Factors Altering the Sleep of Burned Children

Mary Rose PsyD,1 Art Sanford MD,1 Christopher Thomas MD,2 and Mark R. Opp PhD2,3

1Shriners Burns Hospital, Galveston, TX 77555-0803 USA
2Department of Psychiatry and Behavioral Sciences, University of Texas Medical Branch, Galveston, TX 77555-0431 USA 3Present Address: Department of Anesthesiology, University of Michigan, Ann Arbor, MI 48109-0651

Abstract: Although few studies have been conducted on burn patients, they indicate that sleep of burned children is altered. We suggest in this review, on the basis of the limited data available that factors contributing to sleep disruption in burned individuals may be broadly categorized as pathophysiological responses to the injury, the pain and discomfort experienced by the patient and medications used to treat these symptoms, and the physical environment in the Burns Intensive Care Unit. The responses to thermal injury include alterations in circulating neuropeptides, hormones, and immune-active substances, many of which are known to regulate/modulate sleep. Medications for the management of pain and for treating symptoms of various injury-induced stress and anxiety disorders may also alter sleep. Finally, frequent disruptions of the patient by medical staff is but one of the many environmental factors that may contribute to disrupted sleep. Severe burns induce a hypermetabolic response that may result in peripheral wasting, that depletes substrates necessary for tissue repair, and is associated with reduced growth hormone. Burn-induced growth hormone insufficiency is aggressively treated to counteract peripheral wasting and to aid in wound healing of skin graft donor sites. We speculate that improvement of sleep quality would result in a less severe reduction in growth hormone due to the well documented relationship between slow-wave sleep onset and growth hormone secretion. Such improvement in spontaneous growth hormone secretion patterns may aid in recovery by supporting tissue repair and by minimizing the hypermetabolic response to thermal injury. The experiments to test such hypotheses remain to be conducted, yet the results of such experiments may provide the basis for beginning to answer the question of whether or not sleep aids in recovery from injury.

Key words: Growth hormone; cytokine; wound healing; trauma

INTRODUCTION

SLEEP IS A COMPLEX BEHAVIOR THAT IS REGULATED BY INTERACTIONS OF MULTIPLE ANATOMICAL AND NEUROCHEMICAL SYSTEMS WITHIN THE CENTRAL NERVOUS SYSTEM (CNS). Although sleep is a CNS phenomenon, it is susceptible to alteration by stressors that originate outside the CNS. These peripheral stressors may include infection, inflammation, tissue injury or trauma, to name but a few. The modalities by which these stressors impinge on the organism differ, and the degree to which sleep and other behaviors is altered depends to a large extent on the magnitude, timing, and extent of the stressor and the resulting damage. We now know there are several mechanisms by which stressor-induced alterations in the homeostasis of peripheral systems may be detected by the CNS with subsequent effects on sleep.1 These mechanisms include actions of various neuropeptides, hormones, and immune-active substances such as cytokines, as well as direct neural inputs such as those emanating from the vagus nerve. There is a relatively large literature detailing mechanisms by which sleep may be altered in response to infection.2 Much less effort however, has been devoted to determining mechanisms and factors responsible for altering sleep in response to other types of insult. In this review, we focus on alterations in sleep following burn. There have been few studies to date that focus on the effects of this type of trauma on sleep. We first present some demographic information concerning the incidence and treatment of severe burns. We then review the limited information available on this topic and suggest potential factors that may mediate burn-induced alterations in sleep.

