Kingman P. Strohl

Competencies in Sleep Medicine

An Assessment Guide

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Kingman P. Strohl
Case Western Reserve University
Cleveland, OH, USA

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I dedicate this book to my family (Linda McIntosh and Nicholas, Anna, and Madeleine Strohl), and to my many colleagues, students, and friends in academic medicine.

Preface

This book describes goals, curricula, and post-learning, formative assessments for the knowledge and skill sets that could be developed and acquired in training programs, for instance, an ACGME-accredited program for Sleep Medicine. Each chapter is designed to address the needs of Training Directors and Training Programs presenting material in a unique educational goal-based format, rather than an approach focused on content, and accordingly provides examples for assessment. Thus, each chapter has a focus on an area or cluster of areas of knowledge or skills in sleep medicine and articulates appropriate means and examples of instruction for an assessment of the knowledge or skill set in that topic. These principal components and assessments could be used by a program to respond to ACGME calls for such material in the broad range of sleep medicine, address weaknesses in existing program material, and assess trainees in a standardized fashion with the potential for measurable benchmarks.

Each ACGME program should tailor this template to its own program and determine "passing scores", which, when used alongside clinical assessments of trainees, provides a platform for judging whether or not training goals have been individually met. Such a program also can serve international training, as it is based on a curriculum and competencies and therefore not confined to a set time for lectures or an arbitrary time limit for acquiring training.

Each chapter on content areas has the following items:

- Introduction to the content area where the scope of the chapter is discussed.
- A concept Map of the content area aligned with ACGME competencies.
- Suggested "Objectives" for instructional material and how to deliver it.
- Matching Questions. This formative test is designed to provide a language context for the content area, and is presented in three parts: the longer list of answers, the shorter list of questions, and answer sheet.
- Essay Questions. Sample questions are to be provided before or after a presentation to assess the written skills of the trainee. "Ideal" answers are provided. In the Essay Questions, a case description is provided followed by a number of follow-up questions related to the physiology or pathophysiology related to the content area.

In most of the chapters there is a group learning exercise called an IQ group.

- InQuiry (IQ) Learning case. (Note that not all chapters will have one.) These cases can be initially presented in one session to a learning group (e.g. the IQ "team") with no prior knowledge of what is to be covered, emulating what a physician would experience when seeing a new patient. The IQ team concept involves a small, student-centered learning team that uses elaborate patient cases and discussion to learn, retain, synthesize and integrate knowledge. At the first session, the case is read one paragraph at a time, after which team members ask pertinent questions. At the end of the first session, each IQ Team develops its own learning objectives that will help to generate a clinical framework and to guide their learning over the time until the second session. At the second session, the IQ team presents to each other the results of their homework on the group objectives from the first session. At the end of the second session, the Learning Objectives developed by the Sleep Medicine Faculty are disclosed. Learning this way ensures an experiential, not passive, learning experience, and permits identification of learning objectives for basic sciences in the clinical context.

This resource is designed as a first draft for development of competencies in any Sleep Medicine training program with the intent that the program may focus on the trainees and refine the material for their own purposes.

Competencies define the curriculum and inform students about what they must be able to demonstrate to succeed. No one instructional approach provides the knowledge and skills for a Sleep Medicine trainee. Rather a collective hierarchy of clinical and teaching approaches can define the program. Clear objectives will direct students towards higher quality learning by indicating the intended achievements, but leave room for "emergent" learning. Emergent learning occurs when a student actively seeks for information to answer a question, and bumps into other ideas, concepts or facts tangentially related to the case. It is estimated that in an IQ case the student will encounter ~20 % more content than what is really needed. Constructively aligning learning and assessment tasks can lead learners to spend focused time on the topics in the field.

This book hopefully will be used to augment current activities by faculty, staff, peers and others who judge trainee progress and achievement. Multiple assessments like those presented here can empower a program to define and achieve the student learning outcomes, and encourage autonomous learning. Evaluation of the quality of written and oral responses informs on communication skills.

We have developed a complementary online resource for the sharing of content developed through writing this resource (http://competenciesinsleepmedicine.weebly.com/) On this resource will be additional material like PDF presentations in the topic areas, and other games. It will include links to additional learning opportunities.

As a final thought, this is a decent start, but unlikely to be the last word. I think that the Objectives and Matching Questions list most of the terms we encounter as a specialty now and stretch the program to discuss history, physiology, pathophysiology, and new terms. The Essay Questions provide a good start. The IQ groups are uneven for a specialty program. We are still searching for the right balance of levels.

Some seem very basic without challenges to a fellow in the latter half of a 1-year program. Of course, many of the professional societies have developed illustrative cases or PSG fragments that would complement this book, but I think that the stories themselves are important. I hope the interesting cases being presented across the country in training programs could be de-identified and deposited so that other IQ cases could be created.

Luck.

Cleveland, OH, USA Kingman P. Strohl

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Contributors

Hrayr Attarian Department of Neurology, Northwestern University, Chicago, IL, USA

Dennis Auckley Division of Pulmonary, Critical Care and Sleep Medicine, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH, USA

Charles Bae Sleep Disorders Center, Cleveland Clinic Main Campus, Cleveland, OH, USA

Jonathan Baskin Department of Otolaryngology and Head & Neck Surgery, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Michael Decker Francis Payne Bolton School of Nursing, Case Western Reserve University, Cleveland, OH, USA

Thomas E. Dick Division of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Xiao Song Dong Sleep and Pulmonary Medicine, Tito Castro Ponce, Puerto Rico

George P. Fahed Sleep and Pulmonary Medicine, Tito Castro, Ponce, Puerto Rico, Cleveland, OH, USA

Pingfu Feng Division of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Nancy Foldvary-Schaefer Sleep Disorders Center, Cleveland Clinic Main Campus, Cleveland, OH, USA

Fang Han Department of Pulmonary Medicine, Peking University People's Hospital, Beijing, China

Lamia Ibrahim Department of Pulmonary and Critical Care Medicine, University Hospitals Case Medical Center, Cleveland, OH, USA

Dennis Kelley Sleep Disorders Program, Louis Stokes DVA Medical Center, Cleveland, OH, USA

Amit Khanna Lawrence + Memorial Hospital Sleep Center, Groton, CT, USA

Brian B. Koo Department of Neurology, University hospitals and Case Western Reserve University School of Medicine, Cleveland, OH, USA

Vidya Krishnan Department of Pulmonary, Critical Care and Sleep Medicine, MetroHealth Medical Center, Cleveland, OH, USA

Coleen G. Lance Department of Pulmonary and Critical Care Medicine, University Hospitals Case Medical Center, Cleveland, OH, USA

Reena Mehra Department of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Nikolaus Netzer Research Program for Hypoxia and Sleep Medicine Research, Research Program of the Paracelsus Medical University, Hermann Buhl Institute and Clinic Ghersburg for Geriatric Rehabilitation, Germany

Rory Ramsey Sleep Medicine Specialist, Private Practice, Boise, ID, USA

Carlos Rodriguez Sleep Disorders Center, Cleveland Clinic Main Campus, Cleveland, OH, USA

Carol Rosen Pediatric Sleep Center, Rainbow Babies & Children Hospital, University Hospitals Case Medical Center, Cleveland, OH, USA

Kristie R. Ross University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Jessica Vensel Rundo Sleep Disorders Center, Cleveland Clinic Main Campus, Cleveland, OH, USA

Roobal Sekhon Sleep Medicine Specialist, Fairfield, CA, USA

Ziad Shaman Division of Pulmonary, Critical Care and Sleep Medicine, MetroHealth Medical Center, Case Western Reserve University, Cleveland, OH, USA

Clint W. Snyder Department of Family Medicine and Community Health, Case Western Reserve University School of Medicine, Cleveland, OH, USA

Kingman P. Strohl Case Western Reserve University, Cleveland, OH, USA

Shyam Subramanian Department of Pulmonary, Critical Care and Sleep Medicine, Mercy West Hospital, Cincinnati, OH, USA

Salim Surani Department of Pulmonary, Critical Care & Sleep Medicine, Texas A&M University, College Station, TX, USA

J. Daryl Thornton Department of Pulmonary, Critical Care and Sleep Medicine, MetroHealth Medical Center, Cleveland, OH, USA

Harneet Walia Sleep Disorders Center, Cleveland Clinic Main Campus, Cleveland, OH, USA

Tina Waters Sleep Disorders Center, Cleveland Clinic Foundation, Cleveland, OH, USA

Motoo Yamauchi Department of Respiratory Medicine, Nara Medical University, Kashihara, Nara, Japan

Han Yan Department of Pulmonary Medicine, Peking University People's Hospital, Beijing, China

Phyllis Zee Center for Sleep and Circadian Biology, Northwestern University Institute for Neuroscience, Chicago, IL, USA

Chapter 1
Sleep Medicine and Competency Training

Kingman P. Strohl

Introduction

Sleep Medicine is new and remarkable for its multidiscipinary history and training requirements [1]. Its future will depend on a sustained effort not only at a post-graduate level but up and down the spectrum from medical graduate education to CME programs. To promote the value of and outcomes for clinical Sleep Medicine, fellowship programs need to rapidly expand their educational sophistication to effectively address the need for sleep specialists now and in the future. This has led to the delineation of "competencies" at the fellowship level [2] and soon will extend to recertification programs [3].

ACGME Competencies

The general competencies required by the Accreditation Council for Graduate Medical Education (ACGME) include six focal areas: (1) patient care, (2) medical knowledge, (3) professionalism, (4) interpersonal and communication skills, (5) practice-based learning and improvement, and (6) systems-based practice [4]. The ACGME's next accreditation system for graduate medical education (GME) will be fully implemented by core programs in 2014 and then move towards subspecialty training [4]. When the new system goes into effect, each accredited medical fellowship program must declare core competencies and clinical skills developed for delivering quality patient care and to prepare trainees for the dynamic changes occurring in health care delivery. Teaching institutions will publish more specific

K.P. Strohl, M.D. (✉)
Case Western Reserve University, 11100 Euclid Avenue, Cleveland,
OH 44106-1716, USA
e-mail: kpstrohl@aol.com

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learning outcomes that their fellows demonstrate as they progress through training. Programs must submit reports to the ACGME every 6 months that document each resident's accomplishments in meeting their own benchmarks for physician growth and development as a Sleep Medicine specialist. Finally, the ACGME will update the accreditation "yearly" based on trends in key performance parameters developed by the program. The ACGME expects this process will enhance accountability for the effectiveness of graduate medical education. Moreover, the ACGME's new system will continue to set requirements for teamwork, clinical responsibilities, communication, professionalism, duty hours, personal responsibility, and transitions of care. Such guidelines are in part directed towards public perception of current practice in medicine that is more directed at knowledge through the certification or specialty examination than at physician competencies in all areas of "real-world" practice.

While the critical program requirements are published by the ACGME, how the objectives are achieved is the responsibility of each program. Each program is to identify teaching strategies for the 1-year program. There is a generic teaching toolbox proposed to expand the ACGME core communication competencies and suggests some 20 sub-competencies connecting each competency to teaching strategies [5].

This collection of material is designed to propose model instructional methods for Sleep Medicine that might be especially useful for programs that may not have specific expertise, material, or assessments in all the areas of instruction in this multidisciplinary field. The challenge will be comprehensive assessments and measureable outcomes [6].

Formative Evaluations

The ABIM Certification in Sleep Medicine is a "summative assessment" intended to set a bar for a fellow's attainment at a particular time. The ACGME is asking each program to develop a "formative assessment" to address the impact of the program on the fellow during the fellowship and to identify gaps in knowledge, skills, or behavior. The difference is that the latter is the assessment for learning and behavior which differs from an examination for certification. The ABIM examination is an assessment of knowledge, generally used for purposes of external accountability to training programs and hospital privileges.

Formative assessments can encompass a range of formal and informal assessment procedures. Generally the field has done this by collecting information on rotations and providing qualitative feedback to the fellow at least at 6-month intervals. This exercise focuses on the details of performance in practice and procedures. What is now asked of programs is to develop a strategy to assess the delivery of knowledge and skills during the fellowship itself. We have done this traditionally by developing "shelf examinations" that mimic the national board, but this approach teaches to the examination rather than assess the competencies that ACGME programs are expected to address.

In this book, there are a number of exercises that can address the various knowledge and skills and present formats where professionalism, attitudes, and personal learning skills can be assessed. The short-term impact of assessments is to focus attention on a subject, consolidate learning, hopefully leading to learning activities outside the instructional venue. The Matching Exercise is based on theory of how doctor's think, i.e., recalling a diagnosis or process or test that addresses a need identified by a patient presentation. We have included inscription exercises where an answer is written because this line of assessment permits the fellowship program to see how the fellow can respond in written work, noting the sentence structure, the logic, and the ability to address nuances. Such skills may also be assessed from patient notes and assessments, but the focus here is on synthesis and use of content knowledge. Moreover, formative assessments can illuminate a fellow's motivation as a learner, ideas about their capabilities, and development as a specialist – i.e., self-efficacy and choice of learning and problem solving strategies.

Group Learning Exercises

Group learning is a subset of instruction and formative assessment, but it is rarely a focus in a postgraduate residency program. Using a group process for active learning and instruction is derived from the literature on adult learning and business school group problem solving strategies. The problem for the program director is how to develop desired standards of problem solving as it occurs in the multidisciplinary world of medicine. In a group there is the opportunity for fellows to learn and acquire from one another's learning strategy, skills, and study practices.

At Case Western Reserve University, the undergraduate medical education in the first 2 years is presented in small learning groups ~60 % of the time, with lectures and other small group topic instruction comprising the rest of the curriculum. The "IQ" group is a name for the learning group (http://casemed.case.edu/admissions/education/iq-learning.cfm). Students review these cases with no prior knowledge of what is to be covered, much as a physician would when seeing a new patient. At the first session, the case is read one paragraph at a time, for team members develop pertinent questions. At the end of the first session, the group develops its own learning objectives that will help to generate a clinical framework and to guide their learning over the time until the second session. At the second session, the IQ team presents to each other the results of their homework on the group objectives from the first session. At the end of the second session, the learning objectives as articulated by the Sleep Medicine faculty are disclosed.

A "faculty" facilitator presides over each group and ensures that learning stays on track, but the qualifications of this facilitator is not as the content expert. That is, the facilitator's role is not to provide knowledge or answer questions but rather to guide the students through the process of discovery of the objectives, encourage

articulation of good questions from the case, and insist on high-quality discussions. Additionally, the faculty facilitator provides feedback to each student to help improve individual performance and observes and reflects back on group performance.

InQuiry Group (IQ) learning helps a fellow:

- Integrate the core concepts of health and disease.
- Permit students to exhibit skills of scholarship, critical thinking, and personal learning style.
- Encourage and assess the active interchange of ideas between learners.
- Create expectations for independent study and self-directed learning.
- Practice the ability to work in teams, a skill that is critical in medical systems.
- Integrate basic science knowledge in a clinical context, using population, social, and behavioral sciences.

There is a process to beginning as well as ending a two- or three-session IQ presentation. In our experience in a Sleep Medicine fellowship, a two-session period a week apart can be scheduled within the usual conference schedule, although it might be preferable to have a shorter period of time. There is a "check-in" process, where the group members agree on the terms of the process that stresses the importance of group dynamics and interactions in the WR2 curriculum. One member is appointed by the group as a "scribe," responsible for taking notes while the team is brainstorming learning objectives. The scribe captures key questions and comments from the group and then works with the group to consolidate these points into learning objectives after reading the case in the first session. A fellow "team leader" is assigned by the group to have responsibility for running the session. The "leader" keeps the team discussion on time and on track, setting the stage for the second session. It is important that over several sessions, the people appointed as "scribe" or "team leader" rotate among members.

The goal of the first session, the reading of the case, is for the group to develop its learning objectives at the end of the first session. All members of the group are to be responsible for all "learning objectives," and each is to use any and all resources to contribute to the discussion of the learning objectives in the second session. It appears that in this process, the motivated student will examine about 20 % more information that is needed to address the problems, but students will be judged by each other in regard to depth and sources of information.

After each session there is the "check-out," a process for quality improvement in which the function of the team and the teammates (but not the content) is discussed. It is the time for a commentary on the group as a whole, individual members and the facilitator, focused on constructive criticism. It is a time to reflect on group process and function. It serves as a way for team building in a fellowship program through sharing compliments and concerns.

Personal Learning Plans and Milestones

We have found that one way to focus the fellow and the program on progress and milestones is the use of a portfolio, maintained by the trainee. This is a collection of all written material, assessments, recounting praise and constructive criticism, and printouts of PowerPoint presentations. At the outset of the year, the trainee would be asked to set goals and then periodically assess his/her progress and provide brief, written self-evaluations on progress in self-reflective manner. In Table 1.2 we present the themes for each quarter of the 1-year fellowship program in our program.

There are ACGME milestones for the upcoming NEXT Accreditation System that are directed at immediate postgraduate training programs (Fig. 1.1) [4]. Presumably for the Sleep Medicine programs, there will be the expectation that these competencies have been assessed and trainees identified as to the level of accomplishments. While there may be further guidelines for 1-year programs (as opposed to 2–3-year programs), at the present time we envision these milestones to be at levels 4–5, and these probably should be confirmed with a plan with the individual to develop the next step. In our Sleep Medicine program, we plan an early, first-quarter assessment and a later third-quarter assessment on each of the categories (Table 1.3).

The overall goal is to establish rungs on a ladder for the development of a professional in the field of Sleep Medicine (Table 1.4).

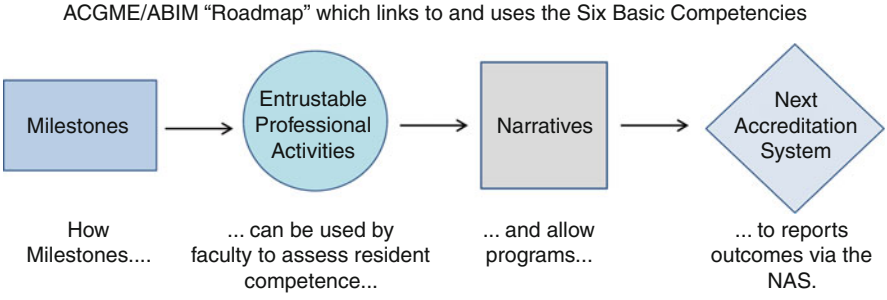

Fig. 1.1 The six competencies are linked to a broader context of a roadmap for training and assessment of Sleep Medicine fellows and fellowship programs that are more process and outcome based. The milestones, entrustable professional activities, and narratives are to be developed by the subspecialty in collaboration with the accrediting agencies. These form the basis for the ACGME "NAS"– NEXT Accreditation System

Table 1.1 Structure for Developing an Essay Question

Essay Question

INSTRUCTIONS
Where you find multiple questions within the same question subpart, label your answer using the letter that corresponds to the letter in the question. Example: Question: A) what is ... B) explain.... C) describe... Answer: A) definition is..., B) the explanation is, C) description.

STEM CONDITION HERE….

A. Identify the factors that contribute… (2-3 short sentences)

B. Explain the rationale for……. (2-3 sentences)

C. List….. (2-3 sentences)

D. Summarize the outcome measures that are… (2-3 sentences)

Ideal Answer:

A.

B.

C.

D.

Table 1.2 Focus of Instruction at Case Sleep Medicine Fellowship over the 1-year Program

First quarter: Neurophysiology/neuropharmacology, patient assessment, differential diagnosis, international classification, research in the program (each fellow produces some scholarly work)
Second quarter: Techniques of monitoring (PSG, MWT, MSLT), neurologists for non-neurologists, pulmonary for non-pulmonologists
Third quarter: Sleep disorders of medical and psychiatric illness, psychology and psychological testing, psychiatry for non-psychiatrists (medicine for psychiatrists)
Fourth quarter: Sleep Medicine systems (administrative and societal issues), presentation of yearly scholarly work

Table 1.3 General Competencies

Milestone	How	Evaluation I	Evaluation II	Evaluate program
Professionalism	Supervised clinicals, feedback from peers and others on the health team			Annual retreat
Interpersonal skills and communication	Feedback Semiannual 360° assessment			Annual retreat
Practice-based learning and improvement	Feedback Semiannual faculty Portfolios Conference attendance			Annual retreat
Systems-based practice	Feedback Semiannually 360° assessment			Annual retreat

Table 1.4 Evaluation of Progression During a Sleep Medicine Fellowship

Reporter (3–6 months)
Obtains and reports basic information for the procedure
Has basic knowledge to know what to look for in the primary tests in Sleep Medicine
Has the ability to recognize normal from abnormal and confidence to label a new problem
Reliable in the context of a rotation for interpretation
Laboratory staff exhibiting solid professional qualities
Interpreter (4–8 months)
Good working fund of knowledge
Consistently prepared for attending input
Consistently able to interpret data: can identify and prioritize new problems
Can offer reasonable possibilities for new problems or outcomes and cite reasons they may apply to this patient
Not always correct, but has a higher level of knowledge, more skill
Answers the "*how and why*" questions about polysomnography, actigraphy, and MSLT/MWT
Manager (8–12 months)
Excellent general fund of knowledge
Broad/deep knowledge of the testing
Actively suggests management options, answers the "*what's next*"
Is proactive rather than reactive, actively suggests management options
Confidence/willingness to state own preferences
Diagnostic plans include more than one appropriate treatment option and considers reasonable therapies

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Educator (10–12 months)
Can cite evidence citing pros and cons of testing and interpretations
Takes an active role in educating themselves, colleagues, and patients
Skilled in identifying questions that cannot be answered from textbooks
Superior fund of knowledge
Consistently possesses superior knowledge and skill and can tailor management pathways for patients and for hospital systems

This table is a composite adapted from Emory University School of Medicine & Pangaro LN. Academic Medicine 1999; 74:1203–7

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Chapter 2
Neurophysiology of Sleep

Thomas E. Dick and Pingfu Feng

Introduction

Consideration of the neurophysiological mechanisms of sleep and wakefulness emerged with the ability to measure "sleep" via the electroencephalogram (EEG), developed by Hans Berger in the 1920s–1930s. (Interestingly, this period overlaps Nathaniel Kleitman's work on circadian rhythm published in 1929, which has been tied to sleep ever since.) The EEG clearly showed various patterns; the first being what Hans Berger described were "alpha" waves over the occipital cortex in awake relaxed humans with their eyes closed. In subsequent recordings, EEG synchrony was identified during the initial stages of sleep. Desynchronized or REM sleep was not discovered until 1953, when Aserinsky and Kleitman recorded people at night. Thus being able to distinguish EEG in wakefulness from sleep allowed scientists to address the neural origins of sleep.

