Sleep in the ICU

Richard J. Schwab, M.D.
Professor of Medicine
Division of Sleep Medicine
Pulmonary, Allergy and Critical Care Division
University of Pennsylvania Medical Center
Philadelphia, Pennsylvania

Sleep in the ICU - Disclosures

- NIH grants - PPG (Phenotyping and OSA)
- ResMed Grant/Registry to study OSA/ CSA and CPAP in hospitalized patients
- Jazz clinical trial for EDS in OSA
- Consultant:
  - Apnicure
  - Foramis Medical Group
  - CryOSA

Sleep in the ICU

ATS Official Statement: The Importance of Healthy Sleep

- Sleep appears to be important for a number of vital functions:
  - Neural development
  - Learning
  - Memory
  - Cardiovascular and metabolic function
  - Cellular toxin removal

Mukherjee S, et al. Am J Respir Crit Care 2015; 191(12):1450-1458.

ATS Official Statement: The Importance of Healthy Sleep

- Major Conclusions of the Statement:
  - Short sleep duration (≤ 6 hours/ 24 hour period) is associated with adverse outcomes, including mortality
  - Long sleep duration (> 9-10 hours/ 24 hour period) may be associated with adverse health outcomes
  - Although individual variability exists, the optimal sleep duration for good health in an adult population is 7-9 hours

Mukherjee S, et al. Am J Respir Crit Care 2015; 191(12):1450-1458.

Sleep Deprivation in the ICU

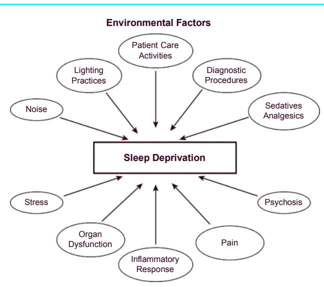


Figure 1. Factors related to sleep deprivation in critically ill patients.

Pisani MA, et al. Sleep in the ICU. Am J Respir Crit Care Med Vol 191; 731 – 738, 2015

Sleep in the ICU

Table 1. Sleep Disturbances in Critically Ill Patients

Patient-related factors	
Preexisting sleep disorders	
Pain	
Anxiety	
ICU-related factors	
Noise	
Light	
Patient care activities	
PSG findings in critically ill patients	
TST	Unchanged/decreased
TST occurring during daytime hours	50%
Sleep latency	Unchanged/increased
Sleep efficiency	Decreased
Sleep fragmentation	Increased
Arousals	Increased
NREM stage 1 (N1)	Increased
NREM stage 2 (N2)	Increased
NREM stage 3 (N3)	Decreased
REM	Decreased

Definition of abbreviations: ICU = intensive care unit; NREM = non–rapid eye movement; PSG = polysomnographic; R&K = Rechtschaffen & Kales; REM = rapid eye movement; TST = total sleep time.

Pisani MA, et al. Sleep in the ICU. Am J Respir Crit Care Med Vol 191; 731 – 738, 2015

Sleep in the ICU

Table 1. Sleep Disturbances in Critically Ill Patients (Continued)

Challenges with scoring PSG in critically ill patients	
NREM stage 1 and 2	Poor interobserver reliability with R&K
NREM stage 2	Difficulty classifying
Absence of K complexes	20–44%
Absence of sleep spindles	20–44%
Use of sedating medications	
Alternative PSG scoring strategies	
Pathologic wakefulness	Visual assessment of EEG reactivity using spectral analysis with eyes open and closed
Atypical sleep	Absence of K complexes and sleep spindles High-amplitude continuous irregular delta frequency EEG No fast frequencies, no REM Low-amplitude chin EMG

Definition of abbreviations: ICU = intensive care unit; NREM = non–rapid eye movement; PSG = polysomnographic; R&K = Rechtschaffen & Kales; REM = rapid eye movement; TST = total sleep time.

