:00 in the morning and waking up at 1:00 p.m. and you want to eventually move them closer to 11:00 p.m. bedtime, you would have them go to bed 2 hours later every night, consecutively. Bedtime would be 3:00 a.m., 5:00 a.m., 7:00 a.m., 9:00 a.m., et cetera around the clock. It is very difficult to do chronotherapy in the opposite direction because our natural circadian rhythm is a little bit longer than 24 hours. If you are going to use chronotherapy, you have to have a person commit to a week or ten day schedule. Typically, teenagers love this. On spring break or summer vacation, I have used that to their benefit. Because teenagers see this process as a little rebellious, and a little out of the realm of the ordinary, they embrace it. If you do not have the time to commit to chronotherapy, it is really very difficult and can be disruptive to the social interactions of the patient.

When applying bright light, what effect is it going to have on shifting sleep phase? If you apply bright light after the core temperature minimum, you are going to advance the sleep phase or push it earlier in the night. If you apply bright light before the core temperature minimum, you are go-

ing to actually delay the sleep phase. This can be problematic if you have a patient who is really sleep phase delayed. They are getting up at 1:00 in the afternoon and they may have their core temperature minimum at 11:00 a.m. If you tell them to use bright light therapy at 7:00 a.m. when they get up for work, what are you doing? You are delaying their sleep phase. Think about this concept carefully when you are applying bright light therapy or else you will create the opposite effect.

What are some of the parameters of light therapy? First of all, the intensity is important. It is generally measured in lux, which is a photometric unit of illuminance. The lux is not an absolute value. It depends on the distance from the light source. When you buy a light box and it says 10,000 lux, you have to ask at what distance? For example, 10,000 lux at 24 inches is not going to be the same as 10,000 lux at 48 inches. In fact, the lux intensity varies as the inverse square of the distance. The intensity drops off quickly the further away you get from the recommended distance. If you are going to use limited spectrum light make sure it has green light because green is the most potent.

The duration of exposure depends on the dosage. Typically, 10,000 lux is recommended for 30 minutes. That dose is just as effective as 2500 lux for 2 hours but you will have compliance problems if you ask people to sit in front of a light box for 2 hours. I think 10,000 lux at 30 minutes is the target when you are using light therapy for circadian rhythm disorders. The timing of the light exposure determines the direction of the phase, whether it is delay or advancement.

A typical fixed light box is 10,000 lux at 24 inches. It is fluorescent. It is important that it have a filter for UV spectrum because the light is damaging to the eyes. This kind of device typically costs about \$289.00. The limitations with these kinds of light boxes is they are a fixed device but the patient is not. Patients are moving about in the morning. They might be getting ready for work and they might not maintain a gaze to keep a constant dose. Second, it is inconvenient to be fixed in a certain position. What do you do in those circumstances? We use a more mobile device like a light visor specific with green light at 8,000 to 12,000 lux. The beauty of this device is that it can go in anybody's visor or the bill of a baseball cap. No matter which direction the person moves, it keeps the light at the appropriate orientation to their eyes.

You generally see a response to light therapy within two to four days but do not consider a trial adequate until after two to four weeks. Light therapy is a fairly rapidly titrating process. There are no absolute contraindications to light therapy but there are certain individuals at higher risk that we have to consider. Typical side effects, if they occur, include headaches and eye strain. If you have a bipolar patient or someone prone to hypomania or agi-

tation, light therapy can be activating but the therapy can be quickly stopped. Educate patients at risk prior to light therapy, and have them immediately stop the therapy if they have side effects. The effect of the light therapy will diminish much more quickly than, for example, withdrawing a medication. It is very uncommon for patients to discontinue treatment for side effects from light therapy but I do want you to be aware of potential concerns. All patients considering light therapy should be asked about previous eye conditions or retinal disease. If there is a positive history of preexisting retinal disease, systemic illnesses that affect the retina, or cataract surgery and lens removal, a base line ophthalmological examination should be done. Elderly patients who may have a greater risk of age-related macular degeneration should also be referred for an ophthalmic evaluation.