The Shriners Burns Hospital in Galveston is one of four pediatric burn hospitals sponsored by the Shriners Hospitals of North America. These hospitals provide free care to children, from birth through age 21. In recent years, the Shriners Burns Hospital at Galveston has become the most active of the four Shriners Burns Hospitals, due primarily to a shift in patient referral base that now includes a significant population from Mexico. During the last decade, the Shriners Burns Hospital in Galveston has averaged 204 acute admissions annually, although this number appears to be increasing; in 1998, there were 236 new acute patients treated; in 1999, 282 new acute patients were treated. Based upon review of medical records at Shriners Burns Hospital in Galveston, the total body surface area (TBSA) burn of patients admitted in 1999 covered about 28.4 % (± 0.3 % SEM), up from about 23% in 1990. During the four year period 1990 to 1994, the number of catastrophic (greater than 80% TBSA) burn patients treated at the Galveston Shriners Burns Hospital ranged from four to nine per year. The number of admissions of patients with catastrophic burns in our hospital increased sharply during the years of 1995 and 1999, when from six to sixteen catastrophic burn patients were treated annually. The reasons for increases in TBSA burn size and in the numbers of catastrophic burns are not known. One reason may be more rapid transportation of catastrophic burn patients to burn centers. In addition, our hospital is now receiving referrals from hospitals in Mexico and...
Alterations in the sleep of burned children

Although there have been few studies that have specifically investigated the effects of large thermal burns on sleep, it is clear that pediatric burn patients suffer severe sleep disturbances. To date, there is only one polysomnographic study of the sleep of burned children of which we are aware. This study was conducted by Gottschlich and colleagues at the Cincinnati Shriners Burns Hospital. These investigators obtained recordings from 11 acutely burned children 1.4—16 years of age (mean 8.3±1.5 years) with an average TBSA burn of 55.1±6.5% (range 17.5%—90.5%). They used continuous 24-hour monitoring and generated 43 records for the 11 subjects (though 14 of the 43 evaluations were obtained from one child). All parameters measured exhibited a large amount of variability. Total sleep time (TST) averaged 625.1±31.6 min/patient/24-h (range: 509.1±52.2 min /24-h—940.8±103.1 min/24-h), an amount greater than age- and gender-matched control subjects. These increases in TST were due to large increases in stage 1 (87.1±11.9 min/patient/24h) and stage 2 (423.8±34.1 min/patient/24-h) sleep, which were 505% and 141% of age and gender norms, respectively. However, these increases in stage 1 and stage 2 sleep were accompanied with a reduction in amounts of the deeper, more restorative stages 3 and 4 slow wave sleep (50.4±10.9 min/patient/24-h) and in REM sleep (63.8±9.4 min / patient/ 24-h), which represented 35% and 40% of amounts exhibited by control subjects, respectively. In addition to alterations in the amount of time spent in sleep stages, there was an increase in number of arousals, which averaged 62.9±7.0/patient/24-h. As such, sleep alterations in burned children are characterized by both changes in duration in state and fragmentation.

In addition to the polysomnographic sleep study, patient self-reports and/or observed estimation of sleep by nursing staff have been used to determine the effects of burn on sleep. Kravitz et al. used information obtained from self-reports of 82 children and adolescent burn patients, 30 months to 20 years of age (mean 11.8 years) to determine that sleep disorders persist at home for at least one year after discharge from the hospital. Common self-reported nighttime sleep disturbances included nightmares (37%), bed-wetting (24%), and sleep-walking (18%). No relationship was detected between the factors of age at time of burn, length of time after burn injury, or cause of burn injury and any of the aforementioned sleep disturbances. It is of interest to note however, that 50 subjects (63%) reported daytime napping, although 46 of these 50 individuals were well beyond the normal age for napping (mean age: 11.7 years). Information about sleep disturbances obtained from self-reports of burn patients may not correlate with observations made by nursing staff trained on visual judgement and quantitation of sleep. Dotson et al. report a low correlation between nursing reports and patient self-reports on sleep quality. Such low correlations may be due to the burn patients inability to remember multiple awakenings, they may have a poor concept of time as a result of the trauma, or nursing staff may be too busy to accurately and consistently determine when subjects are awake or asleep. In a study of 237 adult burn patients, Lawrence and colleagues report that responses to sleep items on the Beck Depression Inventory and the Davidson Trauma Scale indicate that 50% of patients complained of sleep disturbance while in the hospital, and this number was only moderately reduced to 40% two months after discharge. Although the limitations of such types of studies must be recognized, information from self-reports and/or observations of sleep by trained staff corroborate polysomnographic findings and intuition; sleep is disrupted in individuals subjected to burn trauma.