Pisani MA, et al. Sleep in the ICU. Am J Respir Crit Care Med Vol 191; 731 – 738, 2015

Potential Physician/Nursing Factors Causing Sleep Disruption in the ICU

- Diagnostic testing and invasive procedures
  - Chest radiographs, phlebotomy (4 AM to 6 AM)
  - Intravenous or central catheters
- Nursing interventions
  - Vital signs
  - Administration of medications

Pisani MA, et al. Sleep in the ICU. Am J Respir Crit Care Med Vol 191; 731 – 738, 2015; Freedman N, Schwab RJ. Sleep in the Intensive Care Unit. In: *The Intensive Care Unit Manual*, 511-519, 2001

Potential Environmental Factors Causing Sleep Disruption in the ICU

- Lighting
- Noxious odors
- Noise (75 dB is as loud as a cafeteria at noon)
  - Mechanical devices and alarms, including ventilators, infusions pumps, telemetry and oximetry (45 - 76 dB)
  - Background noise (55 - 72 dB)
  - Nursing or respiratory care (55 - 83 dB)
  - Hospital staff conversations (60 - 74 dB)
  - Beepers (70 - 84 dB)

Pisani MA, et al. Sleep in the ICU. Am J Respir Crit Care Med Vol 191; 731 - 738, 2015; Freedman N, Schwab RJ. Sleep in the ICU. *The Intensive Care Unit Manual*, 511-519, 2001

A Total of 203 Patients Completed Sleep ICU Questionnaire

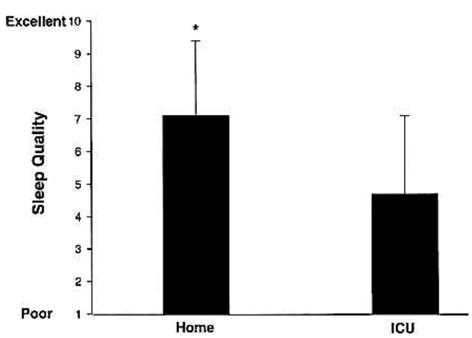
TABLE 1
DEMOGRAPHICS OF STUDY POPULATION*

Unit	n	Gender (*M/F*)	Mean Age (*yr*)	Ventilated Patients (*n*)	Mean ICU Stay (*d*)
CCU	60	40/20	61.1 ± 11.5 (38–78)	1	7.2 ± 14.9 (1–32)
CICU	39	23/16	62.6 ± 12.4 (30–83)	0	12.62 ± 22.38 (1–98)
MICU	56	28/28	51.4 ± 17.8 (19–79)	20	11.3 ± 24.6 (1–134)
SICU	48	30/18	61.4 ± 15.4 (26–86)	11	8.3 ± 11.8 (1–60)
Totals	203	121/82	58.6 ± 15.4 (19–86)	32	8.6 ± 17.5 (1–134)

Definition of abbreviations: CCU = coronary care unit; CICU = coronary intensive care unit; MICU = medical intensive care unit; SICU = surgical intensive care unit.
* Mean ± SD; range in parentheses.

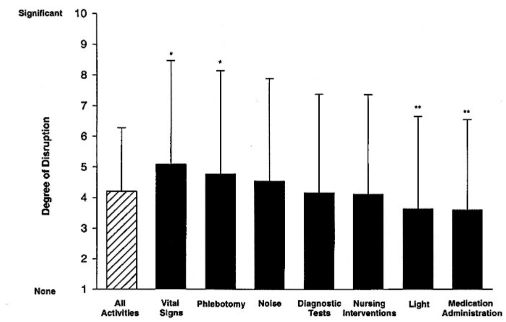
Freedman et al, AJRCCM 159:1155-1262, 1999

Perceived Sleep Quality between Home and ICU (N = 203; p = 0.0001)



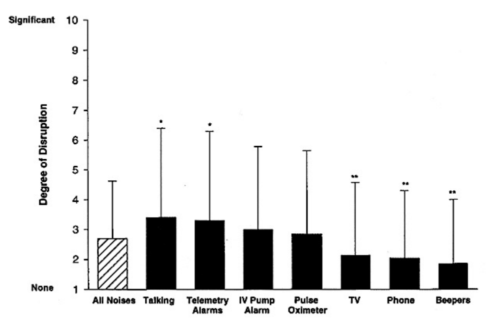
Freedman et al, AJRCCM 159:1155-1262, 1999