We often see patients that have post-traumatic brain injury with headaches and photosensitivity. Many of these patients use tinted lenses chronically which impairs their circadian rhythm. Patients with severe photophobia who wear darkly tinted lenses should be encouraged to reduce dark adaptation. They are denying the brain's ability to entrain to light daily by walking around in dark glasses. Often they also have a hat on to block light from above. This behavior can perpetuate and aggravate a circadian rhythm disorder because of excessive exposure to dim light when what patients need is bright light. This scenario will progressively delay sleep phase in the morning. Wearing sunglasses chronically and blocking out light increases the perception and the pain of light sensitivity. This behavior can significantly impact an individual's circadian rhythm cycle.

There are some common themes to evaluation and treatment of circadian rhythm disorders. All diagnoses except jet lag disorder require at least 7 days of actigraphy monitoring or sleep logs. The goal is to create alignment between circadian phase and social and work requirements. We want the circadian phase to be wakefulness when you have to be awake. And we want to be sleeping in the hours that the circadian phase is promoting sleep. When there is a misalignment, sleep is never going to feel restorative.

Light is the most potent shifter of the sleep phase and should be considered as the first-line treatment with the exception of patients with bipolar disorder. Treatment includes both the application of bright light at the appropriate phase of the circadian rhythm but also dim light at the opposite end. When we are talking about advancing a sleep phase, we want bright light in the morning but we also want dim light at night. If we want to advance a sleep phase or delay the sleep phase, we want bright light at night and dim light in the morning. Think about dim light as the opposite of your bright light therapy and an equally important aspect of maintaining the stability of the circadian rhythm.

Exogenous melatonin is effective and works as a complementary coun-

terpart to light therapy. Chronotherapy works well for teenagers who are on vacation but is very difficult to do in adults with work responsibilities. You will apply bright light in the morning in order to advance the sleep phase. You will apply melatonin at night in order to advance the sleep phase. If you give melatonin in the morning time after the core temperature minimum, you will delay the sleep phase. If you apply light before the core temperature minimum, you will delay the sleep phase. Phase shifts are critically determined by the timing that you administer the treatment.

Here is a specific example illustrating delayed sleep phase disorder. Typically the patient presents with difficulty going to sleep. This may make you think that they have insomnia but they also have difficulty getting up because the hour that they have to arise is not when their circadian rhythm wants them to get up. When they are allowed to sleep on their own schedule, the preferred schedule, they have no complaints of sleep quality or duration. A typical patient would be someone who cannot go to sleep before 1:00 a.m. or 6:00 a.m., and they may sleep from 9:00 until 2:00 p.m. When they sleep during those hours, they feel great and have no complaints but they may have to get up at 7:00 in the morning to go to work or to go to school.

I have just described the most common circadian rhythm sleep disorder. The estimated prevalence in the general population is 0.2% but prevalence in the adolescent population is 7 to 16 percent. This is what you will see in your practice. We are talking about a disorder imposed in an adolescent population who typically has to get up fairly early during the school year. This creates very real problems.

There are non-photic influences on the circadian rhythm that may be behavioral. Not every single adolescent who goes to bed late has this but it is fairly easy to remove the non-photic or behavioral influences such as playing video games late at night, chatting with their friends, having their social time through their iPad, and spending time on their computer. When you remove non-photic influences, children who truly have circadian rhythm disorder are still going to want to go to sleep later and get up later. The children that have the behavioral aspects will see improvement in the alignment of their sleep phase.

It has been estimated that 5–10% of patients that present with chronic insomnia actually have delayed sleep phase disorder. It is important to ask patients about their quality of sleep when they are able to sleep the hours that they want. Is their sleep improved or do they still report insomnia? Treatment for insomnia is very different from treatment for delayed sleep phase disorder.

Several studies indicate there is a genetic predisposition for delayed sleep phase disorder in certain individuals. Typically, these patients will present in childhood. For example, these are the 4 year old children that go to sleep

at 1:00 in the morning. These patients may require lifelong therapy because they have a genetic defect.

There seem to be higher rates of delayed sleep phase disorder in patients with traumatic brain injury (TBI) but the data is very limited. In a sample of 42 patients with mild TBI and insomnia, 17% of them had delayed sleep phase disorder. Prevalence in the general population is 0.2 percent.