Although there is limited information about the precise sleep alterations of children subjected to severe burn, results of studies conducted in other Intensive Care Units (ICUs) may contribute to an understanding of how extended stays in an ICU might influence sleep alterations observed in response to severe burns. Sleep studies conducted in ICUs have focused primarily on how sleep is altered by the hospital environment, factors related to the specific illness and its treatment, and less so on the potential importance of sleep in recovery from illness or surgery. Sleep restriction is believed to be a prominent feature associated with stays in a variety of inpatient units, including pediatric intensive care, medical intensive care, cardiac care, cardiac step down, and surgical intensive care. Though some studies report total sleep times that are near normal, studies that use polysomnography frequently indicate shortened episodes of REM sleep and stages 3 and 4 slow-wave sleep, that may or may not be accompanied by increases in stage 1 sleep. Generally, sleep of infants and toddlers in ICUs is fragmented, and sometimes severely restricted. In a study of pediatric intensive care unit patients age 15 months to 10.5 years (mean, 4.7), Cureton and Fontaine report that increased fragmentation due to frequent awakenings results in sleep restriction, which in this study reduced total sleep time to a mean of about 4.7 hours/patient/night. Compared with their sleep at home, sleep of these patients when in the ICU was reduced by more than 50%. Sleep of adults in ICUs has also been studied, with generally similar findings that total sleep time is reduced. ICU patients frequently obtain less total sleep due to reductions in stages 3 and/or 4 slow-wave sleep and REM sleep.
that may or may not be accompanied by increases in stage 1 sleep.10 Chronic sleep restriction may lead to cognitive and emotional impairment, and has for many years been recognized as a potential problem for patients in ICUs. The effects of prolonged sleep deprivation may result in what has been referred to as the “ICU syndrome” or “ICU psychosis.”11 Symptoms of the ICU syndrome include delirium and emotional lability, and it is possible that ICU patients may be misdiagnosed or mismanaged when exhibiting these symptoms.

Based upon the few studies that have been conducted of burn patients, and findings on disturbed sleep in patients in other ICUs, sleep appears to be (severely) disrupted in burned children. Thus, it is important not only to determine more fully the extent to which sleep of burned children is disturbed, but to also determine the potential causes of disordered sleep so that interventions may be developed that will improve the quality of sleep for these patients. Although it is intuitive that sleep should promote recovery, to date there is no empirical evidence to support this hypothesis with regards to trauma, although there are limited data suggesting sleep may aid in recovery from infection.12 Nevertheless, even if there is presently a lack of evidence supporting the notion that sleep facilitates recovery per se, it seems likely that improved nighttime sleep quality would contribute to improved daytime functioning. The first step in addressing this issue is to determine to what magnitude particular factors contribute to disrupted sleep. Although there are many factors that contribute to the sleep disturbances of burned children, they can be generally classified into three broad categories: a) pathophysiological responses to the injury itself, b) patient discomfort, pain, acute stress disorder, and the medications used to treat these symptoms, and c) environmental factors associated with prolonged stays in the ICU.

Factors contributing to sleep disturbances of burned children

Pathophysiological responses to thermal injury: Severe full thickness thermal burns result in substantial cutaneous wounds and multiple systemic physiological alterations. The constellation of hormonal and metabolic responses result in hypermetabolism, weight loss, poor wound healing, and susceptibility to infection.13

There is a tonic and dramatic increase in metabolic rate after an acute burn, sometimes by as much as 100%.14 In addition, the changes in metabolism normally associated with sleep—wake behavior do not appear to be present in acutely burned children,15 perhaps due to disturbed sleep and circadian rhythms. There are several hormones that have secretory patterns normally associated with sleep-wake behavior, that are known to modulate/influence sleep and whose secretory patterns may be altered either in direct response to burn, or as a secondary response to environmentally-induced alterations in circadian rhythmicity. These include growth hormone (GH), cortisol, and prolactin.16-19 We focus on GH because it was the first hormone for which a sleep-related secretory pattern was described, because burned children exhibit GH insufficiency, and GH is commonly used as part of the treatment regimen for burn patients.