Perceived Sleep Disruption from Factors in the ICU Environment



Freedman et al, AJRCCM 159:1155-1262, 1999

Perceived Sleep Disruption from Specific ICU Environmental Noises



Freedman et al, AJRCCM 159:1155-1262, 1999

Sleep/Wake Cycles and Effect of Noise on ICU Sleep (Freedman et al, AJRCCM 163, 451-457, 2001)

- Studied 22 (20 ventilated) MICU patients with continuous polysomnography and environmental noise measurements over a 24 - 48 hour period
  - To determine the underlying mechanisms of altered sleep/wake patterns in ICU patients
  - To objectively determine the effect of ICU environmental noise on sleep fragmentation
    - Simultaneous real time recordings of environmental noise (Quest 1900 portable sound level meter) and polysomnography

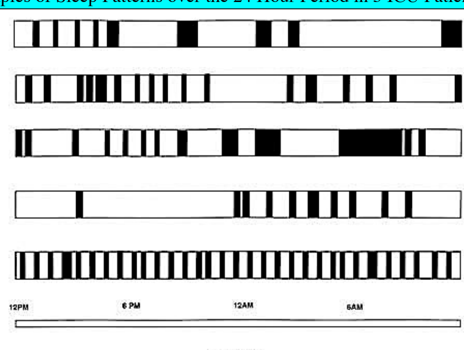
PSG Demonstrating Noise Causing an Arousal from Sleep in an ICU Patient

Freedman et al, AJRCCM 163: 451-457, 2001

Sleep/Wake Cycles in the ICU
(Freedman et al, AJRCCM 163, 451-457, 2001)

- Mean total sleep time per 24 hr period: 8.8 ± 5.0 hrs
- Sleep typically occurred in short bouts (41 ± 18 bouts/24 hrs) with 57% of total sleep during daytime
- Abnormal sleep architecture with a predominance of stage 1 sleep and decreased or absent stages 2, 3, 4 and REM sleep
  - Stage 1 (mean 59 ± 33%)
  - Stage 2 (mean 26 ± 28%)
  - Stage 3/4 (mean 9 ± 18%)
  - REM sleep (mean 6 ± 9%)
  - Twelve of the patients demonstrated no REM sleep

Examples of Sleep Patterns over the 24 Hour Period in 5 ICU Patients



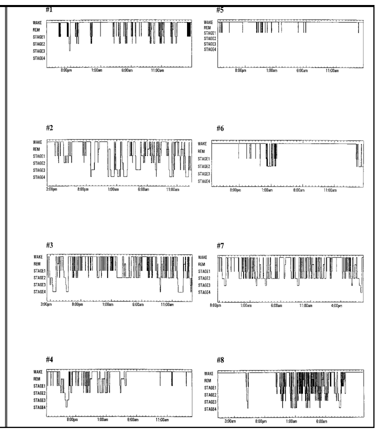
Freedman et al, AJRCCM 163: 451-457, 2001

Sleep in Mechanically Ventilated Patients

- The sleep of a mechanically ventilated ICU patient suffers from all the problems known to affect the sleep of non-ventilated patients plus:
  - Dyssynchronous breathing
  - Ventilator mode
  - Discomfort from the endotracheal tube
  - Stress related to increased difficulty communicating
  - Possibly a greater severity of illness

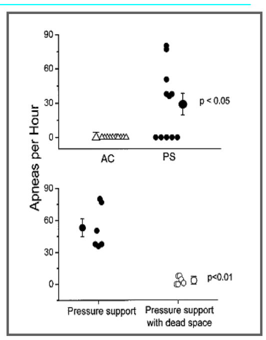
- Hypnograms of 8 ventilated ICU patients
- Sleep fragmented with frequent awakenings
- Distribution of sleep over the 24 hour period
- Prolonged wake

Cooper, et al (Chest 2000;117:809-818)



Ventilator Mode and Sleep Disruption Parthasarathy et al (AJRCCM 2002;166:1423-1429)

- - More apneas per hour with pressure support ventilation compared to assist control
- - Addition of dead space reduced the number of apneas