Patients with psychiatric comorbidities are also at higher risk. The prevalence rate of delayed sleep phase disorder is 17–42% in populations with obsessive compulsive disorder. Adolescents with comorbid depression and delayed sleep phase disorder are very difficult to treat. Adolescents who do not have comorbid depression usually have a rapid response to light therapy and melatonin. Finally, there is an increased rate of seasonal affective disorder in patients that have delayed sleep phase disorder. Delayed sleep phase disorder is partially comorbid with seasonal affective disorder.

In conclusion, an example treatment approach to delayed sleep phase disorder was described: We have a patient who has average sleep onset of 2:00 a.m. calculated by actigraphy or sleep logs. They wake up at 10:30 a.m. on weekends. Their estimated temperature minimum occurs at 8:30 a.m. Their estimated dim light melatonin onset is 12:00 a.m. The desired rise time is 7:00 a.m. on weekdays for work. You want to advance their sleep phase by applying bright light therapy at 9:30 a.m. for one hour and advance 30 minutes each day to target wake up time. It is best to commence this therapy on the weekend. You do not allow them to retreat to darkness or dim light following the bright light pulse. Then, very specifically, you would give melatonin, 0.5 milligrams at 9:00 p.m. based on the dim light melatonin onset estimate and advance at 30 minute intervals per day to a target of 6:00 p.m. This process would target a sleep onset of 11:00 p.m.

Speaker Biographies

Samuel A. Fleishman, MD

Dr. Fleishman is Director, Cape Fear Valley Sleep Center in Fayetteville, NC. The Sleep Center staff treats a variety of sleep disorders, including sleep apnea, insomnia, narcolepsy, periodic limb movement disorder and restless leg syndrome. The Sleep Center is accredited by the American Academy of Sleep Medicine and The Joint Commission.

Dr. Fleishman graduated from the East Carolina University School of Medicine and completed his Psychiatry residency at the Medical College of George where he also completed a fellowship in Sleep Disorders. He is board certified in Psychiatry & Neurology/Sleep Medicine.

Christopher J. Lettieri, MD, FACP, FCCP, FAASM Lieutenant Colonel, Medical Corps, US Army

Christopher J. Lettieri, MD is Professor of Medicine and currently serves as Assistant Deputy Commander for Medicine and Sleep Medicine Fellowship Program Director at Walter Reed National Military Medical Center. Dr. Lettieri received his Doctor of Medicine degree from the Uniformed Services University of the Health Sciences. He completed his residency in Internal Medicine at Tripler Army Medical Center and received his fellowship training in Pulmonary, Critical Care and Sleep Medicine at Walter Reed Army Medical Center.

Prior to his current position, Dr. Lettieri has served as the Chief of Medical Residents, medical liaison to the US Secret Service and FBI Hostage Rescue Team, a team leader for the US Army Special Medical Augmentation Team, Chief of Critical Care for the 14th Combat Support Hospital during Operation Enduring Freedom, and the Chief of Walter Reed's Sleep Disorders Center. He was previously the Chair of the American Thoracic Society's section of Terrorism and Disaster Medicine and the Chair of the American Academy of Sleep Medicine's Education Committee.

Dr. Lettieri has received several teaching, research, and achievement awards. Most recently, these include the Surgeon General's Physician Recognition Award, the Admiral James Zimble Award for the Outstanding Pro-

gram Director, The Major General Lewis A. Mologne Award for Outstanding Academic Medicine, the William Crosby Excellence in Research Award, and the Faculty Teacher of the Year Award. He is a recipient of the US Army's "A" proficiency designator and was selected into the Order of Military Medical Merit. Dr. Lettieri has received several military awards, to include five Meritorious Service Medals, and seven Army Commendation medals.