Beneficial metabolic effects for GH have been for some time demonstrated in burn patients.16 GH is a potent anabolic agent that induces net protein synthesis directly, or indirectly through the actions of insulin-like growth factor-1 (IGF-1). The systemic effects of GH administration include increased appetite, decreased nitrogen loss, increased retention of nitrogen and potassium, weight gain, more rapid wound healing, increased oxygen utilization, and decreased respiratory quotient.20 In a study of burned adolescents that were hypermetabolic and had burns covering approximately 70% TBSA, GH administration (0.2 mg/kg/day) increased both protein synthesis and degradation, but protein synthesis exceeded degradation and resulted in a 50% net reduction in protein loss compared to control patients.21 Other benefits of GH administration to burned individuals include actions of GH on skin. Skin is a target for GH, either by direct receptor-ligand interactions on the surface of epidermal and dermal cells, or indirectly via circulating IGF-1.22 GH increases collagen content and tensile strength of skin and granulation tissue in animal models.23 Use of GH at 0.2mg/kg/day in massively burned children accelerates wound healing of skin graft donor sites.24 This means that surgical procedures for the grafting of skin may be done at shorter intervals and translates to a substantial reduction in the amount of time it takes for a burn wound to heal. For example, in one study the closing of a 60% TBSA burn occurred in 32 days with GH treatment compared to 46 days without GH treatment.24 In the same study, infants less than two years of age also benefited from GH treatment, without detectable adverse effects. Similarly, adult burn patients25 and patients presenting late in the course of burn-induced hypermetabolism26 also exhibit more rapid graft donor site healing times, even though in these latter patients there was by this time a generalized appearances of poor nutrition and cachexia.26

The substantial body of knowledge concerning the association between burns and GH, and the of the benefits of GH administration to burned individuals suggests at least one line of inquiry directed at improving disturbed sleep in these individuals (see later). Less information is available concerning responses of immune-active substances to thermal injury, specifically somnogenic cytokines, and the impact these alterations may have on sleep. Thermal injury induces alterations in acute phase responses and cytokine expression.27 Circulating cytokines, particularly interleukin-1 (IL-1), tumor necrosis factor (TNF), and IL-6 are increased in response to burn. The alterations in these aforementioned cytokines, coupled with changes in liver morphology and acute phase reactant proteins,27 likely contribute to increased susceptibility to opportunistic infection in response to burn.28 It is also possible that alterations in circulating cytokines may contribute to disruptions of sleep in burned individuals. There is an extensive literature indicating a role for IL-1 and TNF in sleep regulation. A comprehensive review of the literature indicating a role for cytokines in sleep regulation is beyond the scope of this paper, and the interested reader is referred to recent reviews by Krueger and colleagues.29,30

Although it is not apparent to what extent circulating cytokines may reflect cytokine status within the CNS, it is clear there are mechanisms by which circulating cytokines signal the brain, and that sleep may be subsequently altered in response to changes in peripheral cytokine concentrations. The best evidence that circulating cytokines are capable of modulating sleep is simply the observation that peripheral administration of somnogenic cytokines alters sleep.31,32 As such, it is reasonable to hypothesize that alterations in peripheral cytokines in response to burn...
may be another factor contributing to alterations in sleep in these individuals.

Previous work by Drs. Herndon, Wolf, and colleagues at the Shriners Burns Hospital at Galveston has demonstrated alterations in several classes of circulating cytokines in response to burn. We have begun a series of mechanistic studies in collaboration with Dr. Regino Perez-Polo in the Department of Human Biological Chemistry and Genetics to determine alterations in cytokine gene expression in areas of skin subject to thermal injury. Our preliminary results indicate that cytokine mRNA expression is up-regulated in samples from skin subject to thermal injury relative to samples taken from normal skin of the same animal. Of what may be relevant to sleep, IL-1β mRNA appears to exhibit a large increase. The ability to detect IL-6 mRNA expression in samples subject to thermal injury but not from normal skin samples suggest large increases in mRNA for this cytokine as well; IL-6 may also be a modulator of sleep. These observations indicate that local tissue responses to thermal injury include increases in proinflammatory cytokine mRNA expression, including those such as IL-1 that are capable of modulating sleep. Additional studies are underway to determine the extent to which local tissue responses may contribute to alterations in circulating cytokine concentrations, and perhaps to alterations in sleep.