Initial experiments began by addressing what EEG patterns were present in the isolated the central nervous system. Two preparations, *encephale isole* and *cerveau isole*, were created in cats. The *encephale isole* had the CNS transected near the caudal medulla, and the cats were kept alive on ventilators. Following this transection the cats went through oscillating periods of EEG synchrony and desynchrony. In contrast the *cerveau isole* is a transection through the midline separating the brainstem from the hypothalamus and cortex. Following this transection, the EEG was synchronized. One difference between the preparations was cranial sensory input, and the chronic EEG synchrony in the absence of sensory input resulted in deafferentation theory of sleep, sleep as a passive state resulting from the absence of

T.E. Dick, Ph.D. (✉) • P. Feng, M.D., Ph.D.
Division of Pulmonary, Critical Care and Sleep Medicine,
Case Western Reserve University School of Medicine,
11100 Euclid Avenue, Cleveland, OH 44106-5067, USA
e-mail: ted3@case.edu; thomas.dick@case.edu

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sensory input. However, the other difference between the two preparations was the loss of brainstem structures. In the 1930s these were poorly defined, but since then many nuclei that determine state have been identified. In 1943, Moruzzi and Magoun identified the ascending reticular activating system (ARAS or RAS) and an area in the mesencephalon, which when selectively lesioned leaving the sensory pathways to the thalamus intact, synchronized the EEG, whereas when activated, desynchronized the EEG. This finding destroyed the passive theory of sleep – even though you as an individual do your best to reduce sensory input when you go to sleep by finding a warm comfortable place, turning off lights, and reducing noise.

The subsequent experiments combined recording activity and selective pharmacology with the lesioning and stimulation protocols to identify sites which are critical to state. Multiple sites have been identified that either promote wakefulness or promote sleep. Indeed, a current theory is that the balance between these mechanisms determines your state; ideally it is toggle switch, a "flip-flop" mechanism. The mutual inhibitory network between the wakefulness and sleep-promoting mechanisms ensures stable states. We present the material in this chapter to be consistent with both ACGME and ABIM requirements as both clearly mandate a comprehensive knowledge of the neural mechanisms underlying state.

The chapter will not be a review of the literature (See References 1–3) but will focus on findings that are fundamental to sleep practitioner's knowledge and will provide specific examples of how topics in this area could be taught and then assessed for competency. Table 2.1 is a map of content domains showing how subtopics may be related to the ACGME general competencies for training in sleep medicine. Table 2.2 lists examples of content-specific questions for generating learning objectives and for assessing the competency regarding these objectives. The raised questions can be the basis for instructional classes and incentives for journal club discussions.

This chapter also provides specific examples of assessment tools. The matching test is included to review factual knowledge of the neurophysiological basis of sleep. As knowledge develops in this field, questions can be added or modified. Essay questions are provided to assess an integrated understanding of an approach. These questions can be provided in many contexts and can be adopted to provide a direction of the discussion. The IQ cases offer examples of IQ group exercises, in which the learning objectives are disclosed later, requiring the learners to seek and evaluate information to achieve the learning objectives of the case. These group discussions assist learners to share knowledge and to improve their learning techniques. The IQ cases can assess where the group training is.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/neurophysiology.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case

State-specific neuronal discharge patterns		
Discharge type	Cell location	Transmitter
Wake-on/REM-off	DR, LC, PH	5HT, NE, HA
	LH	HCRT
REM-on	LDT/PPT	Ach
Wake-on/REM-on	LDT/PPT	Ach
	BF	
NREM-on	POA/AH/BF	GABA
State independent	VTA, SN	DA

Table 2.1 Cognitive Map of the Content Domains Relevant to the Neurophysiology of Sleep and Circadian Rhythm

		Knowledge	Skills	ACGME competency
I	*Epidemiology*	Yes	Yes	B, F
	Demographics			
	Risk factors			
	Special populations			
II	*Mechanisms*	Yes	Yes	A, B, E
	Central nervous system			
	Somatic nervous system			
	Autonomic nervous system			
III	*Risk factors*	Yes	Yes	A, B
	Psychiatric			
	Genetic/gender			
	Developmental/aging			
IV	*Patient assessments*	Yes	No	A, C, F
	Adult			
	Pediatrics			
	Special populations			
V	*Diagnostic measures and interpretation*	Yes	No	A, C, F
	Polysomnography			
	History and physical examination			
	Patient-based testing			
VI	*Disease management*	Yes	Yes	A, E, D, F
	Decisions on therapy			
	Type of therapy			

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		Knowledge	Skills	ACGME competency
VII	*Health and disease clinical pathways* Neural disorders Psychiatric disorders Medical comorbidities	Yes	Yes	A, C, F
	Code for ACGME competencies A. Patient care B. Medical knowledge C. Practice-based learning and improvement			D. Interpersonal skills E. Professionalism F. System-based practice

Table 2.2 Examples of Topics with Educational Objectives

Item I. Genetics

- Define genetic functional systems in sleep and wakefulness – GABA, orexin, and monoamines
- Become familiar with the terminology of neuroscience of sleep:
  1. Brain structures: suprachiasmatic nucleus (SCN), ventrolateral preoptic area (VLPO), tuberomammillary nucleus (TMN), subparaventricular zone (SPZ), dorsomedial nucleus of the hypothalamus (DMH), pedunculopontine tegmentum/lateral dorsal tegmentum (PPT/LDT), retinohypothalamic tract (RHT), dorsal raphé, locus coeruleus, medial pontine reticular formation, ascending reticular activating system, lateral hypothalamus, inhibitory area of Magoun and Rhines, peri-locus coeruleusα area
  2. Neurotransmitters: melatonin, orexin (hypocretin), GABA, serotonin (5HT), acetylcholine (ACh), histamine, adenosine, catecholamines, histamine, monoamines
  3. Effective drugs: modafinil, armodafinil, benzodiazepines, almorexant, Rozerem (ramelteon), Lunesta (eszopiclone), longdaysin
- List how proteins affect cortical membrane potential, hyperpolarizing versus depolarizing

Item II. Anatomy and physiology

- Describe the location and role of the hypothalamus (ventrolateral preoptic (VLPO), ventrolateral hypothalamus, pedunculopontine tegmentum/lateral dorsal tegmentum (PPT/LDT), reticular activating system (RAS)
- Understand the balance of excitatory and inhibitory input in controlling thalamocortical loops
- Understand the difference in the neurophysiologic basis between NREM and REM sleep
- Understand the control of motor activity during REM sleep

Item III. Clinical syndromes

- Describe from a neural systems viewpoint
  - Narcolepsy
  - Insomnia
  - Restless legs syndrome
  - REM sleep disorders
  - Sleep apnea

Item IV. Diagnostic measures as a reflection of circadian and sleep neural systems

- Multiple sleep latency onset
- Questionnaires
- Polysomnography (especially EMG)

(continued)

(continued)

Item V. Therapeutics

- Drug actions that promote wakefulness (modafinil, armodafinil)
- Drug actions that promote sleepiness (benzodiazepines, nonbenzodiazepines)
- Drugs actions that treat cataplexy (tricyclic antidepressant, sodium oxybate)

Item VI. Prognosis, complications, and comorbid conditions

- Discuss interactions of sleep neural systems with pathophysiologic and treatments for primary neurologic and psychiatric disorders
- Understand the interaction of drug addiction and recovery and sleep neurophysiology

Matching Test

Questions

The sleep-promoting actions of this neurotransmitter are antagonized by caffeine. ☐

These neurons release the inhibitory neurotransmitters galanin and GABA to inhibit the monoaminergic cell groups in the locus coeruleus, the raphe nucleus, and the tuberomammillary nucleus. ☐

This hypothalamic region is critical for the integrating circadian rhythms of sleep-wakefulness, feeding, locomotion, and temperature. ☐

G-protein-coupled receptor that binds both orexin A and orexin B and is present mainly in GABAergic putative brainstem interneurons. ☐

This neurotransmitter is synthesized in raphe neurons whose activity varies with state greatest in wakefulness and least in REM sleep. ☐

This brainstem region contains serotonergic cells that become quiescent during REM sleep. ☐

Its release in the cortex is high during waking and REM sleep and lowest during deep NREM sleep. ☐

This brainstem structure described in 1949 receives input from many sensory modalities and sends output to the thalamus and cortex. Its activity is state dependent. ☐

Synthesized in tuberomammillary nuclei of the posterior hypothalamus, this neurotransmitter is released extensively throughout the brain. ☐

Arousing neurotransmitter; formed in the CNS by tuberomammillary neurons in the posterior hypothalamus. ☐

This brainstem region contains neurons that are active during, and may even initiate, REM sleep. ☐

Stimulation of this cranial nerve is hypnogenic. ☐

A hormone synthesized in the paraventricular nucleus of the hypothalamus which is released in response to stress. ☐

Nearly 50 years before the description of REM sleep, it has been known that carbachol administered to this brainstem area produced a state change which we now refer to as "REM-like." ☐

This structure is critical for integrating sleep and metabolism physiologically and behaviorally. ☐

A drug that enhances the action of GABA at the GABAA receptor and promotes sleep. ☐

Medullary area which mediates muscle atonia. ☐

A class of neurotransmitters with an amino group connected to an aromatic ring. Examples include histamine, catecholamines (dopamine, norepinephrine, and epinephrine), and tryptamines (serotonin (5-HT) and melatonin). ☐

This brainstem nucleus contains norepinephrine neurons that are active during wakefulness. ☐

Bilateral lesions in this pontine area result in animals "acting out" their dreams. ☐

This hypothalamic structure is critical for determining circadian rhythm. ☐

The circadian rhythm of this hormone's levels is disrupted by light in the blue-light wavelength (~440 nm). ☐

Loss of this nucleus after bilateral destruction of the posterior hypothalamus results in hypersomnolence. ☐

Deficiency in this neuropeptide modulator underlies the most common form of narcolepsy, in which the sufferer briefly loses muscle tone (cataplexy). ☐

This hypothalamic nucleus receives a strong projection from the SCN and contains subnuclei that regulate circadian rhythms of body temperature and sleep separately. ☐

Answers

1. Suprachiasmatic nucleus (SCN)
2. Ventrolateral preoptic area (VLPO)
3. Tuberomammillary nucleus (TMN)
4. Paraventricular nucleus
5. Subparaventricular zone (SPZ)
6. Dorsomedial nucleus of the hypothalamus (DMH)
7. Pedunculopontine tegmentum/lateral dorsal tegmentum (PPT/LDT)
8. Retinohypothalamic tract (RHT)
9. Median preoptic nucleus
10. Dorsal raphé
11. *Locus coeruleus*
12. Kölliker-Fuse nucleus
13. Medial pontine reticular formation
14. Ascending reticular activating system
15. Pineal body
16. Lateral hypothalamus
17. Inhibitory area of Magoun and Rhines
18. Peri-locus coeruleusα area
19. Pontine gray
20. Vagus
20. Vagus
21. Melatonin
22. Orexin (hypocretin)
23. Orexin 1 receptors
24. Orexin 2 receptors
25. GABA
26. Glycine
27. Serotonin (5HT)
28. Acetylcholine (ACh)/ cholinergic
29. Histamine
30. Adenosine
31. A1 receptors
32. A2 receptors
33. Caffeine
34. Epinephrine/catecholamines
35. Histamine
36. Monoamines
37. Catecholamines
38. Excitatory amino acids
39. Benzodiazepine
40. Corticotrophin-releasing factor

Questions with Answers

The sleep-promoting actions of this neurotransmitter are antagonized by caffeine. 30

These neurons release the inhibitory neurotransmitters galanin and GABA to inhibit the monoaminergic cell groups in the *locus coeruleus*, the raphe nucleus, and the tuberomammillary nucleus. 2

This hypothalamic region is critical for the integrating circadian rhythms of sleep-wakefulness, feeding, locomotion, and temperature. 6

G-protein-coupled receptor that binds both orexin A and orexin B and is present mainly in GABAergic putative brainstem interneurons. 24

This neurotransmitter is synthesized in raphe neurons whose activity varies with state greatest in wakefulness and least in REM sleep. 27

This brainstem region contains serotonergic cells that become quiescent during REM sleep. 10

Its release in the cortex is high during waking and REM sleep and lowest during deep NREM sleep. 28

This brainstem structure described in 1949 receives input from many sensory modalities and sends output to the thalamus and cortex. Its activity is state dependent. 14

Synthesized in tuberomammillary nuclei of the posterior hypothalamus, this neurotransmitter is released extensively throughout the brain. 29

Arousing neurotransmitter; formed in the CNS by tuberomammillary neurons in the posterior hypothalamus. 35

This brainstem region contains neurons that are active during, and may even initiate, REM sleep. 7

Stimulation of this cranial nerve is hypnogenic. 20

A hormone synthesized in the paraventricular nucleus of the hypothalamus which is released in response to stress. 40

Nearly 50 years before the description of REM sleep, it has been known that carbachol administered to this brainstem area produced a state change which we now refer to as “REM-like.” 13

This structure is critical for integrating sleep and metabolism physiologically and behaviorally. 16

A drug that enhances the action of GABA at the GABAA receptor and promotes sleep. 39

Medullary area which mediates muscle atonia. 17

A class of neurotransmitters with an amino group connected to an aromatic ring. Examples include histamine, catecholamines (dopamine, norepinephrine, and epinephrine), and tryptamines (serotonin (5-HT) and melatonin). 36

This brainstem nucleus contains norepinephrine neurons that are active during wakefulness. 11

Bilateral lesions in this pontine area result in animals “acting out” their dreams. 18

This hypothalamic structure is critical for determining circadian rhythm. 1

The circadian rhythm of this hormone's levels is disrupted by light in the blue-light wavelength (~440 nm). 21

Loss of this nucleus after bilateral destruction of the posterior hypothalamus results in hypersomnolence. 3

Deficiency in this neuropeptide modulator underlies the most common form of narcolepsy, in which the sufferer briefly loses muscle tone (cataplexy). 22

This hypothalamic nucleus receives a strong projection from the SCN and contains subnuclei that regulate circadian rhythms of body temperature and sleep separately. 5

Essay Questions

Familial Advanced Sleep Phase Syndrome (FASPS)

A 22-year-old male complains of early morning (~4:00 am) wakening and difficulty to go back to sleep. He usually gets out of bed at 5:00 am. The early wakening cannot be explained by anxiety regarding the day's commitments or by jet lag, recent travel crossing time zones. He is energized and performs well in the morning. However, his energy runs out much earlier than what he expected in the afternoon. He does not watch TV or movies in the evening due to difficulty in maintaining wakefulness after 7:30 pm. He has to go to bed at 8:30 pm. This started several years ago but over the past 2 years has worsened. Otherwise he is generally healthy and has maintained a good GPA at both high school and college. He knows that his father and one of his cousins have the similar problem. His Horne-Östberg score was 75. His Morningness-Eveningness Questionnaire (MEQ) showed he is M-type.

Questions

1. What is the most likely diagnosis?
2. How may patient's melatonin phase change?
3. What gene mutation may patient have?
4. What are the treatments and their long-term effectiveness/outcome?

Answers

1. *Familial advanced sleep phase syndrome (FASPS):* Patients with FASPS have about a 4-h phase advance, which causes arousal in the morning and sleep onset in the evening earlier than normal population. In general, patients arouse at 4–5:30 am and fall to sleep at 7:30–8:30 pm. Although their biological rhythms and major sleep timing are all advanced, they are in phase with each other much like healthy controls. FASPS has familial factors. The complaints of early wakening and sleeping and the similar symptoms of their family members are a good indication of FASPS.
2. The patient's dim-light melatonin onset (DLMO) should be phase-advanced by 3–4 h. This phase change should be distinguished from changes due to stress, sleep deprivation, or unconventional sleep-wake schedules.
3. The patient may have either hPER2 or CK1 gene mutation. In this scenario, CLOCK and BMAL1 are transcriptional factors that heterodimerize and induce the expression of *Per* and *Cry* genes by binding to their promoters at E-boxes. CK1 isoforms bind and phosphorylate PER and CRY and subsequently cause the degradation of Clock/Bmal1 stopping the transcription of *Per* and *Cry*. Recently, a missense mutation at a putative phosphorylation site in hPER2, Ser-662, was identified in patients that suffer from FASPS. This is a serine-to-glycine point mutation in the CK1 binding domain of the hPER2 protein that resulted in hypophosphorylation of PER2 in vitro. Interestingly, a mutation of CK1δ was found separately in Japanese family that suffers from FASPS as well.
4. ASPD can be treated with bright light therapy in the evenings or behaviorally with chronotherapy. Unlike other sleep disorders, ASPD does not disrupt normal

functioning at work during the day, and the patient does not complain of excessive daytime sleepiness. If their ASPD is causing patients to miss evening activities, including putting their own normal children to bed, then with this treatment they can stay awake later than their circadian rhythm. A sufferer of ASPD will still wake very early, and if this cycle continues, it can lead to chronic sleep deprivation and other sleep disorders.

Neurophysiology of Sleep and Circadian Rhythm

A 16-year-old male finds it hard to function at school and home and in social situations because of extreme tiredness. He has trouble sleeping at night, but can fall asleep suddenly, even in the middle of talking, eating, or other activity. When he falls asleep suddenly, he suffers loss of muscle tone. Strong emotions can often trigger these episodes, which may last seconds or minutes.

Questions

1. What is the most likely diagnosis?
2. What are the probable neurophysiologic pathways that are disrupted to cause narcolepsy?
3. How do treatment strategies intervene in these probable pathways?
4. What neurophysiologic pathways control muscle atonia during REM sleep?

Answers

1. Narcolepsy, which is a disorder that causes periods of extreme daytime sleepiness. The disorder also may cause muscle weakness.
2. Orexin-producing neurons in the lateral posterior hypothalamic nuclei (perifornical area, lateral hypothalamus, and posterior hypothalamus). These "orexin" neurons activate monoaminergic neurons in the hypothalamus (tuberomammillary nucleus) and brainstem (raphe, locus coeruleus) that promote wakefulness.
3. Treatment strategies depend on the differential symptoms of sleepiness and cataplexy. Excessive daytime sleepiness (sleep attacks) is responsive to stimulant medications that promote wakefulness. Modafinil (Provigil) has FDA approval for the treatment of narcolepsy and may act as an agonist of the orexin receptors. Sodium oxybate (Xyrem) is approved for use in the treatment of narcolepsy to reduce cataplexy and excessive daytime sleepiness (EDS).
4. Muscle atonia results from two complementary mechanisms: disfacilitation, decreased noradrenergic and serotonergic excitatory input, and inhibition, glycinergic and GABAergic inputs hyperpolarizing the membrane (making the membrane potential more negative). Both disfacilitation and inhibition are brainstem mechanisms that can be elicited by acetylcholine placed in the brainstem. Disfacilitation results from the loss of noradrenaline from locus coeruleus and serotonin from caudal raphé. These neuronal transmitters decrease because activity of the groups is state dependent and decreases in REM sleep. On the other hand, stimulation of the inhibitory area of Magoun and Rhines in the medullary reticular formation mediates inhibition in REM sleep. These pathways are involved in the muscle atonia of REM sleep.

IQ Case

Evaluate Neurophysiology of Sleep and Diagnosis of Insomnia for Student

Goal: Understand the tools, especially how with an available history and clinical data one can utilize knowledge of the neurophysiology of sleep.

Case Vignette

Insomnia description: A 22-year-old girl is self-referred to the sleep clinic because she has been unable to fall asleep every night for several years. She also cannot maintain a good sleep during the night due to frequent wakening up. This could be a self-wakening up or wakening up by gentle noise. She finds it very difficult to go back to sleep again if she wakes up. She said she dreamed a lot and she can remember almost everything that happened during the night. When she goes to school in the morning, she feels tired. She is in her last year of college and majors Biology. She feels nervous about exams. The sleep problem would be worsened if she has an important schedule the next day. Sometimes she feels sad and lonely and is not interested in any classes, but that is not often and lasts very briefly. Her GPA was 3.7 in high school and is around 3.3 currently.

The predominant complaint of primary insomnia is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least 1 month. This may cause significant distress in the daytime or during work and impact social or occupational functioning. The sleep disturbance may associate with daytime fatigue and be worsened by stress overloading. Primary insomniacs do not have a history of substances usage or diagnosis of mood disorders. However, literature reports that chronic insomnia may lead to depressive disorders.

Major symptom of insomnia is difficulty in falling asleep and maintaining sleep. Thus, patient may have extended sleep latency, increased number of wakefulness after sleep onset, reduced total sleep, and decreased deep sleep such as N3. If the power spectral density of the EEG is analyzed, the delta power band may be decreased. This could be partially reflected in the PSQI and should have all in the PSG data. Patients diagnosed with primary insomnia should have a normal PHQ-2.

Insomnia is a highly prevalent sleep disorder, yet little is known about the role of genetic factors in its pathophysiology. Primary insomnia may have PSG hyperarousal and elevated hypothalamic-pituitary-adrenal (HPA) axis. Elevated brain level of CRF or orexins may be involved. However, there is no literature regarding the measurement of CSF orexin levels in primary insomniacs. Primary insomnia has to be treated individually and can be treated with cognitive behavioral therapy such as reducing usage of caffeine, tobacco, or alcohol near bedtime and avoiding daytime sleep. Antidepressant trazodone has been selected as the initial treatment in a considerable percentage of patients. Newer classes of benzodiazepine and nonbenzodiazepine are also used substantially. Primary insomnia is treatable but may be difficult to cure.

Evaluate Neurophysiology of Sleep and Diagnosis of Insomnia for Facilitator

Goal: Understand the instrument available for the examination and assessment of sleep quality and how to interpret them.

Objectives (Revealed at the End of the Session)

A. Describe the different sleep states and their neurophysiologic basis.
B. Interpret polysomnography (EEG, EOG, EMG, and cardiorespiratory) patterns.
C. Discuss the neurophysiologic basis of common sleep disorders.
D. Describe the impact of disturbed sleep on patient's quality of life.
E. Propose a diagnostic plan to properly assess the neurologic function in sleep disorders.