Sleep in Mechanically Ventilated Patients - Ventilator Synchrony

- Mechanical ventilator settings may also worsen sleep continuity by causing dyssynchronous breathing or by being set to a range of respiratory frequencies to which the patient cannot entrain (Weinhouse and Schwab {Sleep 29: 707-716, 2006})
- Sedated individuals are believed to entrain to a wide range of respiratory frequencies
- Optimizing ventilator settings for patient comfort and sleep and the role of pharmacologic sedation is an area that needs active investigation

Effect of Medications on Sleep

Table 20.1 ■ *The Effects of Common Medications on Sleep in Hospitalized Patients*

Medications (Examples)	Sleep Alterations	Adverse Effects
Analgesics		
■ Opioids (M.S., Codeine, Demerol)	↓TST, REM, SWS; ↑W	Sedating properties may worsen SDB
■ NSAIDs (Ibuprofen)	↓TST, SE	
Antidepressants		
■ Tricyclics (Amitriptyline, doxepine	↓W, REM; ↑TST	Drowsiness; CNS depression enhanced by alcohol intake
■ SSRIs (Paroxetine, fluoxetine	↓TST, SE, REM; ↑W	Insomnia, agitation; extensive drug interactions
Antiepileptics		
■ Phenytoin	↓SL; ↑SWS, TST	CNS effects; extensive drug interactions
■ Phenobarbital	↓W, SL, REM; ↑TST	Sedating effects common
■ Carbamazepine	↓LS, REM; ↑SWS	Drowsiness, fatigue
■ Gabapentin	↓W; ↑TST, REM, SWS	Dream disturbances, emotional lability, dizziness, drowsiness

Abbreviations: NA, not available; REM, rapid eye movement sleep; SDB, sleep-disordered breathing; SE, sleep efficiency; SL, sleep latency; SWS, slow-wave sleep; W, wakefulness; TST, total sleep time.

Redeker, NS, et al. Sleep Disorders and Sleep Promotion in Nursing Practice: Springer Publishing Company; 2011.

Effect of Medications on Sleep

Table 20.1 ■ *The Effects of Common Medications on Sleep in Hospitalized Patients* (Continued)

Medications (Examples)	Sleep Alterations	Adverse Effects
Anti-Parkinsonian drugs		
■ Levadopa	↓SWS; nightmares	Disturbing dreams, mood changes, malaise
■ Methyldopa		Drowsiness, nightmares
Antipsychotics		
■ Haloperidol	↓W, SL; ↑SE	Insomnia, restlessness
Cardiovascular agents		
■ f3 antagonist (propanolol, metoprolol)	↑W, SL; ↑REM	Drowsiness, fatigue
■ Calcium channel blockers (Nifedipine, verapamil)	NA	Drowsiness, weakness
		Fatigue, syncope
■ ACE Inhibitors (lisinopril)	No known sleep effects	Insomnia, weakness, nocturia
■ Diuretics (HCTZ, furosemide)	NA	

Abbreviations: NA, not available; REM, rapid eye movement sleep; SDB, sleep-disordered breathing; SE, sleep efficiency; SL, sleep latency; SWS, slow-wave sleep; W, wakefulness; TST, total sleep time.

Redeker, NS, et al. Sleep Disorders and Sleep Promotion in Nursing Practice: Springer Publishing Company; 2011.

Effect of Medications on Sleep

Table 20.1 ■ *The Effects of Common Medications on Sleep in Hospitalized Patients* (Continued)

Medications (Examples)	Sleep Alterations	Adverse Effects
Corticosteroids		
■ Prednisone; cortisone	↓REM, SWS; ↑W	Insomnia, restlessness, behavior changes
H2 Antagonists		
■ Cimetidine	↑SWS	Hallucinations, somnolence
Mood Stabilizers		
■ Lithium	↑TST, SWS; ↓REM	Drowsiness, lethargy
Respiratory		
■ Theophylline	↓TST, SE, REM, SWS; ↑W	Agitation, insomnia
Sedatives/Hypnotics		
■ Benzodiazepines (Midazolam)	↓W, REM, SWS, SL; ↑TST	Delirium, dreaming, insomnia, nightmares
■ Propofol	↓W, SL; ↑TST	CNS depressant; hypnotic

Abbreviations: NA, not available; REM, rapid eye movement sleep; SDB, sleep-disordered breathing; SE, sleep efficiency; SL, sleep latency; SWS, slow-wave sleep; W, wakefulness; TST, total sleep time.