Pain, Discomfort, Medications, and Acute Stress Disorder

A significant factor that may affect the sleep of burn patients is the pain they experience. Pain can interfere with sleep onset, maintenance and quality (see papers in this issue of Sleep). Sources of pain include not only the injury itself, but also subsequent treatments such as wound cleaning, surgical procedures, skin grafts from non-burned donor sites and physical rehabilitation. In addition to the pain itself, many of the medications used to manage pain and discomfort also affect sleep. Minor burn-related pain can often be controlled with just acetaminophen, but major burn injuries usually require narcotic analgesics, such as morphine or codeine. Morphine and other opioid analgesics have a sedative effect. Opioids may decrease REM sleep, abolish stage 4 sleep, and increase stage 1 sleep and arousals. While typically not given when the patient is asleep, analgesic medication is used to relieve pain that is preventing sleep. In addition to direct effects of pain medications on sleep, the discontinuation of medication may also affect sleep, especially if tolerance has developed. For example, withdrawal of methadone increases REM sleep and slow-wave activity during sleep.

Itch is another source of distress that can interfere with the sleep of burn patients. As with pain medications, many of the systemic medications used to control itch also have sedative effects. Antihistamines, such as diphenhydramine, are characterizedly sedating and produce daytime drowsiness. Other antihistamines, such as loratadine for example, do not seem to induce drowsiness. The sedative effect of antihistamines is likely related to shortened sleep latency and sleep onset. However, the use of certain antihistamines to facilitate sleep is probably a result of other effects, like central adrenergic activity. Ciproheptadine is a phenothiazine used in treating itch that typically produces sedation.

Sleep is also altered in individuals suffering from depression, anxiety, or from various stress disorders, and the sleep of children is particularly susceptible to stressors. Nightmares and altered sleep patterns are among the first symptoms observed in burned children suffering from stress disorders. As many as one half of all children traumatized by burn injury will suffer from anxiety, and as many as one third will meet criteria for a diagnosis of post-traumatic stress disorder. Burn patients often receive benzodiazepines and barbiturates to treat anxiety, as well as pain. Benzodiazepines are frequently used to treat sleep disturbance and facilitate sleep onset and maintaining sleep. Acute discontinuation of benzodiazepines can result in insomnia that in some cases is worse than before treatment began. At Shriners Burns Hospital in Galveston we have treated sleep disturbances as part of a constellation of symptoms comprising Acute Stress Disorder (ASD). In a study of burned children with ASD, Robert et al., report that 60% of the subjects suffered from nightmares and 56% had difficulty falling asleep. In another study by the same group, nightmares and/or difficulty falling asleep were disturbances reported by nearly all of the 25 participants. This particular study evaluated the use of imipramine vs. chloral hydrate in treating symptoms of ASD and found that imipramine was significantly more effective than chloral hydrate in reducing symptoms of ASD in this patient population.

Sleep disturbances are a hallmark of major depression, and while less common than post-traumatic stress disorder, major depression is also observed in children that survive serious burns. The specific type of sleep disturbance appears to vary with the age of the individual. Before puberty, children with depression more often report insomnia, whereas hypersomnia is more prevalent in post-pubescent individuals. The medications used to treat anxiety disorders and depression can also alter sleep. As already mentioned, benzodiazepines are used for both the treatment of symptoms of anxiety and depression and as sleeping aids, and produce marked changes in sleep architecture. Reduced REM sleep is a characteristic feature of antidepressant medications, including tricyclics, monoamine oxidase inhibitors, tetracyclics, and serotonin reuptake inhibitors. Sedation is a common effect with the tricyclics and tetracyclics but not characteristic of monoamine oxidase inhibitors or serotonin reuptake inhibitors. In contrast, the serotonin reuptake inhibitors and certain monoamine oxidase inhibitors can produce insomnia.