Greg W. Morgan, MD

Dr. Morgan is Medical Director, Sleep Laboratory at National Intrepid Center of Excellence. He is board certified in neurology, electrodiagnostic medicine, as well as sleep medicine. After graduating from Johns Hopkins University School of Medicine in 1989, he completed his internship in Internal Medicine and residency in Neurology at Lackland Air Force Base. Dr. Morgan completed a fellowship in Clinical EMG/Neuromuscular Disease at Cleveland Clinic. The focus of Dr. Morgan's career has been in the practice of neurology with a subspecialty focus in sleep disorders. Additionally, he has served as the Medical Director at Solstice Pharmaceuticals, as Assistant Professor of Neurology at the Uniformed Services University, published various publications in the field of neurology, and served as medical director of several sleep labs.

Brett J. Schneider, MD

Colonel Brett J. Schneider, MD is Deputy Commander for Behavioral Health, Walter Reed National Military Medical Center, Bethesda, MD. He also serves as the appointed Child and Adolescent Psychiatry Consultant to the US Army Surgeon General. Dr. Schneider graduated from Creighton University with a co-major of Biology and Philosophy. He attended Creighton University School of Medicine and after graduation he did his psychiatry residency and a child and adolescent psychiatry fellowship at Walter Reed Army Medical Center. After completing his training, Dr. Schneider served as the Division Psychiatrist for the 1st Infantry Division in Vilseck Germany for two years before returning to Walter Reed to do a fellowship in Forensic Psychiatry. He served two tours in Iraq for Operation Iraqi Freedom. Dr. Schneider served as the Chief of Telepsychiatry and the Chief of Child and Adolescent Psychiatry prior to being named the first Chief of Psychiatry, WRNNC.

Rear Admiral Alton L. Stocks, U.S Navy Medical Corps

Born in Baltimore, Rear Adm. Stocks comes from a family with careers in medicine and the military.

Graduating from the U.S. Naval Academy with a Bachelor of Science degree in Mathematics in 1972, Stocks completed the Navy's Nuclear Power

Training and Submarine School prior to serving on USS Andrew Jackson (SSBN 619) and USS Long Beach (CGN 9).

Stocks transferred his commission to the Medical Corps and received his medical degree from Georgetown University School of Medicine. Stocks commanded Naval Hospital Corpus Christi and its clinics in Fort Worth, Ingleside and Kingsville, Texas. In October 2007, he served his first flag officer tour as the U.S. Fleet Forces fleet surgeon and deployed as the Joint Task Force Haiti surgeon in January 2010. In May 2010, Stocks transitioned to commander, Navy Medicine East and Naval Medical Center Portsmouth. In September 2011, he assumed command of Navy Medicine National Capital Area and Walter Reed National Military Medical Center at Bethesda.

His personal awards include the Legion of Merit (5), Defense Meritorious Service Medal, Meritorious Service Medal, Joint Commendation Medal, Navy Commendation Medal, Humanitarian Service Medal, Sea Service Deployment Ribbon, Overseas Deployment Ribbon (7), and he is designated as a surface warfare medical officer.

Robert J. Ursano, MD

Robert J. Ursano, MD, is Professor of Psychiatry and Neuroscience and Chairman of the Department of Psychiatry at the Uniformed Services University of the Health Sciences, Bethesda, Maryland. He is founding Director of Center for the Study of Traumatic Stress. In addition, Dr. Ursano is Editor of *Psychiatry*, the distinguished journal of interpersonal and biological processes, founded by Harry Stack Sullivan. Dr Ursano completed twenty years of service in USAF medical corps and retired as Colonel in 1991. He was educated at the University of Notre Dame and Yale University School of Medicine and did his psychiatric training at Wilford Hall USAF Medical Center and Yale University.

Dr. Ursano served as the Department of Defense representative to the National Advisory Mental Health Council of the National Institute of Mental Health and is a past member of the Veterans Affairs Mental Health Study Section and the National Institute of Mental Health Rapid Trauma and Disaster Grant Review Section. He is a Distinguished Life Fellow in the American Psychiatric Association. He is a Fellow of the American College of Psychiatrists. Dr. Ursano was the first Chairman of the American Psychiatric Association's Committee on Psychiatric Dimensions of Disaster. This work greatly aided the integration of psychiatry and public health in times of disaster and terrorism. Dr. Ursano was an invited participant to the White House Mental Health Conference in 1999. He has received the Department of Defense Humanitarian Service Award and the highest award of the International Traumatic Stress Society, The Lifetime Achievement Award, for "outstanding and fundamental contributions to understanding traumatic

stress.” He is the recipient of the William C. Porter Award from the Association of Military Surgeons of the United States, and a frequent advisor on issues surrounding psychological response to trauma to the highest levels of the US Government and specifically to the Department of Defense leadership.