Redeker, NS, et al. Sleep Disorders and Sleep Promotion in Nursing Practice: Springer Publishing Company; 2011.

Does Sleep Deprivation Impair Clinical Performance?

- Data are not definitive but:
  - Anesthesiologists take longer to intubate
    - Gaba et al, Anesth 1998
  - Affects hand-eye coordination in surgeons performing laproscopy
    - Taffinder et al, Lancet 1998
  - Medical errors in ICU (*NEJM October 28, 2004)*
  - Professionalism is compromised/increased risk of depression
  - No procedures post call

Potential Deleterious Effects of Sleep Deprivation in the ICU

- Respiratory System
  - ? Adversely affect weaning
- Immune Function
  - ? Adversely affect healing
- Neuroendocrine System
- ICU syndrome/Delirium

Effects of Sleep Deprivation on the Respiratory System

- Decreased forced vital capacity
- Decreased maximum voluntary ventilation
- Decreased hypercapnic ventilatory response by 20% - 24%
- Decreased hypoxic ventilatory response by 29%
- Decreased inspiratory muscle endurance by 24%
- Decreased genioglossal EMG activity
- Increased upper airway collapsibility

Freedman N, Schwab RJ. Sleep in the Intensive Care Unit. *The Intensive Care Unit Manual*, 511-519, 2001; Schwab RJ. Disturbances of Sleep in the Intensive Care Unit. Critical Care

Poor Sleep Quality is Associated with Late Non-Invasive Ventilation Failure

- Prospective observational cohort of 27 patients requiring non-invasive ventilation
- Hypercapnic respiratory failure
- Proportion of patients with abnormal sleep (abnormal EEG, disrupted circadian rhythm and decreased REM) in non-invasive ventilation failure verses success: 50% vs. 8% (P=0.03)
- Non-invasive ventilation failure was associated with delirium (64% vs. 0%)

Roche Campo et al; Crit Care Med 38:477- 485, 2010

Effects of Sleep Deprivation on the Immune System

- Poor sleep is thought to increase susceptibility to illness; however, this association is controversial
- Sleep deprivation in rats leads to death in 2-3 weeks
- Studies of humans undergoing *total* or *partial* sleep deprivation have shown non-specific changes in immune response and decreases in aspects of cellular immune function
  - Orzeł-Gryglewska, Int J Occup Med Environ Health 23; 95-114, 2010
- Sleep deprivation (4 hours) in 30 healthy adults increased monocyte production of interleukin 6 and tumor necrosis factor alpha
  - Irwin et al, Arch Int Med 166; 1756-1762, 2006

Effect of Sleep Deprivation on Neuroendocrine System

- Studies have shown that partial sleep deprivation is associated with high sympathetic tone
  - Spiegel K et al. Impact of sleep debt on metabolic and endocrine function. Lancet 354:1435-39, 1999
- Cortisol levels have been found to increase on the night following one night of sleep loss
  - Orzeł-Gryglewska, Int J Occup Med Environ Health 23; 95-114, 2010
- Neuroendocrinologic changes may be much greater in critically ill patients

Interventions to Improve Sleep in the ICU

Table 20.2 ■ *Interventions to Promote Sleep During Hospitalization*

Assessment	Interventions	Evidence
Goal: Reduce Effects of Environmental Stimuli		
Monitor noise, lighting, frequency/timing of patient care interactions; patients, perceptions of environmental stimuli and potential stress	Decrease noise; low light at night; normal lighting during the day Cluster patient care interactions; "Quiet Time" ear plugs/eye masks Massage, music, white noise Provide a structured bedtime routine "PM Care"	Gardner et al. (2009), Hu et al. (2010), Richards (1998), Richardson et al. (2007), Olson et al. (2001)
Goal: Modify Illness and Treatment Related Effects on Sleep		
Assess changes in sleep patterns associated with medications, surgery, and other treatments Treat pain, dyspnea, and other symptoms Assess for signs of delirium	Review drug interactions affecting sleep phases; evaluate sleep effectiveness on all hospitalized patients. Hypnotic medications Prescribe/administer analgesics; Anti-anxiety drugs Behavioral treatments for pain	Bourne and Mills (2004), Hardin (2009), Weinhouse and Watson (2009)

Abbreviation: CPAP, continuous positive airway pressure; SDB, sleep-disordered breathing.