Case Vignette

Insomnia description: A 22-year-old girl is self-referred to the sleep clinic because she has been unable to fall asleep every night for several years. She also cannot maintain a good sleep during the night due to frequent wakening up. This could be a self-wakening up or wakening up by gentle noise. She finds it very difficult to go back to sleep again if she wakes up. She said she dreamed a lot and she can remember almost everything that happened during the night. When she goes to school in the morning, she feels tired. She is in her last year of college and majors Biology. She feels nervous about exams. The sleep problem would be worsened if she has an important schedule the next day. Sometimes she feels sad and lonely and is not interested in any classes, but that is not often and lasts very briefly. Her GPA was 3.7 in high school and is around 3.3 currently.

Probing Questions

1. What kind of sleep disorder is most probable?
2. What conditions may predispose to this disorder?
3. What complications may arise from this if left untreated?
4. How would you proceed with a diagnostic plan?

The predominant complaint of primary insomnia is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least 1 month. This may cause significant distress in the daytime or during work and impact social or occupational functioning. The sleep disturbance may associate with daytime fatigue and be worsened by stress overloading. Primary insomniacs do not have a history of substances usage or diagnosis of mood disorders. However, literature reports that chronic insomnia may lead to depressive disorders.

Probing Questions

5. What do the PSQI (Pittsburgh Sleep Quality Index) and PHQ-2 (Patient Health Questionnaire-2) show?
6. What do the multiple sleep latency test and polysomnography show?
7. What is your diagnosis based on the PSQI and polysomnography?
8. What is the concordance between PSQI and polysomnography?

The major symptom of insomnia is difficulty in falling asleep and maintaining sleep. Thus, the patient may have extended sleep latency, increased number of wakefulness after sleep onset, reduced total sleep, and decreased deep sleep such as N3. If analyzed using EEG power frequency, the delta power band may be decreased. This could be partially reflected in the PSQI and should have all in the PSG data. Patients diagnosed with primary insomnia should have a normal PHQ-2.

Probing Questions

9. What can you tell the patient about inheritability?
10. What is the chance of successful treatment?
11. How can you reduce the chance of other sleep and psychiatric disorders from developing?

Insomnia is a highly prevalent sleep disorder, yet little is known about the role of genetic factors in its pathophysiology. Primary insomnia may have PSG hyperarousal and elevated hypothalamic-pituitary-adrenal (HPA) axis. Elevated brain level of CRF or orexins may be involved. However, there is no literature regarding the measurement of CSF orexin levels in primary insomniacs. Primary insomnia has to be treated individually and can be treated with cognitive behavioral therapy such as reducing usage of caffeine, tobacco, or alcohol near bedtime and avoiding daytime sleep. Antidepressant trazodone has been selected as the initial treatment in a considerable percentage of patients. Newer classes of benzodiazepine and nonbenzodiazepine are also used substantially. Primary insomnia is treatable but may be difficult to cure.

Probing Questions

12. What is the long-term efficacy of treatment?
13. What other insomnia disorders can you name?

Evaluate Neurophysiology of Sleep and Diagnosis of Insomnia: Final Handout/Objectives

Goal: Understand the instrument available for the examination and assessment of sleep quality and how to interpret them.

Objectives (Revealed at the End of the Session)

A. Describe the different sleep states and their neurophysiologic basis.
B. Interpret polysomnography (EEG, EOG, EMG, and cardiorespiratory) patterns.
C. Discuss the neurophysiologic basis of common sleep disorders.
D. Describe the impact of disturbed sleep on patient's quality of life.
E. Propose a diagnostic plan to properly assess the neurologic function in sleep disorders.

Evaluation of Neurophysiology of Sleep for Student

Case Vignette

A 53-year-old man is at the sleep clinic because since the age of 44 he has been unable to fall asleep easily. When he goes to bed at night, he feels urges to move his legs due to uncomfortable sensations coming from his legs. Stretching and even just moving the legs brings temporary relief. However, walking for an extended period before going to bed effectively relieved these urges in the past, but it has gotten progressively less effective. Further, on long plane trips or long classical music concerts, he has to get up and walk around to relieve the discomfort. In the morning, he doesn't have these symptoms while lying in bed. He is physically fit with no other apparent medical problems.

Restless legs syndrome (RLS) or Willis-Ekbom disease: Surprisingly up to 10 % of the US population may have RLS, but most have a mild form of the disorder that is relieved by physical activity and is intermittent. Nevertheless severe, sleep disruptive RLS affects millions of individuals. Support groups have formed a website: http://www.rls.org.

The patient is diagnosed with restless legs syndrome (RLS) or Willis-Ekbom disease based on self-reported symptoms and the absence of causes due to vitamin or iron (serum ferritin) deficiencies, vascular insufficiency, and thyroid hormone abnormalities. No specific test exists for restless legs syndrome; rather eliminate secondary, highly treatable causes of RLS.

More than 60 % of cases of RLS are inherited in an autosomal dominant fashion with variable penetrance (Lavigne and Montplaisir 1994). Treatment is first to reduce symptoms and second, if necessary, pharmacologic. Many drug treatments have been proposed; one discussed on the restless legs website is ropinirole, a dopaminergic agonist. Interestingly in states that have medical marijuana laws, RLS is a treatable illness.

Evaluation of Neurophysiology of Sleep for Facilitator

Goal: Understand the tools, especially history available to evaluate of neurophysiology of sleep and how to interpret the data.

Objectives (Revealed at the End of the Session)

A. Describe the neurophysiologic basis of motor control during different sleep states.
B. Interpret EMG and what other measurement can be used to confirm the EMG findings.
C. Discuss the neurophysiologic basis of NREM sleep and disorders associated with movement during NREM sleep.
D. Discuss the neurophysiologic basis of REM sleep and disorders associated with movement during REM sleep.

Case Vignette

A 53-year-old man is at the sleep clinic because since the age of 44 he has been unable to fall asleep easily. When he goes to bed at night, he feels urges to move his legs due to uncomfortable sensations coming from his legs. Stretching and even just moving the legs brings temporary relief. However, walking for an extended period before going to bed effectively relieved these urges in the past, but it has gotten progressively less effective. Further, on long plane trips or long classical music concerts, he has to get up and walk around to relieve the discomfort. In the morning, he doesn't have these symptoms while lying in bed. He is physically fit with no other apparent medical problems.

Probing Questions

1. What kind of sleep disorder is most probable?
2. What conditions may predispose to this disorder?
3. What complications may arise from this if left untreated?
4. How would you proceed with a diagnostic plan?
5. What would you say to the sufferer? What is the prevalence? What is the success of treatment?

Restless legs syndrome (RLS) or Willis-Ekbom disease: Surprisingly up to 10 % of the US population may have RLS, but most have a mild form of the disorder that is relieved by physical activity and is intermittent. Nevertheless severe, sleep disruptive RLS affects millions of individuals. Support groups have formed a website: http://www.rls.org.

Probing Questions

6. Are there specific tests for this disorder? What will polysomnography show?
7. On what is your diagnosis based?
8. Would blood tests help?

The patient is diagnosed with restless legs syndrome (RLS) or Willis-Ekbom disease based on self-reported symptoms and the absence of causes due to vitamin or iron (serum ferritin) deficiencies, vascular insufficiency, and thyroid hormone abnormalities. No specific test exists for restless legs syndrome; rather eliminate try to secondary, highly treatable causes of RLS.

Probing Questions

9. What can you tell the patient about inheritability?
10. What is the chance of successful treatment?
11. What other sleep disorders are associated with this disease?

More than 60 % of cases of RLS are inherited in an autosomal dominant fashion with variable penetrance (Lavigne and Montplaisir, 1994). Treatment is first to reduce symptoms and second, if necessary, pharmacologic. Many drug treatments have been proposed; one discussed on the restless legs website is ropinirole a dopaminergic agonist.

Probing Questions

12. What is the long-term efficacy of treatment?
13. What other motor control disorders associated with sleep and its stage?

Evaluation of Neurophysiology of Sleep: Final Handout/ Objectives

Goal: Understand the tools, especially history available to evaluate of neurophysiology of sleep and how to interpret the data.

Objectives (Revealed at the End of the Session)

A. Describe the neurophysiologic basis of motor control during different sleep states.
B. Interpret the EMG and find other signals to confirm EMG findings.
C. Discuss the neurophysiologic basis of NREM sleep and disorders associated with movement during NREM sleep.
D. Discuss the neurophysiologic basis of REM sleep and disorders associated with movement during REM sleep.

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Chapter 3
Pharmacology of Sleep Medicine

Reena Mehra and Kingman P. Strohl

Introduction

There are two broad categories of pharmacologic action that can be considered in sleep medicine – those that induce sleep and those that inhibit sleep or promote wakefulness.

Sedative hypnotic users often increase their prescribed dose without medical advice, and there is rapid development of tolerance, including those taken for sleep initiation. The sedative effects appear very similar to alcohol intoxication and indeed can mimic this action so that patients who had used alcohol to go sleep now will instead use sedatives. Waking psychosocial potential side effects and symptoms of sedative users include hostility or aggression, swings in mood, poor judgment, anterograde amnesia (memory failure for information presented after drug consumption), inability to function in social settings or at work, and/or inappropriate sexual behavior, all actions also seen with alcohol. The subclasses of sedatives encountered in sleep medicine include benzodiazepines, newer-generation benzodiazepine receptor agonists, hypnotics, antihistamines, antidepressants, and historically barbiturates.

The pharmacology of arousal typically involves stimulants which generally increase the amount of norepinephrine and dopamine in the brain. Such agents are encountered in patients being treated for non-sleep conditions including weight loss, depression, attentional disorders, and fatigue and are used in sleep disorders like narcolepsy, idiopathic hypersomnolence, shift work sleep disorder, or excessive

R. Mehra, M.D. M.S. (✉)
Department of Pulmonary, Critical Care and Sleep Medicine, Case Western Reserve University School of Medicine, 11100 Euclid Ave, Cleveland, OH 44106, USA
e-mail: reena.mehra@uhhospitals.org

K.P. Strohl, M.D.
Case Western Reserve University, Cleveland, OH, USA

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sleepiness after adequate therapy for obstructive sleep apnea. Caffeine is the most widely ingested psychostimulant worldwide. Other examples of stimulants include nicotine, ephedrine, methylphenidate, modafinil, and illicit drugs such as methamphetamine and cocaine and androgenic steroids ("club drugs" such as MDMA). Such stimulants in higher doses may provoke hostility or paranoia, high body temperature, irregular heartbeat, heart failure, and seizures. Withdrawal even from therapeutic doses can be associated with fatigue, depression, and disturbed sleep.

Many commonly used drugs for comorbid, non-sleep conditions affect sleep causing either an increase or decrease in wake tendency. In these domains, the subject perceived therapeutic effect is a composite of not only an effect on neurotransmitters but also the so-called non-sleep effects on circadian rhythm, memory, anxiety, reward systems, etc. There are other instances, such as restless legs syndrome or REM sleep behavior disorder, in which drug side effects cause the presentation of a new sleep complaint which largely resolves with the offending agent withdrawn. In addition to the direct and indirect drug-related effects on normal sleep-wake rhythms compounded by alterations of the circadian rhythm, there is also increasing recognition of the interindividual variability in responsiveness to self-administered drug and pharmacotherapeutics.

As a consequence, pharmacologic knowledge and skills are integral to the practice of sleep medicine (http://www.acgme.org/acWebsite/downloads/RRC_progReq/520_sleep_medicine_06012004_1-YR_u_04122008.pdf: last accessed 9/17/2011). Given the enormity of pharmacotherapeutics for sleep initiation and maintenance in general practice, a training program may need to develop several plans for installing targeted instruction on drugs, drug selection, side effects, withdrawal, chrono-pharmacology, and pharmacodynamics, in contrast to just embedding discussion of drugs with programs that address certain diseases, circadian rhythm, behavioral therapy, epidemiology, etc. Such a curriculum could be based on the highly developed approaches currently incorporated in psychiatry programs. Furthermore, as sleep medicine practitioners manage both adults and children, some understanding is needed as to how pharmacology is presented, evaluated, and approved for both populations.

Content domains were developed through examination of the ACGME requirements, discussions with sleep medicine faculty and prior fellows about current and/or best practice, and collection of existing material on the topic.

Table 3.1 lists content domains relevant to a fellowship. They illustrate the landscape of clinically used material along with corresponding areas for general competencies. While not as comprehensive as one would find in a textbook, these areas are designed to touch upon aspects of clinical practice as well as the basic neurophysiology and neuroanatomic sites of action (see Chap. 2). Some of the areas like epidemiology are solely knowledge based in that through reading about the prescription of sleeping medication across age and ethnic groups, one gains an understanding of how society as well as non-sleep doctors modify sleep-wake behavior. The program could test factual proficiency on drug actions, indications, instructions, and side effects through standardized testing, the matching exercises, or the structured essay answers. Patient assessments, while having theoretical underpinnings, can be

brought up in the clinic and invoke immediate feedback. One should attempt to define trainee comprehension concerning relevant features of a review of current medications, past drug use and abuse, and allergy including the ordering of ancillary tests to assess liver function, pregnancy, abuse, and perhaps genetic polymorphisms for drug metabolism.

In regard to learning opportunities, the delivery of this content would be delivered underpinned by instructional objectives and follow-up assessments. In this regard, some examples of objectives for each content area are presented in Table 3.2. Note that this list tries to focus on practice-related, measureable or verifiable outcomes. One can list the objectives either up front or at the middle or end of the instruction, but the goals should be explicit and objectives verified.

The individual training program should modify this list to address of strength or weakness in overall instructional plan or expertise. One can use these questions as a basis for essay questions to amplify a topic presented in another fashion by visiting faculty or a fellow. The faculty or fellow can use the list and choose to construct lectures based on one or more objectives. Working on this list can be a useful exercise to review prior presentations of topics or used as a springboard for written reviews or research.

Essay questions can be given before or after the presentation, or at intervals in the program. The purpose is to have the learner synthesize the material and re-form it into their own words. You can assess written communication skills. "Ideal" answers would be posted after the fellow submits their answers and discussion ensues.

There are no formal IQ cases in this chapter, as other chapters also address pharmacology and its management. There are objectives and two brief cases which can be presented to the student group. The cases have probing questions and ideal answers. There is also a table that could be filled out as a group one or two times during a 1-year fellowship to review pharmacologic principles.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/neuropharmacology.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or cases.

Table 3.1 Cognitive Map of the Content Domains Relevant to Sleep Apnea and Related Disorders

		Knowledge	Skills	ACGME competency
I	*Epidemiology* Sleep aid use Sleepiness Abuse	Yes	No	B, F

(continued)

(continued)

		Knowledge	Skills	ACGME competency
II	*Mechanisms*	Yes	No	A, B
	Receptor properties			
	GABA receptor subtypes			
III	*Risk factors*	Yes	No	A, B
	Genetic			
IV	*Patient assessments*	Yes	Yes	A, C, D, E
	Side effects			
	Efficacy			
	Special populations, including pregnancy			
V	*Diagnostic measures and interpretation*	Yes	Yes	A, C, F
	Drug screens			A, C
	Liver function tests			A, B, F
VI	*Disease management*	Yes	Yes	A, D, F
	Augmentation in RLS			A, F
	Decisions on therapy			
	Follow-up			
VII	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Withdrawal from alerting agents			A, F
	Contraception effects of alerting agents			A, F
	Commercial driver assessment			F
	Allergic vs. side effects			A
	Code for ACGME competencies			
	A. Patient care		D. Interpersonal skills	
	B. Medical knowledge		E. Professionalism	
	C. Practice-based learning and improvement		F. System-based practice	

Table 3.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
• Illustrate community use and market forces for OTC and FDA-approved sleep aids
• Describe the societal trends and attitudes in sleep, sleepiness, and sleep aids across the last century
• Compare presentation profiles for drug dependent vs. organic EDS
• Recognize the sleep-related side effects of commonly prescribed medications as well as less commonly prescribed medications with well-known effects on sleep physiology
• Understand the appropriate use of sedative hypnotics in insomnia and its role as an adjunct to non-pharmacologic strategies
• Elucidate the indications and effects of commonly prescribed medications for sleep disorders such as restless legs syndrome and hypersomnia disorders

(continued)

(continued)

Item II. Mechanisms of health and disease
- Draw the relationships between drugs that induce sleep and sleep complaints
- Contrast histaminergic and dopaminergic pathways in terms of alertness and sleepiness
- Discuss the actions of sleeping medications in regard to the five subtypes present in the GABA receptor
- List the manner how opioids lead to central apneas and abnormal breathing patterns such as Biot's breathing

Item III. Patient assessments
- Inventory features that indicate "augmentation" in the management of RLS and a plan to mitigate it
- Contrast the elements of NREM to that of REM parasomnia that guide need for and type of pharmacologic treatment
- Review indications of alerting agents in hypersomnia disorders
- Understanding sedating and wakefulness promoting side effects of commonly prescribed medications (e.g., H1-antihistamines, beta-blockers, pseudoephedrine)

Item IV. Diagnostic strategies
- Describe and compare urinary and blood tests for drug addiction vs. prescribed levels of alerting agents and opioids used in sleep medicine

Item IV. Practice-based management
- Compare outcome measures for pharmacologic treatment of sleepiness in the management of narcolepsy and idiopathic hypersomnolence
- Imagine novel pharmacologic approaches to insomnia

Item V. Health and disease management pathways
- Describe the principles in the initiation of therapy for restless legs syndrome
- Now that a patient is placed on therapy, list the factors for management of narcolepsy as a chronic disease
- List patient expectations vs. physician objectives in terms of outcomes

Item VI. Practice-based learning and improvement
- Devise a quality improvement program for management of controlled substances
- Formulate a checklist for adherence for different pharmacologic therapies

Item VII. Interpersonal and communication skills
- Demonstrate and apply motivational interviewing in the proper use of alerting agents for narcolepsy in children and adults
- Evaluate each other's notes and dictations for descriptions of pharmacologic data and prescription practice

Item VIII. Professionalism
- Fabricate a fair and unbiased presentation on the dangers of drowsy driving
- Identify ethical conflicts in prescription of drugs for insomnia

Item IX. System-based practice
- Disease management pathways
  - Concept map a plan to track both prescribed and OTC agents used in a patient with insomnia
  - Develop a family-based plan for drug management of narcolepsy
- Evaluate comanagement with psychology consultations for indications and cost-effectiveness

Matching Test

Questions

Active ingredient in several OTC sleep "aids" like Sominex and Unisom.
Presumed active ingredient producing Thanksgiving postprandial somnolence.
Rozerem.
Only agent with 12-month efficacy data.
While no drug is FDA approved for pediatric sleep use, it has long history of safe use in depression and anxiety.
Prescription strength H1 receptor agonist side effects of weight gain, increased appetite, and liver toxicity.
Most notable of tricyclics used for "sleep" with side effect of diarrhea.
Like its cousin, a prescription also requires asking about birth control pills.
Single isomere of this class.
FDA approved for cataplexy and excessive daytime sleepiness and prescribed at night.
New class of alerting agents.
Non-FDA indication for pavor nocturnus.
Pharmacologic risk for REM sleep behavior disorder (RBD).
Moderate to strong efficacy in PTSD-associated nightmares.
Sedative effects presumably through locus coeruleus.
Some non-GABA efficacy in restless legs syndrome as second-line therapy.
Used in treatment of bruxism.
Act on the pre-Boetzinger complex to alter rhythmogenesis.
Renally excreted benzodiazepine used in cirrhosis.
The only antipsychotic that does not suppress NREM sleep.
Increases the mean MSLT when used by OSA patients by 1 min.
Will interfere with melatonin release.

Answers

1. Melatonin
2. H1 receptor antagonist
3. Tryptophan
4. M1 and M2 agonist
5. Lunesta
6. Temazepam
7. Flurazepam
8. Zolpidem
9. Doxepin
10. Mirtazepine
11. Quetiapine
12. Nefazodone
13. Trazodone
14. NK-1 inhibitor
15. Modafinil
16. Armodafinil
17. Ramelteon
18. Methylphenidate
19. Amphetamine sulfate
20. Dextroamphetamine
21. Gamma-hydroxybutyrate receptor agonist
22. Sodium oxybate
23. H3 antagonists
24. Clonazepam
25. Beta-blockade
26. Prazosin
27. Clonidine
28. Dopaminergic agonist pathway
29. Oxycodone
30. Anticonvulsants
31. Tramadol
32. Monoamine Oxidase Inhibitor
33. Pergolide
34. Aspirin
35. Opioids
36. Lithium
37. Caffeine
38. Lorazepam
39. Bupropion
40. Rotigotine
41. Oxymetazoline
42. Barbiturates
43. Benzodiazepines
44. Benzodiazepine receptor agonists
45. Pramipexole
46. Galanin
47. GABA
48. Ferrous sulfate
49. Carbidopa/levodopa
50. Zaleplon

Questions with Answers

Act on the pre-Boetzinger complex to alter rhythmogenesis. 35
Active ingredient in several OTC sleep "aids" like Sominex ® and Unisom ®. 2
Result in less effects on sleep architecture (less increase Stage 2 and less reduction of slow-wave sleep) than its counterpart class. 44
FDA approved for cataplexy and excessive daytime sleepiness and prescribed at night. 22
Like its cousin, a prescription also requires asking about birth control pills. 15
Antagonist of the adenosine receptor with diuretic properties. 37
Moderate to strong efficacy in PTSD-associated nightmares. 26
Most notable of tricyclics used for "sleep" with side effect of diarrhea. 13
New class of alerting agents. 23
Transdermal dopaminergic agent approved for treatment of restless legs syndrome. 40
Non-FDA indication for pavor nocturnus. 24
Only agent with 12-month efficacy data. 5
Benzodiazepine receptor agonist with the shortest onset of action. 50
Pharmacologic risk for REM behavior disorder. 25
Prescription strength H1 receptor agonist side effects of weight gain, increased appetite, and liver toxicity. 10
Combined with serotonin reuptake inhibitors may result in serotonin syndrome. 32
Presumed active ingredient producing Thanksgiving postprandial somnolence. 3
Renally excreted benzodiazepine used in cirrhosis. 38
Dopaminergic agent most associated with augmentation. 49
Rozerem. 4
Prevalent use of these medications associated with increased recognition of abnormal sleep-related behaviors. 44
Sedative effects presumably through locus coeruleus. 27
Single isomere of this class. 16
This medication delivered as a nasal spray is associated with rebound congestion. 41
Some non-GABA efficacy in restless legs syndrome as second-line therapy. 30
Has been associated with compulsive behaviors such as gambling. 45
Used in treatment of bruxism. 33
Take with Vitamin C to enhance absorption. 48
While no drug is FDA approved for pediatric sleep use, it has long history of safe use in depression and anxiety. 9
Medications associated with sleep spindles. 43
The only antipsychotic that does not suppress NREM sleep. 11
The most abundant neurotransmitter in the brain. 47
Increases the mean MSLT when used by OSA patients by 1 min. 15
Will interfere with melatonin release. 25
Only FDA-approved medication for symptoms of shift work sleep disorder. 15

Salivary levels peak at approximately 120 pM or 30 % of the plasma levels. 1
A less than ideal, but low-cost option for pharmacologic treatment of insomnia. 6
Typically administered in two equal dosages at bedtime. 22
Most commonly prescribed benzodiazepine receptor agonist. 8
An antidepressant which does not reduce REM sleep. 39
Most commonly prescribed non-FDA-approved medication prescribed for insomnia. 13
Can cause nephrogenic diabetes insipidus. 36
Results in REM beta EEG activity. 42
Most common neurotransmitter in the brain. 47

Essay Questions

Case Study 1

A 24-year-old woman arrives in the emergency department (ED) accompanied by her roommate. The roommate states that the patient has been using drugs for sleeping and thinks that an overdose was taken. You administer flumazenil and she recovers. Three hours later you return to find her in a hypnotic state, and the cycle of flumazenil and recovery with relapse repeated itself.