As with studies designed to determine the extent of sleep disturbances in burned children, there are limited studies that have explored the use of medication specifically to improve sleep quality. Jenkins and colleagues administered haloperidol to eight burned children and found that SWS and REMS increased for two to eight hours after administration. Although this study included a small number of patients, some of which may have also been included in a GH study, and not all the details of the study design are provided, the results are encouraging and suggest that neuroleptics may be effective in improving sleep of these patients. The success of neuroleptics in consolidating sleep has not been consistently shown however, and although most neuroleptics do increase stages 3 and 4 slow-wave sleep and decrease waking, their effects on REM sleep are variable. However, since neuroleptics may have profound effects on daytime alertness and may be contraindicated with other medications, and since they may also have extrapyramidal side effects, these drugs may not be ideal as a first line defense against ASD and/or sleep deprivation in burned patients.
Effects on Sleep of Environmental Factors Associated with Intensive Care Units

There are numerous physical factors in the ICU that may affect sleep. These factors include frequent arousals by nursing staff to take vitals and administer medications, medical rounds, and the evaluation of patient wounds by nurses and physicians. The overhead lights in patient’s rooms are often turned on and off during the night, not only causing arousal but affecting circadian rhythms of the secretion of hormones such as melatonin. Burned children are often repeatedly awakened by family members who are desperate to interact with the child, and may believe that alertness and responsiveness to the family is a sign of recovery. Alarms in patient’s rooms often sound, which can also disturb sleep. In addition to noise from alarms, doors to patient rooms are generally left open to speed access of staff to the room and to allow staff to better monitor the patient. Evaluations of noise in ICUs indicate that levels often far exceed the Environmental Protection Agency recommendations for acceptable levels of 45 dBA during daytime and 35 dBA at nighttime;47 sudden noises during the night of up to 95 dBA have been recorded in pediatric ICUs.5

Another general problem contributing to sleep disturbances of patients in ICUs may be that medical staff receive little training on the importance of sleep and the consequences of sleep deprivation. Staff members tend to be task oriented and may focus on accommodating medical orders, while neglecting the patient’s need for rest. Jenkins et al., report that “invasive” care of patients in Pediatric ICU’s contributes to decreased REM sleep and stages 3 and 4 slow-wave sleep.48 Criteria for what constituted invasive care were not provided, so it is not certain which specific factors in this study may have affected sleep, and no attempt was made to reduce the level of invasive care to determine if sleep improved. Nevertheless, these data indicate that the sleep of patients in ICUs is frequently disturbed in the course of providing medical care.

There are several approaches that may be taken to reduce disturbance of patients in the ICU. The policy at the Galveston Shriners Burns Hospital is not to awaken children to give medication for pain or anxiety. There are additional practices by which nursing staff may help to improve the sleep of children in an ICU.49 These include the grouping of tasks (such as a blood draw, taking temperature, and giving medications) to provide blocks of uninterrupted rest that are as long as possible. In our experience, care providers may believe that quickly doing a procedure while the child sleeps is better than awakening the child beforehand. However, burned patients are often hyper-vigilant and frequently awaken in fright during such procedures. If the child has been burned around the face, they may also be unable for physical reasons to see what is happening to them, which may also contribute to a frightened startle response. In addition, just because a procedure is done quickly does not necessarily mean that it will be painless. Although it seems counterintuitive, it is likely that gently arousing the child prior to painful or uncomfortable procedures will facilitate a quicker return to sleep than would occur if attempting to conduct the procedure while the child sleeps.49

On a burn unit, children’s sleep is often also disrupted for emotional reasons. ASD may include symptoms such as fear, nightmares, flashbacks, and re-experiencing of the trauma. Children may feel out of control and confused by their condition. They may be restrained, and have to cope with amputation and/or disfigurement. Because of the specialized nature of a burns unit, some burn ICUs such as ours treat children from countries unable to provide a comparable level or volume of care. For this reason, cultural differences, including language may make it even more difficult for a child to adapt to what is already a frightening environment. As such, attempts to make the environment more “child friendly,” such as allowing security items like blankets, or other familiar objects such as mobiles or photographs, or music may be important in reducing somewhat the fear and anxiety associated with the ICU and medical treatments.