Redeker, NS, et al. Sleep Disorders and Sleep Promotion in Nursing Practice: Springer Publishing Company; 2011.

Interventions to Improve Sleep in the ICU

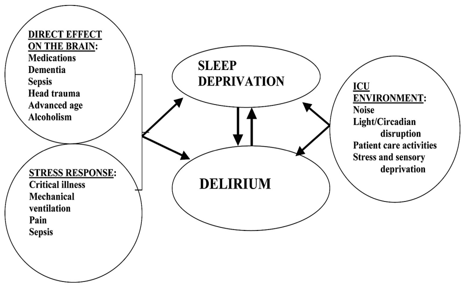
Table 20.2 ■ *Interventions to Promote Sleep During Hospitalization*

Assessment	Interventions	Evidence
Goal: Prevent and Manage the Negative Complications of Sleep-Disordered Breathing		
Assess for oxygenation, snoring, witnessed apnea, dysrhythmias, especially in patients who have undergone anesthesia or used sedative medications or opioid analgesics	Use minimal sedation necessary Use nonsteroidal pain medication rather than opioids as possible Position patients on side with head of bed elevations minimally at 30 degrees unless contraindicated Apply patient's own home CPAP system if patient not mechanically ventilated. If on mechanical ventilation, consult with care provider for support. Apply CPAP following extubation. Monitor ECG rhythms carefully during episodes of hypoxia, apneas or hypopneas, and snoring. Cardiac monitoring in multiple leads is advantageous. Monitor and document any respiratory abnormalities occurring with ventricular or atrial ectopy and bradyarrhythmias. Postoperatively: Monitor SpO2 continuously for patients at high risk for desaturation, including those with prior SDB. Monitor critically ill patients on mechanical ventilation to prevent over ventilation.	Gross et al. (2006), Young et al., 2008. Kaw et al. (2006), Weinhouse and Watson (2009). Drew et al., 2004; Koshino et al. (2008); Ryan, Juvet, Leung, and Bradley (2008)

Abbreviation: CPAP, continuous positive airway pressure; SDB, sleep-disordered breathing.

Redeker, NS, et al. Sleep Disorders and Sleep Promotion in Nursing Practice: Springer Publishing Company; 2011.

Relationship Between Sleep Deprivation and Delirium??



Weinhouse et al, Critical Care 13: 234-241, 2009

Factors Affecting Circadian Rhythms in the ICU

- Altered sleep architecture
- Sleep deprivation
- Aberrant light/dark cycles and social cues
- Severity of illness
- Affect on respiratory muscle strength
  - Implications for weaning

Circadian Rhythms in the ICU

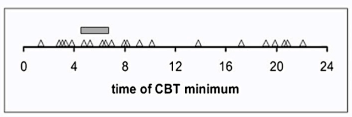
- To investigate circadian rhythms in the ICU, we recorded core body temperature over a 48-hour period in 21 ventilated patients (59 ± 11 years; 8 males vs. 13 females)
- Core body temperature was measured with a swan-ganz catheter or bladder catheter
- A circadian rhythm was detected in the temperature records of every patient
- Substantial variability among patients in the timing (phase) of the circadian rhythm
- Circadian phase position for 17 of the 21 patients fell outside a previously established reference interval for variability among healthy normals

Subject Demographics and Clinical Information

Demographics and Clinical Information	Data
No. subjects	21
Male (female)	8 (13)
Age, mean ± SD, min-max, y	59 ± 11, 33-75
APACHE III score, mean ± SD, min-max	49 ± 22, 29-95
Mechanically ventilated	17
Renal insufficiency	10
Myasthenia gravis	3
COPD exacerbation	6
ARDS	2
First day of CBT recording,[a] mean ± SD, min-max	19.9 ± 18.9, 2-45

Data are presented as No. subjects unless indicated otherwise. APACHE = Acute Physiology and Chronic Health Evaluation; CBT = core body temperature; max = maximum; min = minimum.
[a]Relative to day of ICU admission.