Questions

1. What class of drugs was consumed to have this response? (1–2 short sentences)
2. Why did the intervention ultimately fail? (2–3 sentences)
3. What is a reasonable approach to the patient at this time? (3–4 sentences)
4. What is the relationship of insomnia to depression? (3–4 sentences)

Ideal Answers

1. The somnogenic action of benzodiazepines is reversed by flumazenil.
2. The duration of action by flumazenil is short (20–40 min). In addition benzodiazepines are fat soluble, and there reoccurs redistribution of drug from peripheral fat stores to the brain.
3. One needs to determine patient intent in regard to taking the medication and properly refer when stable for psychiatric evaluation. One of the commonly prescribed benzodiazepines with a long half-life is clonazepam which has a half-life of 8 h. Therefore, 24 h of observation may be required. If high doses of benzodiazepines are being used, there should be a long taper of medications of approximately 10 weeks (Dennis et al. 2006). After evaluation for insomnia, if deemed appropriate, cognitive behavioral therapy targeted towards insomnia (CBT-I) would be the therapy of choice.
4. Poor sleep is captured by 2 of the 5 criteria for depression, making insomnia an essential feature of the diagnosis. In people with insomnia, the risk of developing depression in the next 18 months is high (OR 1.7). Much data have amassed identifying likely bidirectional relationships of insomnia and depression. This in conjunction with recognition that depression and underlying psychiatric disorders occur in approximately half of those with insomnia further solidifies the decision to investigate the diagnosis insomnia.

Case Study 2

A 55-year-old male veteran presents with poor sleep for years whose nightmares have increased over the past 6 months. Two years ago he was started on venlafaxine for depression which helped his mood with new problems in difficulty going to sleep, acting his dreams, and daytime sleepiness; these stopped when the drug was

tapered off. Currently his dreams are more vivid and awaken him at night but without movement; the dreams seem to be the same event or stop at the same point in the dream. He has been placed on flomax for urinary hesitancy and takes hydrochlorothiazide for hypertension. He is frustrated by his sleep. The physical examination is rather unremarkable. He had a negative drug screen.

Questions

1. What explains the venlafaxine effect in this patient? (2–3 short sentences)
2. What are the features of RBD? (3–4 sentences)
3. How do PTSD nightmares differ from RBD, and what neurotransmitters might be involved? (2–3 sentences)
4. What do prazosin and clonidine as treatment of PTSD nightmares have in common? (1–2 sentences)
5. How does one treat RBD? (2–3 sentences)

Ideal Answers

1. Venlafaxine inhibits reuptake of both 5-HT and NE, enhancing vigilance-associated serotonin and norepinephrine networks, producing more wakefulness (insomnia), and decreasing REM while increasing REM fragmentation and non-atonic REM. The literature implicates serotonin, norepinephrine, hypocretin, acetylcholine, and dopamine in the development of RBD. The most likely neuroanatomic abnormality lies in the pons and the regulation of the R-on neurons. The R-on neurons are inhibited by the R-off neurons, which are *activated* by norepinephrine from the locus coeruleus, serotonin from the raphe nuclei, and hypocretin from the lateral hypothalamus.
2. RBD is the motor expression of dreams and is usually not remembered by the patient but inferred through interviews with the bed partner or by a self-report of harm to oneself (or someone else such as the bed partner) during sleep and inferring that a parasomnia is present. The polysomnographic correlate, short of a patient "acting out their dreams," is an increase in muscle tone (generally recorded from the submental muscle EMG) during REM sleep, i.e., non-atonic REM.
3. Dreams in the setting of PTSD are vivid and "stereotypic." Often linked to and recognized as a prior experience, it is the emotive manifestations that carry over from one dream to another. One pathway is that dreams are *activated* by norepinephrine from the locus coeruleus; however, the literature also suggests a role for serotonin from the raphe nuclei and hypocretin from the lateral hypothalamus.
4. Both drugs inhibit alpha-adrenergic receptors and at one level act at the level of the locus coeruleus. This inhibition has blood-pressure-lowering and sedative effects that appear to attenuate over time, but the effects on REM reduction appear to persist.
5. Clonazepam and possibly melatonin are useful medications. Anticholinesterase inhibitors and dopaminergic agents are not of clear benefit. Monoamine oxidase inhibitors, tricyclic antidepressants, serotonergic synaptic reuptake inhibitors, and noradrenergic antagonists can induce or aggravate RBD symptoms and should be avoided in patients with RBD.

Case Study 3

A 16-year-old American male presented for evaluation with his mother a week earlier. He is reportedly very sleepy at school and nods out at home, moody, acts inappropriately with his parents, and has poor impulse control. He reports sleep paralysis and one episode of falling down unexpectedly when told a funny joke. He states that he has vivid dreams, and sometimes at home he awakens from sleep with a start, flailing his arms. His childhood was uneventful and he experienced a normal development. Last winter he had a "viral" illness, after he had been vaccinated for H1N1. He appeared to recover uneventfully. His mother states that he hangs out with the "wrong crowd" and that he is evasive about what he does on the weekends or with his friends. His PCP suspects drug use because it is common in the community, but because of his complex of symptoms, he sends him to you. You decide to perform a polysomnography and MSLT but also order a urinary drug test.

Questions

1. Describe the utility, sensitivity, and specificity of urinary drug testing (UDT) screens in sleep medicine practice (3–5 sentences).
2. List at least three reasons for a false-negative UDT.
3. How would you handle a negative UDT for oxycodone?

Answers

1. Urine drug testing (UDT) results have consequences in regard to diagnostic and therapeutic decisions and the patient-physician trust between physician and patient. Self-reported drug use can be unreliable, and behavioral monitoring lacks sufficient sensitivity to detect substance. Screening methods designed to be sensitive; specificities vary depending on the assay and the likelihood of false-positive results. Confirmatory methods are highly specific but more expensive, and the result arrives days to weeks after the patient-physician encounter. Factors to consider include metabolic conversion between drugs, genetic variations in drug metabolism, and the sensitivity and specificity of the analytical method.
2. A negative urine drug screen can be the result of the following: no drug in the specimen; a drug concentration below the detection threshold; a concentration above the threshold, but the assay is poor; assay interference created (unintentionally) by the administration of other medications or (intentionally) by the addition of adulterants; and a laboratory error.
3. Oxycodone is not detectable by most opiate screening immunoassays. It will require a confirmatory test to indicate that the screen is a true negative.

Quick Exercise: Neurotransmitters Regulating Wakefulness and Sleep

Synaptic network for	Facilitates sleep	Facilitates wakefulness	Brain nuclei or region involved[a]
Acetylcholine			
Adenosine			
Dopamine			
GABA			
Galanin			
Glutamate			
Glycine			
Histamine			
Melatonin			
Norepinephrine			
Orexin			
Serotonin			

[a]Can name more than one

Discussion Cases

Objectives: To review how OTC or prescribed drugs result in sleep complaints

Case Vignette 1

This 40-year-old woman presents with a 12-year history of insomnia. 8 years ago she was prescribed barbiturates which appeared to work, but she was concerned about addiction and so stopped the medications. Currently, she has no difficulty going to sleep but wakes frequently at night and takes 30–45 min to reinitiate sleep. Her general health is good. She has been told she snores if she has a glass of wine about an hour before bedtime. Once she was given a short course of steroids for an arthritic complaint following a viral illness, and it gave her nightmares. She takes ibuprofen for aches and pains prior to going to sleep. She is on no prescribed medications at this time and has no allergies.

Case Vignette 2

A 52-year-old postmenopausal female with a history of depression (for which she has been on long-standing phenelzine) and fibromyalgia comes for evaluation of symptoms of sleep-onset and sleep maintenance insomnia. She states she was

started on a new medication for her fibromyalgia 2 days ago. She has a family history of colon cancer. She describes symptoms consistent with restless legs syndrome as well as night sweats. On examination, you find that she is diaphoretic and tachycardic (regular rhythm) and has hyperreflexia, some muscle rigidity, and pupillary dilation. Her temperature = 100°F, heart rate = 112 bpm, and blood pressure = 189/102 mmHg.

IQ Case for Facilitator

Case Vignette 1

This 40-year-old woman presents with a 12-year history of insomnia. 8 years ago she was prescribed barbiturates which appeared to work, but she was concerned about addiction and so stopped the medications. Currently, she has no difficulty going to sleep but wakes frequently at night and takes 30–45 min to reinitiate sleep. Her general health is good. She has been told she snores if she has a glass of wine about an hour before bedtime. Once she was given a short course of steroids for an arthritic complaint following a viral illness, and it gave her nightmares. She takes ibuprofen for aches and pains prior to going to sleep. She is on no prescribed medications at this time and has no allergies.

Questions

1. You think about prescribing a hypnotic. Discuss which of the following treatments is least likely to be useful (4–5 sentences):

   A. Eszopiclone
   B. Zolpidem
   C. Ramelteon
   D. Zaleplon

2. Compare and contrast the actions of barbiturates and benzodiazepines on sleep. (3 or 4 sentences)
3. Your PCP colleague says he always uses trazodone, because all his patients are depressed. Compare the effects of trazodone to that of zolpidem in the management of insomnia and while not present at this time for the treatment of insomnia in the setting of alcohol rehabilitation. (3–4 sentences)
4. Is there significance to report of steroid effects and the nonsteroidal (ibuprofen) use?
5. How would you image treating insomnia 10 years from now?

Answers

1. All of the drugs listed are FDA-approved hypnotic agents. The patient has difficulty with sleep maintenance. Eszopiclone can improve sleep maintenance as well as reduce sleep latency. Zolpidem reduces sleep latency but does not have a substantial effect on maintenance. Zaleplon has an ultrashort half-life and does not improve sleep maintenance. However, zaleplon (and a newer sublingual formulation of zolpidem, Intermezzo ®) may occasionally be given in the middle of the night as long as at least 4 h remain in the sleep period. Ramelteon is only labeled for sleep-onset insomnia and would not be useful or appropriate for use in the middle of the night.
2. Barbiturates are strong suppressors of REM, while the major benzodiazepine effects are to strongly suppress N3 and mildly suppress REM although these

effects on the sleep architecture are less prominent with the newer-generation benzodiazepine receptor agonists.
3. Both trazodone and zolpidem have similar self-reported efficacy in the first week. By the second week, the effect of trazodone seems to decline. Trazodone is the only medication for insomnia actually tested in an RCT manner for the treatment of insomnia in alcohol withdrawal.
4. Corticosteroid effect on sleep includes a significantly reduced REM sleep and increased arousals; ironically, many patients complain of nightmares with steroids. Nonsteroidal pain relievers decrease synthesis of prostaglandin D. They act to sleep onset by attenuating the normal reduction in temperature with sleep onset and can act to suppress the normal surge in melatonin release**.**
5. Compare your answers with others and consider whether you considered genetics, genomics, genetic manipulation, and neural stimulation in possible approaches.

Case Vignette 2

A 52-year-old postmenopausal female with history of depression (for which she has been on long-standing phenelzine) and fibromyalgia comes for evaluation of symptoms of sleep-onset and sleep maintenance insomnia. She states she was started on a new medication for her fibromyalgia 2 days ago. She has family history of colon cancer. She describes symptoms consistent with restless legs syndrome as well as night sweats. On examination, you find that she is diaphoretic and tachycardic (regular rhythm) and has hyperreflexia, some muscle rigidity, and pupillary dilation. Her temperature = 100°F, heart rate = 112 bpm, and blood pressure = 189/102 mmHg.

Questions

1. Articulate the most likely cause of her symptoms differential diagnosis, rationale, and immediate treatment plan. (4–5 sentences)
2. What key questions regarding her history will you ask to evaluate the etiology of the patient's restless legs syndrome symptoms? (2–3 sentences)
3. Provide a potential pharmacologic approach to the treatment of restless legs syndrome in this patient and cite potential side effects. (5–6 sentences)
4. How would you manage her insomnia symptoms related to postmenopausal status?

Answers

1. The differential diagnosis includes serotonin syndrome, neuroleptic malignant syndrome, anticholinergic toxicity, sympathomimetic toxicity, and hyperthyroidism. Neuroleptic malignant syndrome occurs in the setting of the use of antipsychotics, which is unlikely in her case. Muscle rigidity is not observed in hyperthyroidism. Given her history of depression and fibromyalgia, she most likely has serotonin syndrome in the setting of a recently prescribed serotonin

norepinephrine reuptake inhibitor (duloxetine in this case) in the setting of already prescribed MAO-I. Also, NMS develops over days to weeks and serotonin syndrome develops within 24–48 h. The patient should be admitted to the hospital with continuous cardiac monitoring and intravenous fluids should be administered. Benzodiazepines can be used to treat severe agitation and short-acting agents to address hypertension such as esmolol or nitroprusside should be considered. Control of hyperthermia is important to reduce muscle activity and chance of rhabdomyolysis. Cyproheptadine is considered the antidote due to its nonspecific 5-HT1A and 5-HT2A antagonistic properties and weak anticholinergic effects.

2. The specific temporal relationships of antidepressant medication use and onset of the restless legs syndrome should be investigated as these medications can exacerbate symptoms. The patient has a family history of colon cancer and has not undergone colonoscopy screening. CBC and iron studies including ferritin should be obtained. Review of systems should be focused on symptoms of hematochezia. Iron supplementation is indicated if ferritin < 50 ug/ml.
3. As the dopaminergic pathways are thought to be at the root of the pathophysiology of restless legs syndrome, the use of dopamine D2 and D3 receptor agonists such as pramipexole or ropinirole may be considered. These medications can cause symptoms of mania or illicit compulsive symptoms such as shopping or gambling. Ropinirole is metabolized by the liver and pramipexole is renally excreted. Older-generation dopamine agonists such as carbidopa/levodopa may be considered given these are less expensive; however, proneness to augmentation is increased. Gabapentin or gabapentin enacarbil (the latter considered to have increased oral bioavailability) may also be considered, and dosages should be timed 2–3 h prior to bedtime. The advantage of gabapentin compared to the dopamine receptor agonists is less concern of rebound and augmentation.
4. Although estrogen replacement therapy has been shown to improve postmenopausal symptoms, however, it is not a well-founded approach given from the Women's Health Initiative indicating increased cardiovascular risk and dementia with estrogen replacement therapy. Sleep apnea should be considered as an etiology. Vasomotor symptoms of menopause resulting in sleep disruption may respond to serotonin reuptake inhibitors; however, given the serotonin syndrome diagnosed in the patient, this is not a current option. Recent data from a randomized controlled trial support the use of acupuncture for the treatment of sleep disruption in menopause. Black cohosh (Actaea racemosa, syn. Cimicifuga racemosa) is an alternative treatment consideration in menopause-related insomnia; however, high-quality studies are needed to confirm use.

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Chapter 4
Sleep and Organ Physiology

Dennis Auckley and Ziad Shaman

Introduction

Over the last 15–20 years, there has been rapid advancement in our understanding of sleep physiology and how sleep interacts with a variety of organ systems in the human body. Despite the insights gained in recent years, there is still much that we do not know, and numerous questions remain to be answered. However, the foundation is now in place such that training in Sleep Medicine must include an appreciation of the associations between sleep and organ physiology. The ACGME requirements for a Sleep Medicine Fellowship (http://www.acgme.org/acWebsite/downloads/RRC_progReq/520_sleep_medicine_07012012.pdf: last accessed 2/22/12) state that trainees must demonstrate comprehensive knowledge of a number of organ systems and their physiology and pathophysiology as they relate to sleep. This is most clearly stated in the medical knowledge competency, though elements of this topic can be found in other competencies as well. In addition, 5 % of the content of Sleep Medicine Certification examinations, regardless of the board offering the examination (i.e., http://www.abim.org/pdf/blueprint/sleep_cert.pdf: last accessed 2/22/12), deals directly with organ system physiology in sleep.

During the seemingly passive state of sleep, the brain and the rest of the body organs remain in constant interaction. The physiological effect of sleep on the body's organ systems is modulated by the closed feedback loops of the somatic and the autonomic nervous systems. Pressure receptors in the peripheral circulation allow the brain to regulate its blood flow through efferent projections onto the heart and onto the vascular system. The decreased gastrointestinal tract motility coupled with alterations in gastric acid secretion during sleep has significant implications for

D. Auckley, M.D. (✉) • Z. Shaman, M.D.
Division of Pulmonary, Critical Care and Sleep Medicine,
MetroHealth Medical Center, Case Western Reserve University,
2500 MetroHealth Dr, Cleveland, OH 44109, USA
e-mail: dauckley@metrohealth.org

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sleep and gastrointestinal disease. Several hormones are tightly linked to the circadian rhythm as well as to the sleep/wake state of the brain. This connection allows rapid changes in hormonal secretions, in addition to providing the stability of a day-night routine. Thermoregulation is closely associated with the circadian cycle and plays a role in sleep initiation and problems thereof. The interaction between sleep and the immune system appears bidirectional. Because of the constant feedback system between the brain and the body organ systems, a major disturbance in sleep is highly likely to affect the function and homeostasis of the body as a whole. Similarly, pathological changes in any individual organs may lead to a significant change in sleep structure and organization.

For this chapter, the content and competency examples were developed through discussions with sleep faculty and fellows, review of existing literature in the fields of interest, and examination of the ACGME requirements. The ACGME requirements list comprehensive knowledge in a number of physiological domains, though some of these (i.e., basic neurologic mechanisms of sleep, respiratory physiology during sleep) are covered in other chapters in this book and will not be addressed here. This chapter will focus on the effect that sleep and specific organ physiology have on each other, focusing on the physiology of the autonomic nervous system as well as the cardiovascular, gastrointestinal, endocrine, thermoregulatory, and immune systems.

The chapter is not an inclusive content review, but intended to illustrate some issues expected to be part of a sleep practitioner's knowledge base as well as to provide specific examples of how sleep affects organ physiology and provides some illustrative assessments. Table 4.1 provides a road map of content domains showing how subtopics may be related to the ACGME general competencies for training in Sleep Medicine. Knowledge is most applicable to the topic of organ physiology, though there are areas where patient care and other competencies can be addressed and assessed. Table 4.2 lists objectives for content-specific questions from which presentations can be formulated and then assessed. These objectives can also be used as essay questions, spur journal club discussions, or form the basis of a lecture on the particular issue raised by the question.

Intertwined with the content delivery, as organized and discussed above, is the need to assess competency of the learner in these areas. This chapter provides examples of how this can be accomplished. The matching test is an example of a traditional knowledge assessment tool utilizing matching tests to review factual knowledge of sleep and organ physiology. As more data becomes available in this field, these questions can be modified and additions can be made. The essay questions provide sample essay questions that attempt to assess a more comprehensive understanding of the issue posed. These can be provided as either closed or, if self-directed learning is the goal, open book written questions. However, the most useful method to gauge the learner's comprehension of the topic might be to pose these types of questions as open discussion questions in a one-on-one session. This allows the evaluator to change the direction of the discussion to assess particular subtopics as well as allows the evaluator to judge the learner's ability to "think on their feet."