Conclusions and Perspectives

There is minimal empirical evidence to date to support the hypothesis that good sleep promotes, whereas poor sleep interferes with, recovery process(es) after infection or trauma. There are interesting parallels however, between the sleep deprivation syndrome that develops in rats after prolonged total or partial sleep deprivation50 and responses of children to serious burn. As with chronically deprived rats, the constellation of responses of children to burn include hypermetabolism and inability to thermoregulate appropriately, and susceptibility to opportunistic infections. The invasion of blood of rats by opportunistic microbes suggests that prolonged sleep deprivation results in a breakdown of host defenses against indigenous and pathogenic microorganisms.51 Although there are no comparable studies of humans, rats in which burn wounds are colonized by bacteria exhibit reductions in spontaneously occurring REM sleep that are prolonged relative to the sleep of animals in which wounds were not colonized by bacteria.52

Observations such as these suggest complex relationships between sleep, burns, and multiple facets of wound healing. Once a burn patient is sleep deprived, the interactions between responses to the trauma and sleep deprivation may become synergistic. For example, lack of sleep may retard recovery due to the absence of natural sleep-associated GH surges. Conversely, it may that the administration of GH to counteract hypermetabolic-induced wasting and to promote skin healing at graft donor sites may improve sleep, if the timing of such administrations is appropriate. The experiments to test these hypotheses have not been conducted. One could hypothesize that the consolidation of sleep and improvement in sleep quality would reduce the extent of GH insufficiency and thus promote recovery. It seems somewhat surprising then, that no direct efforts, of which we are aware, have been made to improve sleep quality of burned individuals, either through the use of drugs or modification of the Burns ICU environment.

One medication in particular may be useful in improving sleep quality under these conditions; gamma-hydroxybutyrate (GHB). GHB is a GH secretagogue and GABA metabolite that has been used for almost 35 years as a sedative for ICU patients.53 GHB increases the amplitude and duration of the first, stage 4 sleep-associated GH pulse.54 GHB also improves both pain and fatigue ratings reported by fibromyalgia patients,55 and elevates mood.56 Although GHB may have serious side effects, we suggest its use in burn patients should be cautiously explored
because it may increase GH secretion, and reduce fatigue and pain. It may be that the use of a medication such as GHB, in conjunction with making the Burn ICU a more “sleep friendly” environment, would improve sleep quality and promote recovery. Such experiments have not been conducted, and the question of whether good sleep promotes, or poor sleep interferes with the recovery process remains unanswered.

Although data and empirical studies are limited, intuition and observations of individuals in burn and other ICUs suggest there may be severe disruptions to the sleep of these individuals. It is clear that additional research is needed to determine the extent of sleep disturbances in burn patients. As only one study has examined PSG recordings of sleep in these patients, there remain questions as to what characteristics of the burn (ie; depth, total body surface, pain response) affect the quality and quantity of sleep. The possibility of a synergistic relationship between sleep deprivation and burn wound recovery has not been explored; research into this area may lend valuable insights into potential treatment regimens. The causes of sleep disturbance of burn patients are multiple and varied, but pathophysiological responses to the injury itself, the pain and discomfort experienced and medications used to treat these symptoms, and the physical environment of the ICU are likely major contributors. Treatment of burns may require months of hospitalization, and for the reasons outlined previously are likely to result in prolonged chronic sleep deprivation. There are two fundamental questions that pertain to interactions between trauma and sleep. One is, of course determining the precise nature and causes of the sleep disruption. The other, and more important question is whether appropriate courses of intervention that reduce sleep disruption and promote sleep quality will aid in recovery.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the ongoing support of the Shriners Burns Hospital Corporation, and the Department of Surgery at UTMB. The efforts of Dr. David Herndon, Galveston Shriners Burns Hospital, are particularly appreciated. MRO was supported by National Institutes of Health grants MH 54976, MH 52275, and MH 56873 while writing this manuscript.

REFERENCES


54. Van Cauter E, Plat L, Scharf MB et al. Simultaneous stimulation of slow-wave sleep and growth hormone secretion by gamma-hydroxybu-