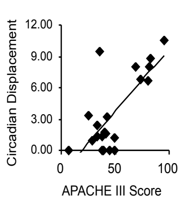
Subjects' Circadian Phase Position



- Each triangle indicates an individual patient's clock time of the estimated CBT minimum, plotted against clock time (in hours)
- In 10 patients circadian phase position (CPP) fell earlier than the reference interval; in 7 patients, the CPP fell later
- The gray bar indicates the reference interval for healthy normal subjects (04:38-06:45), taken from a database of healthy extreme morning- and evening type individuals studied under constant-routine conditions
- The vast majority of healthy normal subjects would be expected to have circadian phase positions inside this relatively narrow reference interval
- In contrast, the circadian phase positions of patients in the ICU were distributed over the entire 24 h of the day
- The mean ± SD of circadian displacement in either direction (advance or delay) was 4.44 ± 3.54 h

Circadian Rhythms in the ICU

- Stepwise linear regression was performed to determine if age, gender, APACHE III score, or day in the ICU could predict the patient-specific magnitude of circadian displacement
- APACHE III score was the only variable found to be significantly predictive of circadian displacement



Gazendam et al. Chest. 2013;144:483-9

Discussion

- Our findings suggest that the severity of illness may directly or indirectly contribute to changes in the circadian rhythms in ICE patients
- Altered circadian phase positions in patients in the ICU may also result from abnormal temporal cues (zeitgebers) in the ICU environment, which can cause desynchronization of the circadian pacemaker
- Light patterns, in particular, appear to be different for ICU patients compared with normal control subjects
- Ambient light is a relatively potent zeitgeber in human beings, but if ICU patients receive insufficient and/or improperly timed light, it may result in changes in the circadian rhythmicity

Gazendam et al. Chest. 2013;144:483-9

Discussion

- Knowledge of the circadian phase position in critically ill patients may also have direct physiologic and therapeutic implications
- Patients with COPD show circadian fluctuations in pulmonary function, with circadian differences between peak and trough values of FEV 1 and peak expiratory flow rates of 25% to 50%
- This time may be predictable based on the temporal relationship between the pulmonary function rhythm and the CBT rhythm
- Healing may be impacted by circadian rhythms, and alignment of central and peripheral oscillators by zeitgebers, such as feeding regimes, may benefit patients

Gazendam et al. Chest. 2013;144:483-9

Discussion

- Drug efficacy and half-life depend on circadian timing
- Chronotherapy may benefit patients in the ICU by potentially enhancing drug efficacy and/or decreasing toxicity
- CBT recordings may be useful as a circadian marker in future research to evaluate the efficacy of circadian-based drug delivery strategies

Gazendam et al. Chest. 2013;144:483-9

Conclusions about Circadian Rhythms

(Gazendam et al. Chest. 2013;144:483-9)

- Circadian rhythm of CBT in critically ill ICU patients to be considerably shifted relative to normal control subjects
- Patients with higher APACHE III scores showed greater circadian phase displacement
- Increased knowledge and consideration of patients' circadian rhythmicity may have a positive impact on therapeutic interventions and the quality of sleep in the ICU
- The finding of abnormal circadian rhythms in the ICU strongly suggests that appropriately timed patient care and treatment strategies aimed at realigning circadian rhythms may be beneficial for clinical recovery in critically ill patients

Sleep and Circadian Rhythms Disturbances in the ICU

- Patients sleep in the ICU but they sleep in short bouts throughout the 24 hour period
- Delta/REM sleep are difficult to achieve in the ICU
- Human ICU interventions appear to be more disruptive to sleep than noise
- The ventilator can disturb sleep in the ICU
- Sleep deprivation may adversely effect immune, respiratory function, neuroendocrine, and cause (?) delirium
- Circadian rhythms are present but displaced in ICU patients
- Consider nonpharmacologic approaches initially

Sleep in the ICU

Thank you for your attention! Any Questions?

rschwab@mail.med.upenn.edu