The IQ case offers examples of IQ group exercises, in which the learning objectives are disclosed only after the fact, requiring the learners to seek and evaluate

Table 4.1 Cognitive Map of the Content Domains Relevant to Sleep and Physiology

		Knowledge	Skills	ACGME competency
I.	*Epidemiology*	Yes	No	B, F
	Age			
	Risk factors			
	Special populations			
II.	*Mechanisms of health and disease*	Yes	No	A, B
	Somatic nervous system			
	Autonomic nervous system			
	Cardiovascular			
	Gastrointestinal			
	Endocrine			
	Immunologic			
	Thermoregulation			
III.	*Risk factors*	Yes	No	A, B
	Environmental			
	Genetic			
	Age-related			
IV.	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatrics			
	Special populations			
V.	*Diagnostic measures and interpretation*	Yes	Yes	A, C, F
	Hemodynamic measurements			
	ECG testing			A, C
	pH probe monitoring			
	Hormone and cytokine measures			
	Temperature measures			
	Patient-based testing			A, B, F
VI.	*Disease management*	Yes	Yes	A, E, D, F
	Presentation of therapeutic options			A, E, D, F
	Decisions on therapy			A, F
	Follow-up			A, F
VII.	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Cardiovascular disease and arrhythmias			
	Gastroesophageal reflux			
	Sleep deprivation, circadian rhythms, and endocrinological diseases			
	Sleep and host susceptibility			
	Thermoregulation and insomnia			
	Code for ACGME competencies			
	A. Patient care		D. Interpersonal skills	
	B. Medical knowledge		E. Professionalism	
	C. Practice-based learning and improvement		F. System-based practice	

[a]Basic neurologic mechanisms of sleep and respiratory physiology are covered in the chapter on sleep-disordered breathing

Table 4.2 Examples of Topics with Educational Objectives

Item I. Epidemiology

- Describe the circadian pattern of cardiovascular mortality
- List the most common cardiac rhythm abnormalities seen during normal sleep
- In individuals with nocturnal gastroesophageal reflux disease (GERD), describe the frequency with which nocturnal GERD symptoms disrupt sleep and affect daytime functioning
- Compare the risk of hypothyroidism in the general population versus in patients with sleep apnea

Item II. Mechanisms of health and disease

- Propose a mechanism by which obstructive sleep apnea (OSA) leads to hypertension through changes in the sympathetic nervous system
- Suggest a pathophysiology for the circadian pattern of sudden cardiac death
- Make a table that details how sleep changes esophageal function. How could the normal physiological effects of sleep on the esophagus and stomach lead to nocturnal GERD?
- Show the interaction between processes C and S on the level of
  - ACTH/cortisol
  - Growth hormone
  - Thyroid-stimulating hormone
  - Melatonin
- Describe how body temperature changes with sleep, focusing on the differences between the effects of sleep and the circadian rhythm on thermoregulation
- Discuss factors that lead to increased sleep as part of an acute-phase response to infection

Item III. Risk factors

- Locate the central station of the autonomic nervous system (ANS) in the brain
- Give three examples of primary and three examples of secondary causes of ANS diseases
- Describe how environmental and behavioral factors may influence risk for sleep-related GERD
- Analyze the effect of sex hormone deficiency on sleep in both genders
- Discuss how long-term severe sleep loss alters host defenses in animal models

Item IV. Patient assessments

- Describe the effect of sleep on the delayed component of blink reflex
- Differentiate the hemodynamic status during NREM versus REM sleep in
  - Systemic blood pressure and its effect on the risk of stroke
  - Blood flow in the cutaneous and in renal circulation
- Relate how you would work up a patient presenting with complaints of nocturnal GERD and sleep fragmentation
- Describe the secretion pattern of these hormones in relationship to sleep
  - Prolactin
  - Gonadotropic hormone
  - Renin/angiotensin/aldosterone
  - Antidiuretic hormone
- Discuss how collecting 24-h core body temperature measurements could be helpful in the evaluation of insomnia

Item V. Diagnostic measures and interpretation

- Propose mechanisms for decreased H-reflex amplitude on nerve conduction studies during sleep
- Compare CNS areas of activity and inactivity during NREM and REM sleep
- Interpret sinus pauses on a polysomnographic cardiac rhythm
- Compare testing technology
  - Level I, II, III, and IV monitoring
- Describe pretest probability and posttest uncertainty for diagnostic testing for sleep apnea
- Explain sensitivity and specificity for clinical outcomes
- Interpret 24-h pH probe readings in relation to sleep
- Discuss how you would obtain 24-h core body temperature measurements

(continued)

Table 4.2 (continued)

Item VI. Disease management
- Discuss the effect of the ANS on heart rate variability during REM sleep and sudden arousals, and propose a management plan
- Advise a patient with long QT syndrome regarding the effect of sleep-disordered breathing on her prognosis
- Describe the impact of CPAP therapy for OSA on nocturnal GERD. Speculate on why this outcome occurs
- Describe thyroid hormone replacement titration in a patient with hypothyroidism and OSA
- Discuss how might maneuvers to impact core body temperature be useful in the management of insomnia
- Compare and contrast the principles of therapy
  - Behavioral
  - Mechanical
  - Surgical
  - Medical
  - Pharmacologic therapy
- Imagine novel approaches

Item VII. Health and disease clinical pathways
- Propose a collaboration pathway in assessing cardiac arrhythmia patients for sleep-disordered breathing
- Analyze the effect of sex hormone replacement on sleep in both genders
- Describe the principles in the initiation of therapy
- Now that a patient has responded to therapy, list the factors for management of apnea as a chronic disease
- List patient expectations versus physician objectives in terms of outcomes

information that they believe will achieve the learning objectives of the case. These group discussions are helpful for the learners in that they can share knowledge and hopefully improve their learning techniques. The IQ cases are probably best used to obtain an overall assessment of where the group or program is in their training and how fellows interact in a learning group.

Two illustrative PowerPoints are presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/organ-physiology.html). These may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Matching Test

Questions

Active during REM. ☐
Association between insomnia and core body temperature. ☐
Atrioventricular block frequency during sleep in healthy volunteers. ☐
Cause of death in chronically sleep-deprived animals. ☐

Central station for autonomic signals. ☐
Decrease in blood pressure during NREM sleep. ☐
Effect of supine posture on core body temperature. ☐
Evening rise inhibited by slow-wave sleep. ☐
Gastrointestinal activity that does not normally occur during sleep. ☐
Influences gastric acid secretion. ☐
Level lowest in early morning. ☐
Level peaks near morning. ☐
Nadir of core body temperature. ☐
Parasympathetic nervous system. ☐
Prevents fecal incontinence in sleep. ☐
Secretion increases during slow-wave sleep. ☐
Sinus pause during sleep occurrence in healthy volunteers. ☐
Site of sleep/thermoregulatory integration. ☐
Sleep response to acute infection. ☐
Sleep stage with lowest primary esophageal peristalsis. ☐
Sympathetic nervous system. ☐

Answers

1. 5 %
2. 15 %
3. 25 %
4. 50 %
5. 75 %
6. 2200–0200
7. 1st sleep cycle
8. 3rd sleep cycle
9. Antidiuretic hormone
10. Cerebral cortex
11. Chewing
12. Chronically decreased core body temperature
13. Chronically elevated core body temperature
14. Circadian rhythm
15. Cortisol
16. Decreased anal canal pressure
17. Decreases core body temperature
18. Growth hormone
19. Increases core body temperature
20. Increased NREM sleep
21. Increased REM sleep
22. Locus coeruleus
23. Melatonin
24. No change in core body temperature
25. Nucleus tractus solitaries
26. Preoptic anterior hypothalamus
27. Pons (medial pontine reticular formation)
28. REM sleep
29. Renin
30. Repeated strokes
31. Retrograde rectal motor activity
32. Septicemia
33. Sleep stage
34. Slow-wave sleep
35. Suprachiasmatic nucleus
36. Swallowing
37. Thyroid stimulating hormone
38. Tone ↑ during NREM and ↑↑ during REM
39. Tone ↑ during NREM and ↓ during REM
40. Tone ↑ during phasic REM and ↓ during tonic REM
41. Tone unaffected by sleep stage
42. Ventrolateral preoptic nucleus

Questions with Answers

Active during REM. 27
Association between insomnia and core body temperature. 13
Atrioventricular block frequency during sleep in healthy volunteers. 1
Cause of death in chronically sleep-deprived animals. 32
Central station for autonomic signals. 25
Decrease in blood pressure during NREM sleep. 2
Effect of supine posture on core body temperature. 17
Evening rise inhibited by slow wave sleep. 37
Gastrointestinal activity that does not normally occur during sleep 11
Influences gastric acid secretion. 14
Level lowest in early morning. 23
Level peaks near morning. 15
Nadir of core body temperature. 8
Parasympathetic nervous system. 38
Prevents fecal incontinence in sleep. 31
Secretion increases during slow wave sleep. 18
Sinus pause during sleep occurrence in healthy volunteers. 4
Site of sleep/thermoregulatory integration. 26
Sleep response to acute infection. 20
Sleep stage with lowest primary esophageal peristalsis. 28
Sympathetic nervous system. 39

Essay Questions

Endocrine

A 55-year-old female presents to the sleep clinic with loud snoring and fatigue. She is found to have severe sleep apnea (AHI 35). Because of mild thyromegaly on clinical examination and a report of sinus bradycardia on the polysomnogram, you suspect hypothyroidism. You confirm the diagnosis by discovering an elevated serum TSH. The patient agrees to initiation of nasal CPAP therapy, but you want to start thyroid hormone replacement.

Questions

1. Compare the risk of hypothyroidism in patients with sleep apnea versus the risk of sleep apnea in patients with hypothyroidism.
2. What are the mechanisms that link hypothyroidism and sleep apnea?
3. How may thyroid replacement therapy adversely affect patients with sleep apnea?

Answers

1. In patients referred for evaluation for OSA, risk of hypothyroidism is similar in those with and those without OSA (<2 %). On the other hand, about 80 % of patients with hypothyroidism are found to have sleep apnea, and hormone replacement has a good chance of reducing the severity of sleep apnea in those patients.
2. Myxedematous infiltration of the upper airway may reduce its patency. Hypothyroidism can impair the function of upper airway muscles by decreasing the central drive to the upper airway muscles or due to direct myopathy.
3. With hormone replacement, long-term changes in upper airway muscle function and breathing control may be slow to recover. However, the increase metabolic rate and oxygen consumption can occur much faster, resulting in supply/demand mismatch and end organ ischemia.

Thermoregulation

A 45-year-old female presents to the sleep clinic with a complaint of difficulty falling asleep for several years. She tends to lie in bed for 1–2 h before being able to initiate sleep. She denies evening caffeine use and has a comfortable and quiet bedroom environment. She also denies symptoms suggestive of an anxiety disorder or restless legs syndrome. Her examination is normal other than her cool hands and feet with grossly normal pulses. A sleep diary and actigraphy confirm a prolonged sleep latency, but once sleep is initiated, there appears to be good sleep maintenance.

Questions

1. Is there significance to the finding of cool hands and feet in the context of her complaint of sleep-onset insomnia?
2. How does changing from an upright to supine posture affect thermoregulation?
3. What thermal interventions might be of benefit for her insomnia?
4. What are the thermal effects of melatonin and benzodiazepines?

Answers

1. The circadian regulation of the heat loss in the evening is closely associated with sleepiness and sleep initiation. The main thermoeffectors leading to a loss of body heat are the small vessels in the distal skin regions, particularly the fingers and toes. It has been shown that individuals with cold hands and feet are prone to sleep-onset insomnia.
2. It causes a redistribution of heat from the core to the periphery, increasing distal skin temperatures, reducing core body temperature, and increasing sleepiness. This effect lasts for 1–2 h.
3. A warm bath 30–90 min before sleep and intense exercise 4–8 h before bedtime both can raise the skin temperature, leading to distal vasodilatation and subsequent heat loss, lowering the core body temperature. This effect can shorten sleep latency.
4. Both will lead to a decrease in core body temperature.

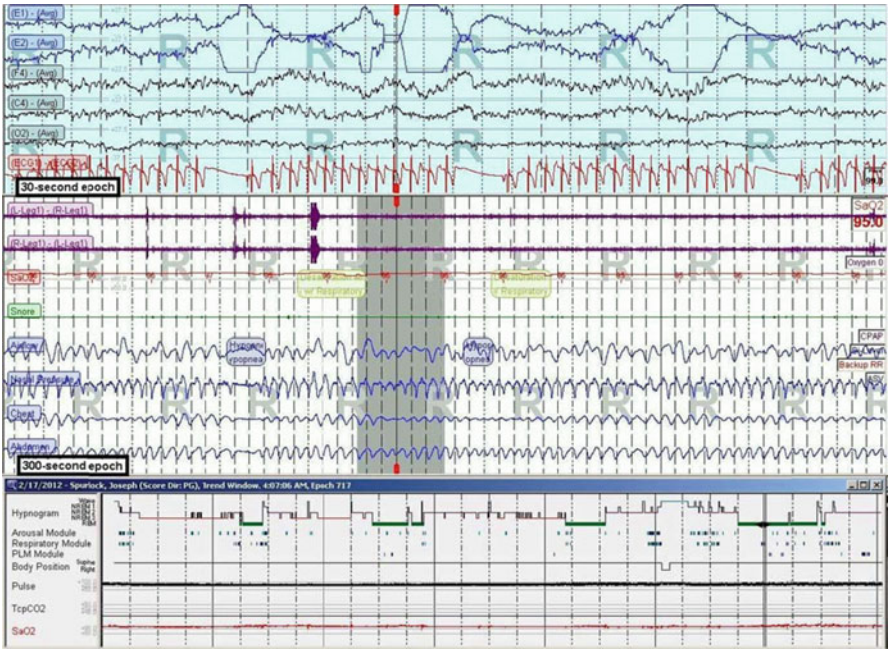

Fig. 4.1 The *top panel* represents a 30 s epoch of REM sleep showing EOG, EMG, and EKG leads. The *middle panel* represents a 5 min time period of REM sleep showing the leg channels, oxygen saturation, snoring, flow channels, and effort channels. The *bottom panel* represents the entire night sleep hypnogram showing sleep stages, respiratory events, and the oxygen saturation tracing

IQ Cases

Cardiovascular for Student

Goal: Understand the effect of sleep/wake state on the cardiovascular system physiology via functions of the autonomic nervous system and how abnormalities in function can result in disease states.

Case Vignette

A 55-year-old man is referred to the sleep clinic from cardiology for evaluation of sleep apnea. The patient was noted to have significant heart rate variability on a Holter monitor during sleep. The patient endorses light snoring, excessive daytime sleepiness (ESS 13), and unrefreshing sleep. The patient has been working long hours and drinking a lot of caffeine. His average sleep duration is 5–6 h per night. He denies witnessed apneas, RLS symptoms, parasomnias, and insomnia. The patient has past history of hyperlipidemia and hypertension. He has no social vices.

He takes an ACE-inhibitor and a statin. The patient's family history is significant for ischemic cardiac disease. On examination, the vital signs are normal other than for a BMI of 30. The JVP is normal. The heart rate and rhythm are normal. Cardiac auscultation is normal. There is no LE edema.

A CXR and an EKG were both normal. The details of the Holter monitor report are not available. An echocardiogram is performed and shows LVH without wall motion abnormalities but significant diastolic dysfunction. A sleep study is performed. The study results (Fig. 4.1) are shown with EOG/EEG/EKG signals in a 30-s epoch in the top panel, EMG/SpO_2/Mic/thermistor/pressure sensor/chest belt/abdominal belt in a 300-s epoch in the middle panel, and a full night hypnogram appearing in the lowest panel.

The patient is diagnosed with sleep apnea (AHI 28) and nasal CPAP is titrated. At therapeutic settings only NSR is seen on EKG. The patient returns to the clinic for advice regarding treatment of sleep apnea. The patient mentions to you that his father used to snore loudly and had died in his 60s during sleep. He wonders if the same thing is going to happen to him.

You send your report to the referring physician (a cardiologist) who started a practice next to your clinic last month. The two of you come up with a management plan that is reassuring to the patient. The patient lives a good 50 more years.

Cardiovascular for Facilitator

Goal: Understand the effect of sleep/wake state on the cardiovascular system physiology via functions of the autonomic nervous system and how abnormalities in function can result in disease states.

Learning Objectives (To Be Shared at the End)

A. List the most common cardiac rhythm abnormalities seen during normal sleep.
B. Interpret sinus pauses on a polysomnographic cardiac rhythm.
C. Discuss the effect of hemodynamic differences during NREM versus REM sleep.
D. Describe the circadian pattern of cardiovascular mortality.
E. Propose a collaboration pathway to assess patients with cardiac arrhythmia for sleep-disordered breathing.

Case Vignette

A 55-year-old man is referred to the sleep clinic from cardiology for evaluation of sleep apnea. The patient was noted to have significant heart rate variability on a Holter monitor during sleep. The patient endorses light snoring, excessive daytime sleepiness (ESS 13), and unrefreshing sleep. The patient has been working long hours and drinking a lot of caffeine. His average sleep duration is 5–6 h per night. He denies witnessed apneas, RLS symptoms, parasomnias, and insomnia. The patient has past history of hyperlipidemia and hypertension. He has no social vices.

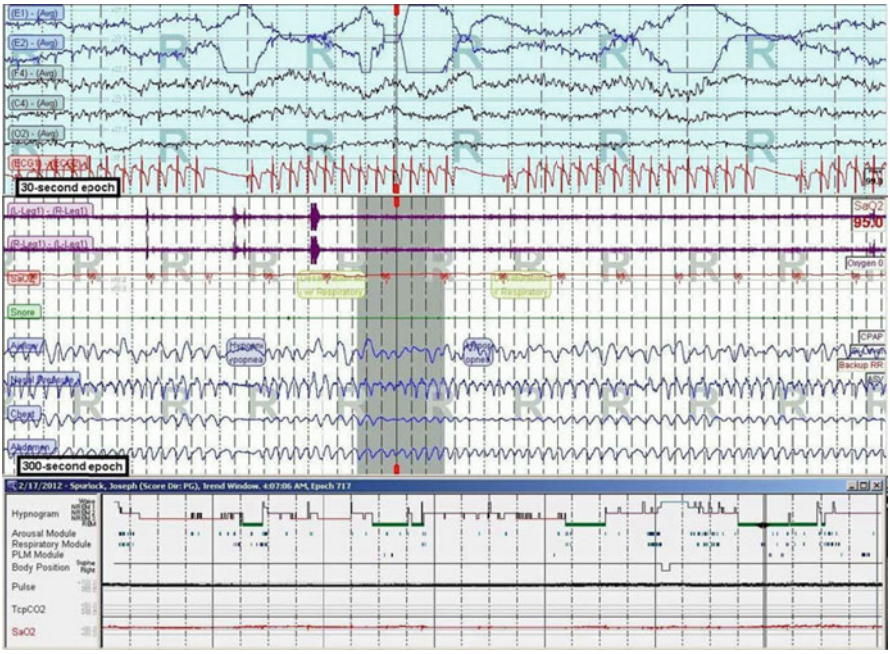

Fig. 4.2 The *top panel* represents a 30 s epoch of REM sleep showing EOG, EMG, and EKG leads. The *middle panel* represents a 5 min time period of REM sleep showing the leg channels, oxygen saturation, snoring, flow channels, and effort channels. The *bottom panel* represents the entire night sleep hypnogram showing sleep stages, respiratory events, and the oxygen saturation tracing

He takes an ACE-inhibitor and a statin. The patient's family history is significant for ischemic cardiac disease. On examination, the vital signs are normal other than for a BMI of 30. The JVP is normal. The heart rate and rhythm are normal. Cardiac auscultation is normal. There is no LE edema.

Probing Questions

1. What benign cardiac rhythms can be seen during sleep?
2. What are the patient's risk factors for cardiac disease?
3. What are his risk factors for a sleep disorder? Which?
4. How would you proceed with a diagnostic plan?

A CXR and an EKG were both normal. The details of the Holter monitor report are not available. An echocardiogram is performed and shows LVH without wall motion abnormalities but significant diastolic dysfunction. A sleep study is performed. The study results (Fig. 4.2) are shown with EOG/EEG/EKG signals in a 30-s epoch in the top panel, EMG/SpO2/Mic/thermistor/pressure sensor/chest belt/abdominal belt in a 300-s epoch in the middle panel, and a full night hypnogram appearing in the lowest panel.

Probing Questions

5. What does the sleep study show?
6. What is the differential diagnosis of the EKG finding?
7. What is the significance of the sleep stage on cardiac rhythm and hemodynamics?

The patient is diagnosed with sleep apnea (AHI 28) and nasal CPAP is titrated. At therapeutic settings only NSR is seen on EKG. The patient returns to the clinic for advice regarding treatment of sleep apnea. The patient mentions to you that his father used to snore loudly and had died in his 60s during sleep. He wonders if the same thing is going to happen to him.

Probing Questions

8. What can you tell the patient about the relationship between sleep and sudden cardiac death?
9. What is the effect of CPAP on autonomic instability in sleep apnea [6]?
10. How can you reduce this patient's risk of sudden cardiac death?

You send your report to the referring physician (a cardiologist) who started a practice next to your clinic last month. The two of you come up with a management plan that is reassuring to the patient. The patient lives a good 50 more years.

Probing Questions

11. Name some primary cardiac diseases that may affect sleep.
12. How would you initiate a collaboration effort between your practice and the cardiologist next door to manage patients with cardiac and sleep disorders most effectively?

Cardiovascular Handout/Objectives

Goal: Understand the effect of sleep/wake state on the cardiovascular system physiology via functions of the autonomic nervous system and how abnormalities in function can result in disease states.

Learning Objectives (To Be Shared at the End)

A. List the most common cardiac rhythm abnormalities seen during normal sleep.
B. Interpret sinus pauses on a polysomnographic cardiac rhythm.
C. Discuss the effect of hemodynamic differences during NREM versus REM sleep.
D. Describe the circadian pattern of cardiovascular mortality.
E. Propose a collaboration pathway to assess patients with cardiac arrhythmia for sleep-disordered breathing.

Gastrointestinal for Student

Goal: Understand the effect of sleep/wake state on the gastrointestinal system physiology and how abnormalities in function are associated with disease states focusing on gastroesophageal reflux disease (GERD) [1, 5].

Case Vignette

A 32-year-old female with a history of obesity (BMI 35 kg/m^2) and gall stones presents with a complaints of frequent nocturnal awakenings, occasional gasping at night, light snoring, and excessive daytime sleepiness. An Epworth Sleepiness Scale score is 12. She denies symptoms consistent with narcolepsy, and she obtains 7.5 h of sleep per night on a regular basis. Her physical examination is notable for a class II Mallampati airway and a mildly hoarse voice, but is otherwise unremarkable. You perform a polysomnogram (PSG) that reveals an AHI of 1.2, intermittent mild snoring, and frequent arousals. The periodic limb movement index is 3.0. The technician notes the patient frequently awakens from sleep coughing.

You perform a repeat PSG with an esophageal pH probe in place, and this reveals that the arousals are associated with frequent significant decreases in her esophageal pH.

The patient is diagnosed with severe nocturnal GERD.

Gastrointestinal for Facilitator

Goal: Understand the effect of sleep/wake state on the gastrointestinal system physiology and how abnormalities in function are associated with disease states focusing on gastroesophageal reflux disease (GERD) [1, 5].

Learning Objectives (To Be Shared at the End)

A. What is the differential diagnosis of recurrent nocturnal awakening?
B. Discuss how sleep physiology predispose to nocturnal GERD.
C. Review the potential consequences of nocturnal GERD.
D. Describe the spectrum of treatments for GERD.
E. Discuss how treatment of nocturnal GERD might affect the patient's sleep.