Dr. Ursano has served as a member of the National Academies of Science, Institute of Medicine, Committee on Psychological Responses to Terrorism, Committee on PTSD and Compensation and the Committee on Nuclear Preparedness; and the National Institute of Mental Health Task Force on Mental Health Surveillance After Terrorist Attack. In addition he is a member of scientific advisory boards to the Secretary of Health and Human Services and the Centers for Disease Control. In 2012, Dr. Ursano was awarded the William C. Menninger Memorial Award for distinguished contributions to the Science of Mental Health by the American College of Physicians. Dr. Ursano has more than 300 publications. He is co-author or editor of eight books.

Harold J. Wain, PhD

Dr. Harold Wain PhD, FAPM, is Chief of the Psychiatry Consultation Liaison Service at Walter Reed National Military Medical Center. He is also a Professor in Department of Psychiatry at the Uniformed Services University, Bethesda, Maryland. Dr Wain was Chief of the Psychiatry Consultation Liaison Service at Walter Reed Army Medical Center. He has previously been Director of the Psychiatry Consultation Liaison Service and the Director of the Psychosomatic Clinic. Dr. Wain has also been Chief of the Psychology Service at Walter Reed Army Medical Center.

Dr. Wain completed his clinical training at Walter Reed Army Medical Center. He has published and lectured extensively both nationally and internationally in the areas of Psychosomatic Medicine, Hypnosis, Somatoform Spectrum Disorders, Trauma, Pain, and Consultation Liaison Psychiatry.

Emerson Wickwire, PhD

Dr. Emerson Wickwire is Sleep Medicine Program Director at Pulmonary Disease and Critical Care Associates in Columbia, Maryland, and serves Assistant Professor, part-time, at Johns Hopkins School of Medicine, where he completed a two-year postdoctoral fellowship in sleep. Dr. Wickwire is board certified in both behavioral sleep medicine and cognitive and behavioral psychology. A recognized expert in the non-drug treatment of sleep disorders and comprehensive approaches to managing chronic disease, Dr. Wickwire has a particular interest in leveraging technology to improve patient care.

Dr. Wickwire has published over two dozen peer-reviewed scientific ar-

ticles, book chapters, and scientific abstracts, and has served as an editor for numerous academic publications. He currently serves on the education committees for both the American Academy of Sleep Medicine and the National Sleep Foundation. Dr. Wickwire is an active and award-winning medical educator.

Michael R. Yochelson, MD

Michael R. Yochelson MD is Vice President of Medical Affairs and CMO for the MedStar National Rehabilitation Network. He is a highly-trained and qualified board certified neurologist and physiatrist.

Dr. Yochelson is a graduate of the George Washington University School of Medicine and Health Sciences and completed his residency training at the National Capital Consortium. Previously, he served as a staff physician in the Navy and has a particular interest in headaches, post-traumatic epilepsy, sleep dysfunction, and spasticity management after traumatic brain injury.

Currently, Dr. Yochelson serves on the Board of Directors for the Brain Injury Association of Washington, D.C. and is an active member of the Brain Injury Association of Maryland. He is a Professor of Clinical Neurology and Clinical Rehabilitation Medicine at Georgetown University in Washington, D.C. He has worked with the RAND Corporation, studying traumatic brain injury in service members returning from deployment. Dr. Yochelson has also served on an FDA Scientific Advisory Board pertaining to the Orphan Products Grant Program.

Dr. Yochelson has received numerous awards, including the Outstanding Educator Award in Physical Medicine & Rehabilitation, Georgetown University/National Rehabilitation Hospital (2008) and the Edward A. Eckenhoff Leadership Award, National Rehabilitation Hospital (2009). Dr. Yochelson is recognized as one of the “Top Rated Doctors” in Northern Virginia (2010 & 2011) and as a “Top Doctor” in *U.S. News* (2011–2013).



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