Case Vignette

A 32-year-old female with a history of obesity (BMI 35 kg/m^2) and gall stones presents with a complaint of frequent nocturnal awakenings, occasional gasping at night, light snoring, and excessive daytime sleepiness. An Epworth Sleepiness Scale score is 12. She denies symptoms consistent with narcolepsy, and she obtains 7.5 h

of sleep per night on a regular basis. Her physical examination is notable for a class II Mallampati airway and a mildly hoarse voice but is otherwise unremarkable. You perform a polysomnogram (PSG) that reveals an AHI of 1.2, intermittent mild snoring, and frequent arousals. The periodic limb movement index is 3.0. The technician notes the patient frequently awakens from sleep coughing.

Probing Questions

1. What is your differential diagnosis for her frequent nocturnal arousals?
2. Can her frequent arousals explain her excessive sleepiness?
3. What is the significance of her hoarse voice?

You perform a repeat PSG with an esophageal pH probe in place, and this reveals that the arousals are associated with frequent significant decreases in her esophageal pH.

Probing Questions

4. What does a normal nocturnal esophageal pH probe reading look like and how might the patient's be different?
5. What are risk factors for nocturnal gastroesophageal reflux (GERD)?
6. What is it about sleep that may predispose to nocturnal GERD?

The patient is diagnosed with severe nocturnal GERD.

Probing Questions

7. What can you tell me about the consequences of nocturnal GERD on health and quality of life?
8. What different interventions can be considered to treat nocturnal GERD?
9. What if she had been diagnosed with obstructive sleep apnea and GERD – what treatment might be beneficial for both conditions?
10. Describe the benefits, as they relate to sleep, that the patient might expect from treatment of the GERD.

Gastrointestinal: Handout/Objectives

Goal: Understand the effect of sleep/wake state on the gastrointestinal system physiology and how abnormalities in function are associated with disease states focusing on gastroesophageal reflux disease (GERD) [1, 5].

Learning Objectives (To Be Shared at the End)

A. What is the differential diagnosis of recurrent nocturnal awakening?
B. Discuss how sleep physiology predispose to nocturnal GERD.
C. Review the potential consequences of nocturnal GERD.
D. Describe the spectrum of treatments for GERD.
E. Discuss how treatment of nocturnal GERD might affect the patient's sleep.

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Chapter 5
Upper Airway Physiology

Jonathan Baskin

Introduction

For the field of sleep medicine, the ACGME notes that a multidisciplinary approach in the instruction of sleep medicine trainees is required (IV.A.2.a).(4). (a)). Upper airway physiology is a fundamental area of study for sleep-related respiratory disorders and obstructive sleep apnea in particular. Inherent in any discussion of upper airway physiology is an understanding of the anatomy (see IV.A.2.b).(1).(b)). It is axiomatic that having this knowledge is critical to diagnosing and treating sleep-related disorders that involve the upper airway. It is also fundamental to proper management when referring patients to consulting physicians or services. All training programs will, by necessity (as stated in Sect. IV.A.2.a.1.a of the ACGME program requirements), spend a significant amount of time teaching fellows how to do a comprehensive examination of the upper aerodigestive tract using tools which are generally accessible in a clinical setting for most patients (including children). Ideally, this training will involve some experience in office-based direct fiber-optic laryngoscopy as this tool can give a great deal of relevant upper airway information with respect to sleep-disordered breathing.

The purpose of this chapter is to provide an overview of upper airway physiology and anatomy with a focus on fulfilling ACGME requirements for training physicians in sleep medicine. In addition to using the ACGME program requirements guide, this chapter is based on feedback from residents in otolaryngology as well fellows in sleep medicine programs and residents in other nonsurgical fields as well. It is assumed that the vast majority of fellows have previously had some training in examining the upper aerodigestive tract. The intent is to help the fellow develop a more discerning eye that is necessary to recognize features of the awake upper

J. Baskin, M.D. (✉)
Department of Otolaryngology and Head & Neck Surgery,
Case Western Reserve University School of Medicine,
Louis Stokes Cleveland VA Medical Center, Cleveland, OH, USA
e-mail: jzb@case.edu

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airway (UA) that can give the practitioner some idea of how the UA might behave during sleep.

The UA is defined as the tube that on expiration transmits air from the laryngeal glottis (true vocal folds) to either the nostrils or the lips; during inspiration the process is reversed using active inspiration. Humans are fairly unique among mammals in our susceptibility to upper airway obstruction during sleep. This is directly related to the anatomy and physiology of the upper airway that evolved special characteristics in association with bipedalism and speech production. The development of speech required not only anatomical features but neural control complexity to function as an aerodigestive tract supporting deglutition and respiration while protecting the distal airways. Anatomically, with basoflexion of the skull base in humans (to orient the axial skeleton perpendicular to the line of sight), there was effectively a migration of the foramen magnum closer to the pharynx, creating a smaller pharyngeal space. The shortening of the splanchnocranium (facial skeleton) and descended larynx in humans, which are associated with the development of speech, result in a tongue that is positioned in the oropharynx as opposed to the oral cavity as in other mammals including nonhuman primates. Even among humans there are further interpopulation craniofacial variations that make some ethnic groups more vulnerable to UA collapse than others, independent from the more common association with obesity. In addition, changes in the cranial base, the mandible, the maxilla, and the face occur during development, so that the normal infant initially has a very stable upper airway that becomes more vulnerable to collapse; another time for great changes is in the transition to puberty and with older age.

In addition to fixed craniofacial anatomical features and soft tissues surrounding the pharyngeal airway that allow for its multiple functions, other factors contribute to the stability (or instability) of the upper airway for the purposes of breathing during sleep. The distensible and relatively small pharynx that extends from the larynx to either the nasal or oral cavities is highly dynamic in terms of its caliber and compliance. Size and stiffness are subject to many influences that include degree of arousal, respiratory control mechanisms, neuromuscular control mechanisms, upper airway reflexes, degree and sites of fat deposition, body position, body fluid distribution, mucosal surface tension, and age.

Complicating matters even more is the differential impact that the various stages of sleep have on UA neuromuscular stimulation. In the awake state, various UA dilators (most notably the genioglossus as well as other tongue protrusors and palatal muscles) contribute to UA patency. As we descend into sleep progressing from NREM to REM, there is progressive loss of efferent neuromuscular stimulation to UA muscles (particularly tonic muscles). This is in contrast to the diaphragm that continues to receive a relatively high level of neuroexcitatory input. This differential leads to continued negative pressure on inspiration in the face of increase UA compliance or collapsibility. As part of a peripheral reflex arc, mechanoreceptors in the UA that respond to negative pressure increase efferent activity to UA dilators, thus providing some compensatory stimulation to UA dilators. When this fails to effect UA patency, the critical closing pressure of the UA (P_{CRIT}) is exceeded, leading to obstruction. There are several drugs including alcohol and commonly prescribed

sedatives that will reduce UA dilator activity but do not suppress diaphragmatic innervation that increase this risk of obstruction. Cortical arousal associated with UA obstruction increases the excitation of UA dilators (not through a reflex arc), resulting in a sturdier and more patent UA. This knowledge of neural control becomes important in understanding the potential for neurological illness, and neuromuscular disease, in particular, to alter the function of the upper airway in the wake and sleep state.

The UA muscles are also linked to the ventilator cycle not only via peripherally mediated reflexes but also via central respiratory control organized at the level of the brainstem. This drive is affected primarily by hypercarbia and to a lesser extent by hypoxia. Central ventilatory control is affected by levels of consciousness as well as by transitions to sleep. Mechanistically, this is thought to be responsible for some types of sleep-disordered breathing whereby the central ventilatory drive is cycling between different states of arousal, thereby causing alternating degrees of UA activation. This cycling can worsen SDB by further destabilizing the UA.

Because the UA is a collapsible tube, it is susceptible to various forces. The "opening" force of the UA is referred to as the transmural pressure (P_{TM}) and is the sum of collapsing or tissue pressures (P_{TIS}) and the opening or luminal pressures (P_{LUM}). The P_{LUM} is equal to the P_{AIRWAY} in addition to the pressures related to airflow (P_{FLOW}). The P_{TIS} is influenced by several factors including neuromuscular tone, vascular congestion, extracellular fluid levels, mucosal surface tension, and adipose content. The critical closing pressure of the UA (P_{CRIT}) is defined as the pressure at which P_{TIS} exceeds P_{LUM} which causes a cessation of airflow. During wakefulness the P_{LUM} exceeds the P_{TIS} (and therefore the UA pressure is above P_{CRIT}) and the UA remains patent. During sleep the P_{TIS} rises to varying degrees depending on sleep stage, body position, and other physiological conditions. At this point, during inspiration, one of the three conditions can exist. In a nonobstructed individual, the P_{TM} is greater than the upstream pressure (P_{US} – ambient pressure at the nose or mouth) which in turn is greater than the downstream (intrathoracic) pressure – P_{DS} ($P_{TM} > P_{US} > P_{DS}$). In the obstructed individual, P_{US} is greater than the P_{DS} which exceeds the P_{TM} ($P_{US} > P_{DS} > P_{TM}$). Stated in another way, the P_{TM} is lower or more negative than the P_{CRIT} and the airway is completely collapsed. The third scenario applies to the snorer. The airway is either opened or closed depending on whether it is exposed to P_{DS} or P_{US}. When the UA is exposed to the more negative intrathoracic pressure, it collapses. As a result of this collapse, it is no longer exposed to the negative P_{DS} but rather is exposed to the positive P_{US} which causes the UA to open. Airflow resumes and the UA is once again exposed to the more negative P_{DS} which causes the UA to collapse. This constant opening and closing of the airway around a pressure point creates the vibrations which result in snoring.

The environment of the UA is fundamentally important to its behavior during sleep. This would include the surface tension or surface adhesive forces of the mucosal lining. For example, nasal obstruction during sleep leads to mouth breathing which in turn contributes to mucosal desiccation and increased surface adhesion. Factors that increase surface lubrication decrease this surface tension and result in less UA collapsibility. The extracellular fluid milieu in the UA can also

affect the pressure dynamics in the UA. Large rostral fluid shifts from the lower extremities to the head and neck tissues are thought to occur in decompensated heart failure when a patient assumes a supine position. This increases P_{TIS} and can contribute to an elevation in P_{CRIT}. Similarly, UA dimensions are affected by vascular congestion. This could be mediated by several mechanisms related to peripheral dilation of vessels but most likely exerts its effect on nasal structures (turbinates) and the lateral pharyngeal walls. The effectiveness of pneumatic splinting of the airway (with CPAP use) seems to indicate that the fluid shifts to and/or venous congestion in the neck region play an important role in a subset of patient with SDB. Fat deposition in various UA structures like the tongue and lateral pharynx also affect the space dimensions and UA collapsibility.

When examining the UA, it is important to bear in mind that the UA is heterogeneous tube and that various subsites of that tube do not behave uniformly. The breakdown of the UA into subsites allows a nuanced understanding of the anatomy which is necessary when contemplating therapeutic interventions. It is even important for approaching CPAP in mask selection and predicting which subset of the population is more likely to have intolerance to this therapy. The subsites include the nose, retropalatal or velopharyngeal region, the oropharynx, the retroglossal or tongue base region, and the epiglottis. The glottis, in the patient with no awake airway obstruction, rarely enters the picture in OSA. The examination begins with an evaluation of the neck circumference and the craniofacial skeletal structure which can reveal a great deal about the UA and where it is predisposed to obstruct (apnea) or narrow (snoring and hypopnea). This includes an evaluation of the teeth and the dental occlusion. Aspects of the oral cavity and pharynx such as tongue size (Mallampati score) and tonsils/palate are easily assessed during the oral cavity exam. The anterior nasal structures such as the caudal and anterior nasal septum and the anterior segments of the inferior turbinates are also easily visualized with the aid of a nasal speculum. The other subsites can only be properly examined with the aid of a fiber-optic laryngoscope. Fiber-optic exam is potentially more useful when done in conjunction with the application of negative pressure by the patient. This is referred to as a Muller maneuver. In this procedure the patient is instructed to close his mouth while the examiner pinches his nose (around the scope). The patient then attempts to inhale and inflate his lungs against high resistance. This causes the soft tissues of the UA to collapse in a pattern that simulates, to a partial degree, UA collapse during sleep. Though certainly not perfect, the procedure does offer some approximation of the site and pattern of UA obstruction in the sleeping state.

Finally, there is a need for appropriate referral not only for consultation but also for imaging studies. For the former the sleep specialist should be quite specific about the questions being-asked of a consulting surgeon or neurologist, and this referral should be grounded in the potential benefits and harm for any procedures involving the upper airway. Patients with complex, congenital or acquired upper airway disorders will be referred to the sleep physician for an opinion or for management. In regard to imaging studies, the sleep physician should be able to interpret the findings in light of the sleep disorder. MRI and CT imaging, along with cephalometrics, are relevant to understanding the static, anatomical features of the

head and neck, and the sleep specialist should be able to apply an understanding of the upper airway to the studies.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/physiology-of-the-upper-airway.html). It may be reviewed by the student and the program or discussed in a group format before or after the Essay Questions or IQ case.

Finally, the sleep specialist may often be asked to prepare lectures to other specialties on sleep disorders, and the material on the anatomical and functional features of the upper airway relevant to sleep-disordered breathing will often be a topic in these presentations.

Table 5.1 Cognitive Map of the Content Domains Relevant to Upper Airway Physiology and Anatomy

		Knowledge	Skills	ACGME competency
I.	*Epidemiology* Age Behavioral risk factors Ethnicity Special populations (obesity, heart failure, etc.)	Yes	No	B,F
II.	*Mechanisms of health and disease* Upper airway physiology Upper airway anatomy Neurophysiology Respiratory physiology Cardiovascular Gastrointestinal	Yes	No	A,B
III.	*Risk factors* Anatomical Medical comorbidities Age-related	Yes	No	A,B
IV.	*Patient assessments* Adult Pediatrics Craniofacial morphology Soft tissue: static and dynamic	Yes	Yes	A,C,D,E
V.	*Diagnostic measures and interpretation* Fiber-optic laryngoscopy Imaging Drug-induced sleep endoscopy	Yes	Yes	A,B,C,E,F
VI.	*Disease management* Presentation of therapeutic options Efficacy of various surgical options Follow-up	Yes	Yes	A,B,C,E,F

(continued)

(continued)

		Knowledge	Skills	ACGME competency
VII.	*Health and disease clinical pathways* Adult OSA Pediatric OSA CHF-related changes to the UA Affects of GERD on the UA Obesity	Yes	Yes	A,B,C,D,F
	Code for ACGME competencies A. Patient care B. Medical knowledge C. Practice-based learning and improvement		D. Interpersonal skills E. Professionalism F. System-based practice	

Table 5.2 Examples of Topics with Educational Objectives

Item I. Clinical epidemiology
- Describe the anatomical changes seen in the UA with growth and aging
- Understand the impact of body position on UA anatomy asleep and awake
- Describe how ethnicity and craniofacial structure impact on UA functions

Item II. Mechanisms of health and disease
- Identify which upper airway muscles are dilators and associated with UA patency
- Recount the functional similarities and differences in the nasal, nasopharyngeal (velopharyngeal), pharyngeal, and laryngeal (hypopharyngeal/retrolingual) segments of the UA
- Understand the difference between UA reflexes and cortical control of the UA
- Describe the pressure differentials that exist between the outside atmosphere, the UA (pharynx), and the intrathoracic environment in the sleeping non-snorer, snorer, and obstructed individual
- Recognize the potential effects of CHF as well as reflux on the UA during sleep

Item III. Risk factors
- Identify UA anatomical risks for OSA
- Understand how a low humidity environment could affect the UA
- Describe UA protective reflexes and any changes with sleep and aging
- List sites for fat deposition in the UA

Item IV. Patient assessments
- What physical factors (that pertain to the UA) are important in the evaluation of the adult and pediatric patients with OSA
- What craniofacial features are particularly important to always note in the initial examination
- Upon which soft tissue structures should the exam (unaided by laryngoscopy) be focused

Item V. Diagnostic measures and interpretation
- List the elements of a dynamic UA examination
- Describe how the UA during sleep can be partially simulated in the awake patient
- What is evaluated using awake fiber-optic laryngoscopy
- List appropriate and inappropriate indications for imaging studies
- Understand the potential contribution of drug-induced sleep endoscopy (DISE) and when it is appropriate

(continued)

(continued)

Item VI. Disease management

- Advise a patient in a nonbiased manner of the benefits and risks of a surgical intervention
- Describe the surgical options available for the different sites of obstruction
- Describe the success rates of procedures using a site-specific approach
  - Note that newer surgical approaches offer improved efficacy relative to prior surgical interventions
- Understanding that the effects of healing from surgery occur over months and even years, Be aware of the optimal follow-up needs for surgical interventions

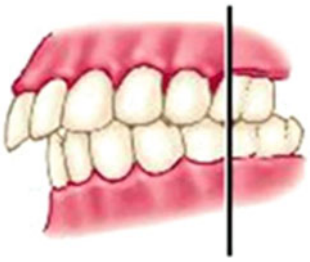
Item VII. Health and disease clinical pathways

- Recognize how the natural disease course of OSA in adults differs from that seen in children
- Understand the potential effects of rostral fluid shifts during sleep
- Indentify conditions like GERD and its effects on UA functions and its relationship to sleep
- Recognize the impact of nasal obstruction on UA functions

Matching Test

Questions

Specific area of obstruction primarily addressed by a UPPP. ☐
The appropriate way to assess the Mallampati score is via…. ☐
The signal transmitted by this respiratory motor nerve is relatively unchanged during the transition from NREM to REM. ☐
The palatine tonsils are a part of this UA subsite. ☐
This tongue muscle is the largest primary upper airway dilator. ☐
Functional stimulation of this nerve increases posterior airway space. ☐
The figure below depicts what type of malocclusion. ☐



What type of obstruction is most alleviated by a mandibular (advancement) dental appliance? ☐
The number of teeth in each dental arch generally required for treatment with a custom mandibular advancement device ☐
A uvulopalatopharyngoplasty (UPPP) is most effective in treating OSA in a patient with the following exam. ☐

An edentulous patient with retropalatal obstruction, minimal tonsillar tissue, and lateral wall oropharyngeal collapse might benefit from this procedure. ☐

This procedure targets both retropalatal and retrolingual obstruction. ☐

A contraindication to a mandibular advancement device in a fully dentate individual. ☐

A 6-year-old child has a 2-year history of snoring and gasping at night. He has had at least 5 episodes of pharyngitis requiring antibiotics in the last year. What is the most likely cause of his OSA symptoms? ☐

A 4-year-old child has a 2-year history of snoring and fitful sleep, nasal drainage, mouth breathing, and recurrent otitis media. Pharyngeal tonsils do not appear obstructing. What is the most likely anatomical cause of his symptoms? ☐

Is an independent risk factor for OSAS in nonobese adults. ☐

During this condition the P_{TM} is less than the intrathoracic pressure but greater than the ambient pressure at the nose. ☐

The afferent nerve that appears to play the most prominent role in the upper airway (negative pressure) reflex arc. ☐

A patient with a history of successful nasal CPAP use becomes intolerant of the therapy after a nasal fracture. What is the most likely site of nasal obstruction? ☐

The pressure at which the transmural pressure in the UA is exceeded (negatively) and the UA collapses. ☐

This structure, innervated by the glossopharyngeal nerve, primarily measures 02 levels. ☐

This blood level is most responsible for triggering the perception of “air hunger.” ☐

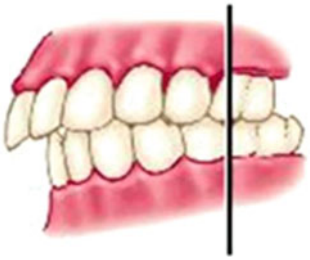
This muscle facilitates the transition from nasal breathing to mouth breathing. ☐

Answers

1. Carbon dioxide
2. 10: molars needed to be present in the lower but not upper arch
3. Large obstructing tonsils and a BMI <30
4. Retrolingual obstruction(tongue base)
5. Facial nerve (cranial nerve VII)
6. Expanded sphincter pharyngoplasty
7. Presence of torus palatini
8. Adenoid inflammation and hypertrophy
9. Mouth opening and active tongue depression
10. Vagus nerve (cranial nerve X)
11. Critical closing pressure (P_{crit})
12. Oropharynx
13. Class III malocclusion
14. Nasopharyngeal airway obstruction
15. Styloid process
16. Uvulopalatopharyngoplasty
17. Phrenic nerve
18. Styloglossus muscle
19. 10: at least 1 healthy molar should be present in each of the 4 quadrants
20. Prior tonsillectomy and a BMI <30
21. Supraglottis
22. 14: all molars need to be present and healthy in each of the 4 quadrants
23. Mouth opening with tongue in resting position
24. Large obstructing tonsils and a BMI>40
25. Arrested dental decay in a premolar (bicuspid) tooth
26. Class II malocclusion
27. Maxillary-mandibular advancement
28. Nasal valve
29. Genioglossus muscle
30. Obesity hypoventilation syndrome
31. Transmural pressure ($P_{TM)}$
32. Spinal accessory nerve (cranial nerve XI)
33. Hyoglossus muscle
34. Posterior nasal septum
35. Sjögren's disease
36. Rhinitis with nasal obstruction
37. Tonsillar hypertrophy
38. Inferior turbinates
39. Class IV malocclusion
40. Moderate OSAS
41. Downstream pressure (P_{DS})
42. Snoring
43. Glossopharyngeal nerve (cranial nerve IX)
44. Palatoglossus muscle
45. 4–6: as long as there is a preponderance of conical-shaped teeth, no molars need to be present
46. Middle turbinates
47. Brachial plexus
48. Vestibulocochlear nerve (cranial nerve VIII)
49. Central nervous system receptors
50. Carotid ganglion
51. Superior concha
52. Carotid body
53. Oxygen
54. Trigeminal nerve (cranial nerve V)
55. Glucose
56. Mouth opening while saying "Ahh"
57. Blood pH
58. Levator veli palatini
59. Carotid sinus
60. Tensor veli palatini
61. Myoglossus
62. Ansa cervicalis
63. Palatoglossus
64. Hypoglossal nerve (cranial nerve XII)
65. Eustachian tube
66. Fossa of Rosenmuller
67. Retropalatal obstruction (velopharyngeal)
68. Glottic obstruction
69. Chronic temporomandibular joint inflammation
70. Carotid body
71. Spheno-ethmoid recess
72. Anterior scalene muscle

Questions with Answers

Specific area of obstruction primarily addressed by a UPPP. 67
The appropriate way to assess the Mallampati score is via… 23
The signal transmitted by this respiratory motor nerve is relatively unchanged during the transition from NREM to REM. 17
The palatine tonsils are a part of this UA subsite. 12
This tongue muscle is the largest primary upper airway dilator. 29
Functional stimulation of this nerve increases posterior airway space. 64
The figure below depicts what type of malocclusion. 26



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The number of teeth in each dental arch generally required for treatment with a custom mandibular advancement device. 19
A uvulopalatopharyngoplasty (UPPP) is most effective in treating OSA in a patient with the following exam. 3
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This procedure targets both retropalatal and retrolingual obstruction. 27
A contraindication to a mandibular advancement device in a fully dentate individual. 69
A 6-year-old child has a 2-year history of snoring and gasping at night. He has had at least 5 episodes of pharyngitis requiring antibiotics in the last year. What is the most likely cause of his OSA symptoms? 37
A 4-year-old child has a 2-year history of snoring and fitful sleep, nasal drainage, mouth breathing, and recurrent otitis media. Pharyngeal tonsils do not appear obstructing. What is the most likely anatomical cause of his symptoms? 8
Is an independent risk factor for OSAS in nonobese adults. 36
During this condition the P_{TM} is less than the intrathoracic pressure but greater than the ambient pressure at the nose. 42
The afferent nerve that appears to play the most prominent role in the upper airway (negative pressure) reflex arc. 10
A patient with a history of successful nasal CPAP use becomes intolerant of the therapy after a nasal fracture. What is the most likely site of nasal obstruction? 28

The pressure at which the transmural pressure in the UA is exceeded (negatively) and the UA collapses. 11

This structure, innervated by the glossopharyngeal nerve, primarily measures 02 levels. 70

This blood level is most responsible for triggering the perception of "air hunger." 1

This muscle facilitates the transition from nasal breathing to mouth breathing. 58

Essay Questions

1. What would explain the association between OSA and Treacher Collins syndrome? What are some of the potential ways to address OSA in such a patient?

   Treacher Collins, also known as mandibulofacial dysostosis, is an autosomal dominant congenital disorder with multiple associated craniofacial deformities. An aspect of this deformity is hypoplasia of the facial bones. Micrognathia, or mandibular hypoplasia, results in prolapse of the tongue base and crowding of the pharyngeal airway (primarily in the retrolingual area). In severe cases neonates are prone early on to airway obstruction and must be tracheostomized to bypass the UA obstruction and secure the airway. In less severe cases there may be no obvious evidence of airway compromise in early childhood. However, on closer evaluation, the child can be found to have sleep-disordered breathing. The range of severity can be broad among people with Treacher Collins and is related to the degree of craniofacial deformity. The SDB is generally addressed by procedures that increase the size and projection of the mandible. By treating the skeletal deformity, the soft tissue obstruction is alleviated. This could include bone grafting or distraction osteogenesis (DO) of the bilateral mandibular rami. DO is compelling as a treatment modality because it gradually lengthens the skeleton in a way that allows the soft tissue to accommodate these changes slowly and fairly atraumatically. There is, of course, a cosmetically compelling reason to do this surgery as well.

2. Describe the pressure differentials that exist between the intrathoracic airway, the UA (pharynx), and the ambient environment at the nose or mouth in a sleeping patient who is experiencing an apneic episode.

   The pharynx is a collapsible tube that is described as a Starling resistor. In the apneic individual the pharyngeal tissue pressure, which is the sum of the elastic forces of the UA tissues and the activity of the UA dilators, is subjected to varying pressures depending on where the patient is in the respiratory cycle. The pressures created in the UA on inspiration are related to airflow as well as the negative downstream pressure generated by intrathoracic airways. In an apneic episode the P_{TM} is exceeded by the negative downstream pressure generated by inspiration. At that point the critical closing pressure (P_{CRIT}) of the UA is exceeded and the UA obstructs. Stated in another way, the P_{US} is greater than the P_{DS} which exceeds the P_{TM} ($P_{US}>P_{DS}>P_{TM}$).

3. Describe the difference between UA the muscles that show respiratory-related activity and those that do not (tonic muscles).

   The genioglossus is the best studied of the UA dilators and is thought to be very important with respect to the pathogenesis of OSA. It is also a respiratory-modulated UA muscle and is thought to represent, to a large degree, the activity of other UA muscles that have respiratory-related activity (such as the levator veli palatini and the palatoglossus). There are UA muscles that are tonic and do not show any respiratory modulation. An example of such a UA muscle would be the tensor veli palatini. In the awake state the genioglossus is influenced by PCO_2

and PO_2 levels, peripheral and central chemoreceptors, the negative pressure reflex, as well as arousal/wakefulness-related input. The activity of the tensor veli palatini and other tonic muscles however is not influenced by these factors. When a person without SDB falls asleep, the activity of both types of muscles decline, but after a brief period, the respiratory-modulated UA dilators exhibit greater activity, thereby reducing UA resistance. OSA patients show more elevated activity in these respiratory-modulated muscles than normal patients, both in sleep and in the waking state. However, the compensatory activity of these muscles is insufficient to prevent obstructive events.

Essay Questions

Case Study 1

CPAP Intolerance in a Patient with OSA

A 56-year-old woman, who is by profession a grade school teacher, presents with a several year history of snoring and a recent diagnosis of OSA based on a laboratory PSG (AHI of 26, supine REM AHI of 38, LSAT=84 %, less than 2 % sleep time with O2sat<90 %). She reports an occasional "stuffy nose" that she does not think is seasonal and for which she has not been treated. She was prescribed CPAP at 12cmH_2O. She appears motivated but after several weeks is reporting difficulty tolerating CPAP. She is uncomfortable with the high pressure blowing in her face. She has hypertension that appears to be fairly well controlled with a beta-blocker. She denies any cardiac disease. She has never had any surgery in the head and neck region (she denies a history of tonsillectomy). Her BMI is 36.

Part I

Questions

1. What are some of the reasons patients struggle to tolerate CPAP?
2. What might explain her nonseasonal nasal obstruction?
3. What can be done to address nasal obstruction nonsurgically?

Answers

1. Nasal obstruction can contribute greatly to CPAP intolerance. This can be caused by turbinate hypertrophy, polyposis, septal deflection, neoplasm and by nasal valve collapse. Nasal valve collapse occurs (in the awake patient) when the nostrils and nasal side walls collapse with negative pressure. In the setting of CPAP, an ill-fitting nasal mask can exacerbate this condition. Other causes include claustrophobia, lack of humidification, incorrect titration, and lack of support and guidance from medical personnel/staff.

2. Anatomical obstruction (e.g., septum deviation, turbinate hypertrophy, nasal valve collapse), allergic rhinitis secondary to nonseasonal antigens (e.g., dust mites, some molds, pets), nonallergic rhinitis, inflammatory conditions, or neoplasm.
3. Depending on the causes, medical treatment can consist of nasal steroids, antihistamines (oral and inhaled), leukotriene inhibitors, and others. Allergic workup is often warranted followed by immunotherapy if indicated.

Part II

You determine that the nasal cavities are not anatomically obstructed. She has Friedman class 1 tonsils. You pass a fiber-optic laryngoscope through the nasal cavity and perform a Muller maneuver. The view just inferior to or beyond the nasopharynx looks like Fig. 5.1. You advance the fiber-optic laryngoscope further into the oropharynx and it shows the view seen in Fig. 5.2. In Fig. 5.3 a maneuver was done to improve the airway.

Questions

1. What UA subsite is shown in Fig. 5.1 and what is the degree of obstruction?
2. What muscle is primarily contributing to the lateral pharyngeal wall obstruction?
3. What UA subsite is shown in Fig. 5.2?
4. What is being done now to create more posterior airway space in Fig. 5.3?

Answers

1. This figure shows the retropalatal airway (also referred to as the velopharynx) and there is severe circumferential obstruction.
2. Palatopharyngeus
3. Retrolingual airway space in the pharynx. This is sometimes referred to as the tongue base area. This is an example of partial or moderate obstruction.
4. Jaw thrust.

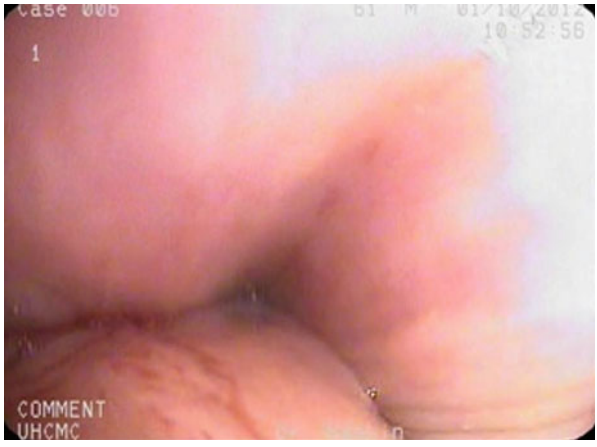


Fig. 5.1

Fig. 5.2

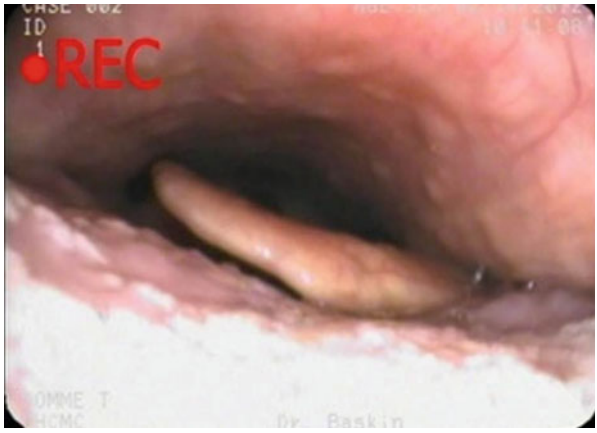
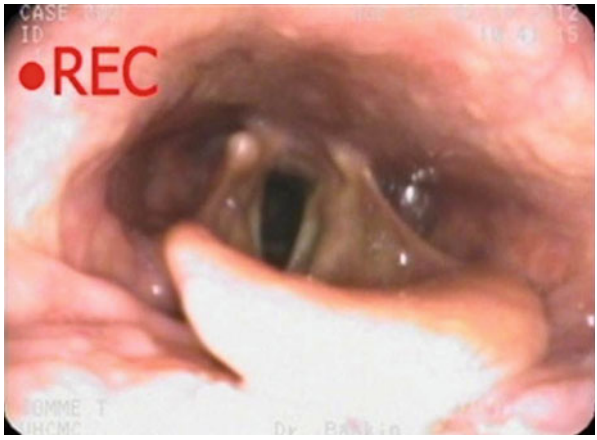


Fig. 5.3



Part III

You prescribe nasal steroids and this does improve her nasal obstruction, but she remains intolerant of CPAP. You have a discussion with the patient about the treatment options. The patient is interested in learning more about surgery as well as other modalities of treatment.

Questions

1. Is a dental appliance a good option for this type of obstruction?
2. What procedure can help alleviate this obstruction?
3. How should you counsel the patient with respect to reasonable outcome expectations?
4. What role does BMI have in influencing your decision to recommend surgery?

Answers

1. Although her overall AHI suggests moderate OSA, she would not likely receive significant benefit from a dental appliance because the primary obstruction is retropalatal and the mandibular advancement dental appliance primarily targets the retrolingual airway. However, it is important to note that mandibular advancement can cause some clinically significant opening of the retropalatal airway as well.
2. A procedure which specifically addresses the lateral pharyngeal walls. An expanded sphincter palatoplasty is designed to do that and can be effective in patients like this one. The palatopharyngeal muscles are mobilized and transposed anteriorly and laterally to reduce lateral tissue prolapse. It can be effective even in patients who have minimal tonsil tissue.
3. Site-specific surgery can be very effective, but realistic expectations need to be counseled. While surgery, in select patients, can eliminate the need for CPAP, it is often used in conjunction with other treatment modalities like weight loss and better sleep hygiene. Or it can reduce UA obstruction to the degree that a lower CPAP pressure is required, making CPAP more tolerable.
4. A BMI of >40 is a relative contraindication to pharyngeal surgery in patients with OSA. However, it must be considered on an individual basis.

Part IV

The patient chooses to do nothing and presents to you 4 years later. She has gained considerable weight and now has a BMI of 42. In addition, her hypertension is no longer well controlled on the previous regimen. She laments that her symptoms have compelled her to move toward early retirement. She recently tried CPAP again but is still struggling with compliance. She has not had a PSG since you last saw her.

Questions

1. What surgical options can you offer this patient with respect to the upper airway?
2. What other surgical options could you consider for this patient?
3. Does surgically induced weight loss result in resolution of obesity-related OSA?

Answers

1. Surgically, the most effective treatment for a patient like this is tracheotomy. However, most patients are loath to consider this option.
2. Bariatric surgery can be considered if conservative measures at weight loss have failed.
3. The proportion of obese patients with OSA has been reported to be as high as 88 % in patients seeking bariatric surgery. Bariatric surgery has been shown to significantly improve OSA, and this improvement appears to be directly proportional to weight loss. However, the surgery also addresses obesity-related hypoventilation syndrome, and there is debate as to the degree to which this is responsible for the reduction in SDB.

Part V

The patient undergoes bariatric surgery. You are asked to make recommendations concerning the postoperative treatment.

Questions

1. Is there benefit to requiring the patient to use the CPAP prior to surgery?
2. What risk is present in treating immediately postoperative bariatric surgery with high-pressure CPAP/BiPAP?

Answers

1. There is no clear evidence that it reduces perioperative morbidity though treatment of OSA is clearly linked to an improvement in other medical problems that are known to increase operative and perioperative morbidity. However, there is no consensus as to how long a patient with OSA would need to be on CPAP to improve operative outcome.
2. There is a theoretical concern that high-pressure CPAP will result in aerophagia, leading to intestinal distention which will stress the anastomosis (depending on the bariatric surgical technique used). There is no strong clinical evidence to prove or disprove this notion.

Case Study 2

Evaluating the Upper Airway

A patient presents with complaints of snoring. He suffers from mild peripheral vascular disease as well as CAD. He does not have any evidence of CHF and is free of any other significant medical comorbidities. He has BMI of 27. He had a tonsillectomy and adenoidectomy when he was a child. PSG has revealed moderate OSA. CPAP has been recommended, but he would like to have a comprehensive UA evaluation to explore other options.

Part I

Questions

1. Prior to evaluating the nasal and oral cavities, what are the important initial components of your physical exam in the office?
2. What information can you expect to obtain from anterior rhinoscopy?
3. The right-sided turbinate is significantly larger than the left turbinate. Do you consider referring the patient for a unilateral turbinoplasty?

Answers

1. Neck circumference, cervical-mental angle, craniofacial morphology with a focus on the development of the mandible and maxilla, vocal quality (upper airway crowding often affects vocalization), and the presence of mouth breathing.
2. The position of the anterior septum, anterior aspect of the inferior turbinates, and the presence of nasal polyposis.
3. The turbinates are vascular organs. The nasal cycle describes alternating vascular engorgement from the left to the right. This can be more pronounced in the supine position. Therefore, this physical finding is not generally of clinical relevance. Enlarged inferior turbinates associated with rhinitis tends to be a bilateral phenomenon and is often associated with other findings like mucosal bogginess.

Part II

The exam demonstrates no significant nasal obstruction but does show a mildly retrusive mandible with a class II molar occlusion. You suspect retrolingual obstruction.

Questions

4. What office procedure can be done to dynamically evaluate the retrolingual/base of tongue subsite of the UA?
5. Does the procedure described in 1 accurately reflect the UA dynamic during NREM sleep? During REM sleep?
6. What imaging studies can be used to evaluate the UA?

Answers

4. Direct (flexible) fiber-optic laryngoscopy with the Muller maneuver (MM). The Muller maneuver is performed by placing the tip of the scope above the site you wish to evaluate. The examiner then pinches the nostrils shut and then asks the patient to close his/her mouth. While the mouth and nose are shut, the patient is asked to try to inhale (against artificially created high resistance), thereby placing the UA under negative pressure.
5. The MM is an approximation of the UA during sleep; however, it is widely regarded as an incomplete reflection of UA behavior during sleep. The neural input related to wakefulness cannot be in eliminated in the awake individual. It is a closer approximation of NREM sleep than REM which exhibits even greater UA muscle relaxation. The Muller maneuver can be done with the patient in a supine position, but this has not been consistently shown to increase accuracy.
6. A cephalometric study can be done to assess craniofacial skeleton morphology though some practitioners replace this study with three-dimensional imaging that can provide highly accurate cephalometry as well as allow for more sophisticated surgical planning. Computed tomography can be used to evaluate the nasal cavities.

Part III

You find no convincing pattern of obstruction using the Muller maneuver, and imaging was similarly unrevealing. The patient is eager to have more information about his UA before deciding on which therapeutic course to follow.

Questions

7. What other diagnostic tests might be useful in this situation?
8. What sites are evaluated in DISE?
9. What pharmacologic agents are typically used in DISE?

Answers

7. Drug-induced sleep endoscopy (DISE).
8. The retropalatal airway, the oropharynx, the retrolingual (base of tongue) airway, and the epiglottis. Some use the acronym VOTE (velopharynx, oropharynx, tongue, epiglottis).
9. Propofol or a combination of Versed and fentanyl. Although this induces a state that is neurologically different from sleep, it appears to cause a similar state of relaxation in the UA. It is considered by many sleep physicians to be the UA evaluation that most closely approximates the state of the UA in natural sleep.

IQ Case Preoperative Assessment for Student

Goal: Few clinical scenarios better illustrate the complexity of UA physiological control mechanisms than the UA response to the administration of different types of anesthesia. The fellow in sleep medicine must understand how to perform a relevant preoperative assessment of the patient with SDB to provide guidance to the referring surgeon and anesthesiologist as they care for a growing population subset that faces significant, and sometimes unrecognized, danger when subjected to anesthesia.

Case Vignette

A 73-year-old man with severe OSA presents for a preoperative evaluation prior to shoulder arthroscopy for repair of a rotator cuff injury. The procedure is scheduled for 1–2 h and is expected to take place as outpatient surgery in an ambulatory center using an interscalene nerve block and sedation.

He quit smoking over 10 years ago and does not consume alcohol. He has a history of CAD that appears well controlled, moderately well controlled CHF, HTN, and mild COPD. He does not have chest pain on climbing one flight of stairs though he does not typically climb more than this.

About a year prior, he was evaluated for sleep apnea and a PSG revealed a supine REM AHI of >100 events/h, with an overall AHI of 55. His OSA symptoms are well controlled since he started regularly using CPAP 3 months ago at a setting of 14cmH_2O, and by report (as well as device usage data), he is compliant. However, he continues to have the occasional urge to move his legs while falling asleep though he was told that he does not have true restless leg syndrome (RLS). He does not suffer from iron deficiency.

You are asked to see the patient by the surgeon to assess his "surgical risk" and to propose management of sleep apnea during his surgery. The anesthesiologist is unwilling to administer anesthetic until the patient's OSA care is "optimized." The consultation is also requesting instruction with respect to patient management through the postoperative period.

On physical exam he has a BMI of 36 and neck circumference of 18.5″. He has an oblique (blunted) cervical mental angle with what appears to be an anteriorly positioned laryngeal complex. He has no trismus and is mostly dentate in the upper and lower arches with an angle class II malocclusion and a moderately retrusive mandible. His upper airway exam reveals a tongue palate relationship (similar to Mallampati) of 3 and no significant tonsillar tissue, but there is oropharyngeal crowding. He has no nasal obstruction with bilaterally patent nasal cavities on anterior rhinoscopy. The rest of his exam is notable for clear lung sounds, normal heart rate and rhythm, and 1+ bipedal edema.

IQ Case: Preoperative Assessment for Facilitator

Goal: Few clinical scenarios better illustrate the complexity of UA physiological control mechanisms than the UA response to the administration of different types of anesthesia. The fellow in sleep medicine must understand how to perform a relevant preoperative assessment of the patient with SDB to provide guidance to the referring surgeon and anesthesiologist as they care for a growing population subset that faces significant, and sometimes unrecognized, danger when subjected to anesthesia.

Learning Objectives

A. Evaluate, preoperatively, the patient with SDB who is expected to undergo surgery while under any type of anesthesia.
B. Understand the risk factors associated with intraoperative difficulty in the patient suffering from SDB.
C. Differentiate between patients who are reasonable candidates for surgery in an ambulatory setting versus a full service hospital.
D. Understand the pharmacologic affects of anesthetic drugs on upper airway physiology
E. Discuss the recommendations for care in the SDB patient in the acute postoperative phase and beyond.

Case Vignette

A 73-year-old man with severe OSA presents for a preoperative evaluation prior to shoulder arthroscopy for repair of a rotator cuff injury. The procedure is scheduled for 1–2 h and is expected to take place as outpatient surgery in an ambulatory center using an interscalene nerve block and sedation.

He quit smoking over 10 years ago and does not consume alcohol. He has a history of CAD that appears well controlled, moderately well controlled CHF, HTN, and mild COPD. He does not have chest pain on climbing one flight of stairs though he does not typically climb more than this.

About a year prior, he was evaluated for sleep apnea and a PSG revealed a supine REM AHI of >100 events/h, with an overall AHI of 55. His OSA symptoms are well controlled since he started regularly using CPAP 3 months ago at a setting of 14cmH_2O, and by report (as well as device usage data), he is compliant. However, he continues to have the occasional urge to move his legs while falling asleep though he was told that he does not have true restless leg syndrome (RLS). He does not suffer from iron deficiency.

You are asked to see the patient by the surgeon to assess his "surgical risk" and to propose management of sleep apnea during his surgery. The anesthesiologist is unwilling to administer anesthetic until the patient's OSA care is "optimized." The consultation is also requesting instruction with respect to patient management through the postoperative period.

Probing Questions

1. What are the important features of the history in determining his fitness for ambulatory anesthesia?
2. Why is the PSG data presented particularly relevant for a patient being considered for ambulatory surgery?
3. What is the significance of restless leg syndrome for anesthesia?
4. If he does not fulfill the criteria for restless leg syndrome, is his complaint of occasional restless legs no longer relevant?

Ideal Answers

1. Obesity, AHI while supine and in REM sleep, restless legs (even if there is no official diagnosis of RLS), medical comorbidities, prior CPAP success, and the nature of the surgical procedure.
2. High supine REM AHI means that with some relaxation he has a reasonable likelihood of obstructing if he is sedated. He has been using his CPAP which means he has been optimized with respect to his SDB. However, there is no consensus as to how long a patient with OSAS needs to be treated for OSA prior to surgery to improve postsurgical outcomes.
3. True restless leg syndrome is a relative contraindication for awake surgery where the patient has to lie still for an extended duration as the motion can be disruptive to surgery.
4. It is still relevant because if he is restless during surgery the motion will present the surgeon and anesthesiologist with difficulty during the case. This will increase the probability of having to convert to general anesthesia.

On physical exam he has a BMI of 36 and neck circumference of 18.5″. He has an oblique (blunted) cervical mental angle with what appears to be an anteriorly positioned laryngeal complex. He has no trismus and is mostly dentate in the upper and lower arches with an angle class II malocclusion and a moderately retrusive mandible. His upper airway exam reveals a tongue palate relationship (similar to Mallampati) of 3 and no significant tonsillar tissue, but there is oropharyngeal crowding. He has no nasal obstruction with bilaterally patent nasal cavities on anterior rhinoscopy. The rest of his exam is notable for clear lung sounds, normal heart rate and rhythm, and 1+ bipedal edema.

Probing Questions

5. What are the important features of the exam with respect to determining his fitness for ambulatory anesthesia?
6. What is significant about the anteriorly positioned laryngeal complex?
7. What is the significance of the bipedal edema?
8. Is this patient a good candidate for a nerve block with sedation?
9. Is he a good candidate to have his surgery in an ambulatory center?

Ideal Answers

5. Obesity, oblique (blunted) cervical mental angle, anterior laryngeal complex, a lack of trismus, a retrusive mandible, bipedal edema, and the tongue/palate (Mallampati) score of 3.
6. If he had to be intubated, it would be more difficult using traditional laryngoscopic blades for visualization. When the large base of tongue is factored into the picture, there is risk of poor visualization of the laryngeal introitus during intubation. The video laryngoscope (one well-known commercial variant is the "GlideScope") is a tool meant to aid in visualization of the laryngeal introitus in these types of instances. It can greatly facilitate intubation in cases such as this one.
7. When the patient lies supine for a significant length of time, a rostral fluid shift from the lower extremities to the head and neck region would result in greater UA tissue congestion and edema. This could potentially elevate Pcrit, gradually, while the procedure progresses, putting the patient at risk for airway compromise.
8. He does not appear to be a good candidate for sedation. Given UA anatomical considerations, his high degree of supine obstruction on PSG, the LE edema, and the restless legs, he would have a fair probability of not tolerating an awake procedure for any length of time. Administration of sedatives during the procedure to help the patient refrain from moving could tip the patient into UA obstruction in the middle of the procedure which poses a risk to surgical outcome as well as to the patient in general.
9. No. The risks are significant for intraoperative airway complications. Any patient with severe OSA in addition to other medical comorbidities (such as heart failure – even if compensated) should be approached cautiously when planning surgery in an ambulatory facility. This is a current and highly relevant issue as the number of surgeries being done in ambulatory centers continues to rise, and there are financial pressures to utilize these centers over full service hospitals. Therefore, these issues will need to be considered with increasing frequency in the future.

Based on your exam you determine that a nerve block with sedation is not safe in this patient. You also recommend that the procedure should not be done in an ambulatory surgical center. You evaluate the patient for general anesthesia.

Probing Questions

10. What are the classes of pharmacologic agents used in general anesthesia and what affects do they have on the UA and ventilation?
11. What are the risks associated with the typically used protocol of induction of anesthesia followed by intubation?
12. Why is it relevant that he has patent nasal cavities?
13. What level of arousal would you prefer on emergence from anesthesia prior to extubation?

Ideal Answers

10. Opioids, propofol, and barbiturates blunt the UA reflexes and affect central respiratory centers. Nitrous oxide and other inhalational agents significantly decrease the ventilatory response to CO_2 and O_2 as well as decrease UA reflexes. Neuromuscular blocking agents can interfere with the UA reflexes.
11. With the physical factors described (obesity, retrusive mandible, anterior larynx, MM 3, LE edema) and the patient in a supine position, he is at risk for obstruction and may not be easily ventilated via face mask once he is asleep. This can be easily managed if it is anticipated and personnel with the proper experience and appropriate equipment are on hand.
12. He may be a candidate for awake nasal fiber-optic intubation if there is a concern about being able to mask ventilate the patient after anesthesia has been induced.
13. The patient should be fully awake and able to respond to some commands. Many anesthesiologists will require the patient to be able to elevate his head off the operating room table for a few seconds prior to removing the endotracheal tube.

You provide your recommendations to the surgeon, and several days later, you receive a phone call from the anesthesiologist. He would like to know your postoperative recommendations.

Probing Questions

14. What recommendations do you have concerning immediate postoperative pain management?
15. Is CPAP administration advisable in the recovery period?
16. In general (for all types of surgical procedures) what are the potential concerns for CPAP use?

Ideal Answers

14. Opioids are best avoided if possible; however, they can be administered judiciously and with the patient under close observation. NSAIDs are specifically indicated for pain control if they are not contraindicated for surgical reasons. Steroid administration can be helpful, in some situations, in lowering the need for other analgesics and for reducing post-intubation edema in the upper airway.
15. Yes. The patient should use his CPAP as soon as he is in the postanesthesia care unit (recovery room). He should continue to use his CPAP at home during all periods of sleep (including naps).
16. CPAP can be disruptive for some types of UA surgery such as nasal structure surgery. However, it is generally advisable in patients with severe OSA if it is practical. In patients with bariatric surgery (depending on the technique) or surgery requiring anastomosis of bowel, there is a theoretical concern that CPAP can cause aerophagia which could put pressure on the anastomosis, leading to anastomotic failure. However, this is somewhat controversial as there is no clear data substantiating this clinically. Nevertheless, the CPAP settings should be titrated prior to surgery to ensure that the pressure levels are not overly high.

IQ Case: Preoperative Assessment Handout/Objectives

Goal: Few clinical scenarios better illustrate the complexity of UA physiological control mechanisms than the UA response to the administration of different types of anesthesia. The fellow in sleep medicine must understand how to perform a relevant preoperative assessment of the patient with SDB to provide guidance to the referring surgeon and anesthesiologist as they care for a growing population subset that faces significant, and sometimes unrecognized, danger when subjected to anesthesia.

Learning Objectives

A. Evaluate, preoperatively, the patient with SDB who is expected to undergo surgery while under some kind of anesthesia.
B. Understand the risk factors associated with intraoperative difficulty in the patient with SDB.
C. Differentiate patients who are reasonable candidates for surgery in an ambulatory setting versus a full service hospital.
D. Understand the pharmacologic affects of anesthetic drugs on upper airway physiology.
E. Discuss the recommendations for care in the SDB patient postoperatively in the acute phase and beyond.

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Chapter 6
Epidemiologic Concepts and Statistics in Clinical Decision Making

Vidya Krishnan and J. Daryl Thornton

Introduction

With the internet and health information technology, health-care providers in training are exposed to more clinically relevant information than ever before. Processing that information and integrating it into clinical practice is a skill that must be developed in a structured and comprehensive fashion. Recently, an increasing number of health-care providers have chosen to pursue research in clinical epidemiology, health services, and quality improvement, collectively called outcomes research. This trend has emerged as more funding agencies, health-care delivery systems, and the government have increasingly emphasized this as an area of focus. In short, such research will shape the financing and administration of health care in the future.

Not surprisingly, the topic of performing, analyzing, and interpreting clinical studies should encompass a curriculum of its own. Epidemiology, biostatistics, clinical decision making, and quality improvement are each areas of study that can require a focus to master and a commitment to maintain skill and knowledge. In this construct, the goals of a sleep fellowship curriculum are to impart interest in basic knowledge of sleep medicine and provide tools to critically interpret a clinical manuscript, to implement the relevant findings of a study, to identify areas of knowledge deficit, and to learn how to address such deficits. These goals are essential to training sleep physicians who will practice high-quality medicine and continually seek to improve their practice. After all, as clinicians, we are trained to be lifelong learners. While sleep fellows do not need to be epidemiologists or biostatisticians,

V. Krishnan, M.D., M.H.S. (✉) • J.D. Thornton, M.D., M.P.H.
Department of Pulmonary, Critical Care and Sleep Medicine,
MetroHealth Medical Center, 2500 MetroHealth Drive,
Cleveland, OH 44109, USA
e-mail: vkrishnan@metrohealth.org

K.P. Strohl, *Competencies in Sleep Medicine: An Assessment Guide*,
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they do need to have foundational understanding of these disciplines to critically evaluate clinical studies in topics related to sleep medicine.

The first step in continuing education is to seek the knowledge – reading updated journals/literature and attending conferences (whether local, national, or international) on the topic of interest – all for the purposes of emphasizing current knowledge, expounding on new findings, and identifying areas needing further investigation. Often this journey of knowledge requires time and effort: (1) protected time on a frequent and regular basis (ideally several hours daily each week) that is spent seeking new knowledge and (2) effort in terms of finding sources of knowledge, whether it be in printed or online journals, books, lectures, or virtual and augmented reality. Adequate, uninterrupted time and effort should be afforded to sleep fellows during their training to obtain and process this information. However, a key component to seeking knowledge is subject interest. A genuine interest in the subject matter by the sleep fellow is an equally important facet of their training. A sleep fellow is expected to learn all aspects of sleep medicine, and to this end it is a two-way street to seek and accept the knowledge that is expected of a sleep fellowship curriculum.

Interpreting a clinical study requires skills in identifying a study question, understanding the background leading to the study question, interpreting study design, and data analysis. A good clinical study clearly identifies the study hypotheses to be tested. As sleep medicine is a relatively young field, there is a plethora of areas of research to be studied. The field of sleep medicine is inundated with new clinical findings for treatment of sleep disorders – new orofacial treatments for sleep apnea, diagnostic modalities for narcolepsy, quality of life consequences of restless legs syndrome – and interpretation and integration of these new findings is essential to providing ongoing quality medical care for patients. Interpreting a clinical study requires knowledge in identifying the strengths and weaknesses of a study. This includes identifying the study hypothesis. This hypothesis should then be adequately addressed by the study design, which includes the subject population, the power and study sample, and the analysis of the data. In interpreting the study results, one must know the background of the field to understand how the present study contributes to the current understanding of the disease or process in question. A basic understanding of these principles is essential to interpreting a clinical study. A forum, such as a journal club, can be valuable for offering such a curriculum. Journal club meetings, which may be on a local level or even online for particular subject matter, can be informative to think through an important journal article and seek the thoughts and input of various experts who will help put the findings in context of the existing knowledge base.

As knowledge is accumulated, processing it is essential to application at the bedside. Often times, studies can offer contrasting results. Understanding the role of meta-analyses and systematic reviews can be helpful to integrate findings from several studies. Cost-effectiveness and comparative effectiveness analyses can be useful in determining the real-world benefit of an intervention compared to current standards of care while simultaneously evaluating associated costs.

Implementing state-of-the-art research findings at the bedside is only the beginning. Quality and continual improvement strive for consistent excellence in care through formally analyzing current performance and systematically working to improve that performance. Important outcomes commonly evaluated include reduction of medical errors, reduction of morbidity and mortality, and improvement in patient satisfaction. A vital part of quality improvement is sustainability – creating systems to ensure that the desired outcomes are uniformly achieved. After topic introduction and study, fellows should develop their own quality improvement projects to better understand how the process works, how to improve their own practice, and how to sustain successful ventures.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/epidemiologic-concepts-and-statistics.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 6.1 Cognitive Map of the Content Domains Relevant to Epidemiology, Biostatistics, and Clinical Decision Making

		Knowledge	Skills	ACGME competency
I.	*Elements of a clinical study* • Research question/hypothesis • Subjects and subject population • Measurements – accuracy and precision • Descriptive measurements – means and standard deviations, medians, and interquartile ranges • Sample size and power	Yes	No	A, F
II.	*Study designs* • Case report • Case series • Cohort studies • Case-control studies • Randomized controlled trials • Meta-analyses and systematic reviews	Yes	No	A, F
III.	*Analysis of data* • Performance measurements – sensitivity, specificity, predictive values • Incidence and prevalence • Relative risk versus absolute risk • Relative risk, odds ratio, and hazard ratios • Number needed to treat (harm)	Yes	No	A, F

IV.	*Clinical decision making*
	• Bayesian theory
	  ○ Pretest probability
	  ○ Likelihood ratios
	  ○ Posttest probability
		Yes	No	A, F

V.	*Quality improvement*	Yes	Yes	C

Table 6.2 Examples of Topics

Item I. Outcome measures of epidemiology
- Death
- Disease/illness – physical signs, laboratory abnormalities
- Discomfort – symptoms of interest (e.g., sleepiness, fatigue)
- Disability – impaired ability to do usual activities
- Dissatisfaction – emotional reaction (e.g., sadness, anger), quality of life
- Destitution – poverty, unemployment

Item II. Measures of disease frequency
- Count
- Proportion
- Ratio – prevalence
- Rate – incidence
- Risk – person-time rate

Item III. Test performance measures
- Test sensitivity/specificity
- False-positive and false-negative rates
- Positive and negative predictive values
- Bayesian theorem and pre-/posttest probabilities

Item IV. Measures of risk
- Odds ratio
- Relative risk
- Hazard ratio
- Risk reduction – absolute and relative
- Number needed to treat (harm)

Item V. Association versus *causality*
- Confounding
- Effect modification

Item VI. Study designs
- Case reports
- Case series
- Case-control study
- Cohort study
- Controlled trials
- Systematic reviews and meta-analyses

Item VII. Chronic disease screening

Item VIII. Quality improvement projects

Item IX. Review quality of a scientific article

Matching Test

Question 1

Choose the most appropriate study design for each scenario.

1. Study of risk factors for narcolepsy, comparing patients with narcolepsy with their healthy siblings

2. In order to investigate OSA and other sleep-disordered breathing as risk factors for the development of cardiovascular disease, a longitudinal study of patients with sleep disorders is followed over time
3. Compare the use of a new dopamine receptor agonist versus placebo to treat RLS
4. Compare the use of a melatonin receptor agonist versus placebo to treat delayed sleep phase disorder, by analyzing data from multiple previous studies

   A. Case study
   B. Case series
   C. Case-control study
   D. Cohort study
   E. Randomized controlled trial
   F. Meta-analysis

Answer 1

1. *C*. Case-control study. Study of risk factors for narcolepsy, comparing patients with narcolepsy with their healthy siblings.
2. Cohort study. In order to investigate OSA and other sleep-disordered breathing as risk factors for the development of cardiovascular disease, a longitudinal study of patients with sleep disorders is followed over time.
3. *E*. Randomized controlled trial. Compare the use of a new dopamine receptor agonist versus placebo to treat RLS.
4. Meta-analysis. Compare the use of a melatonin receptor agonist versus placebo to treat delayed sleep phase disorder, by analyzing data from multiple previous studies.

Question 2

1. Bias
2. Absolute risk reduction
3. Birth cohort
4. Number needed to treat
5. Hypothesis

   A. Term for the systematic deviation of results or inferences from the truth, or the process leading to such systematic deviation.
   B. The number of patients who need to be treated before one person may benefit.
   C. A group of people born during a particular period or year who are then followed up for the incidence of new disease or events.
   D. A supposition that is posed in a form that will allow it to be tested and refuted.

E. The difference in absolute rate of outcome of patients who received an intervention and those who did not.
F. The number of patients who need to be treated before one person is harmed.

Answer 2

1. *A. Bias*. Term for the systematic deviation of results or inferences from the truth, or the process leading to such systematic deviation.
2. *D. Absolute risk reduction (ARR)*. The difference in absolute rate of outcome of patients who received an intervention and those who did not.
3. *C. Birth cohort*. A group of people born during a particular period or year who are then followed up for the incidence of new disease or events.
4. *E. Number needed to treat (NNT)*. The number of patients who need to be treated before one person benefits. NNT is the inverse of ARR:

$$Number\ Needed\ to\ Treat = \frac{1}{Absolute\ Risk\ Rrduction}$$

5. *D. Hypothesis*. A supposition that is posed in a form that will allow it to be tested and refuted.
6. *F. Number needed to harm (NNH)*. The number of patients who need to be treated before one person is harmed.

Essay Questions

Researchers sought to determine the diagnostic accuracy of home nocturnal pulse oximetry to determine the presence of sleep-related breathing disorders (SRBD) in patients with systolic heart dysfunction. Fifty consecutive subjects underwent home oximetry testing and in-laboratory polysomnography (PSG) within 2 weeks of each other (in random order) [5].

Diagnostic value of home nocturnal oximetry in identifying sleep-related breathing disorders (SRBD)

	PSG	
	Normal	SRBD
Nocturnal oximetry		
Normal	13	5
SRBD	1	28

Question 3

With regard to nocturnal oximetry and SRBD, using PSG as the gold standard diagnostic test:

(a) What is the sensitivity and specificity of the test?
(b) What is the positive predictive value and negative predictive value of the test?
(c) Which study tests (sensitivity, specificity, positive predictive value, negative predictive value) are most descriptive of the test? Which are most descriptive of the study population?

Answer 3

		Disease Status	
		Without Disease	**With Disease**
Test Status	**Negative Test**	True Negative	False Negative
	Positive Test	False Positive	True Positive

Sensitivity

- Proportion of people with disease who test positive for the disease.
- $Sensitivity = \dfrac{True\ Positives}{\left(True\ Positives + False\ Negatives\right)}$
- Best for ruling out a disease after obtaining a test result.

Specificity

- Proportion of people without disease who test negative for the disease.
- $Specificity = \dfrac{True\ Negatives}{(True\ Negatives + False\ Positives)}$
- Best for ruling in a disease after obtaining a test result.

Positive Predictive Value (PPV)

- Determines the probability that the patient has the disease given a positive test result.
- $Positive\ Predictive\ Value = \dfrac{True\ Positives}{(True\ Positives + False\ Positives)}$

Negative Predictive Value (NPV)

- Determines the probability that the patient does not have the disease given a negative test result.
- $Negative\ Predictive\ Value = \dfrac{True\ Negatives}{(True\ Negatives + False\ Negatives)}$

A1a. $\text{Sensitivity} = \dfrac{(\text{true positives})}{\text{all positive nocturnal oximetries}} = \dfrac{28}{33} = 84.8\%$

$\text{Specificity} = \dfrac{(\text{true negatives})}{\text{all negative nocturnal oximetries}} = \dfrac{13}{14} = 92.8\%$

A1b. $\text{Positive predictive value} = \dfrac{(\text{true positives})}{(\text{all positive PSGs})} = \dfrac{28}{29} = 96.6\%$

$\text{Negative predictive value} = \dfrac{(\text{true negatives})}{(\text{all negative PSGs})} = \dfrac{13}{18} = 72.2\%$

A1c. Sensitivity and specificity are descriptions of the test that is studied. Positive and negative predictive values are more applicable to the study population. Practically, if the disease is prevalent in the population being studied (or the pretest probability is high), then positive predictive value increases and negative predictive value decreases. Therefore, a negative test is more likely to be a false negative than a true negative.

Questions 4

Compare and contrast incidence versus prevalence.
Compare and contrast risk ratios, odds ratios, hazard ratios.

Which study designs can result in the desired meaningful parameters?

	Case control	Cross section	Cohort	RCT
Incidence				
Prevalence				
Odds ratio				
Relative risk				
Hazard ratio				

Answer 4

1. *Incidence* is the measurement of the number of *new* individuals who contract a disease during a particular period of time.
   Prevalence is the proportion of *all* individuals in a population found to have a condition.
   Odds ratio (OR) is the odds of an event happening in the experimental group expressed as a proportion of the odds of an event happening in the control group.
   Relative risk (also risk ratio, RR) is the ratio of the absolute risk (AR) for each group.
   Hazard ratio (HR) is the ratio of the hazard rates corresponding to the conditions described by two levels of an explanatory variable.
   When the rate of outcome is low, OR and RR are similar, but with increasing rate of outcome, OR overestimates the RR.
   Whereas RR reflects the risk over the entire study period, HR reflects instantaneous risk over the study time period.

	Case control	Cross section	Prospective cohort	RCT
Incidence			X	X
Prevalence	X	X	X	X
Odds ratio	X	X	X	X
Relative risk			X	X
Hazard ratio			X	X

Caveats

1. Nested case-control studies are derived from cohort studies and may have the longitudinal data to produce incidence and prevalence

Question 5

For each study question/study design pair, describe the clinical study that can address the identified study question.

1. Study of risk factors for narcolepsy, comparing patients with narcolepsy with their healthy siblings. Case-control study.

2. In order to investigate OSA and other sleep-disordered breathing as risk factors for the development of cardiovascular disease, a longitudinal study of patients with sleep disorders is followed over time. Cohort study.
3. Compare the use of a new dopamine receptor agonist versus placebo to treat RLS. Randomized controlled trial.
4. Compare the use of a melatonin receptor agonist versus placebo to treat delayed sleep phase disorder, by analyzing data from multiple previous studies. Meta-analysis.

Answer 5

1. Narcolepsy patients have the outcome of study; their non-narcoleptic siblings can serve as the matched controls. Risk factors for narcolepsy including diet, environmental factors, and behavioral factors can be studied.
2. A cohort of patients with OSA can be identified and studied longitudinally. A thorough analysis of cardiovascular risk factors can be evaluated upfront (or patients with certain risk factors can be eliminated to minimize the confounding). Cardiovascular events can be identified prospectively in the study cohort.
3. Patients with RLS without clear reasons to accept the study drug can be identified to participate in a study. Patients can then be randomized to receive study drug, or placebo, and prospectively followed for efficacy or side effects.
4. All clinical studies that have studied melatonin receptor agonists can be examined. The quality of each study, based on study populations, study designs, and evaluation of outcomes, can be used in a meta-analysis. Raw data from these studies can be combined to analyze the total effect of the study drug.

Question 6

What is a confounder and how can it influence the perceived outcomes of a study?

Answer 6

A confounder is a variable that is associated with both the dependent and independent variables, but is not an intermediate step from the dependent and independent variable. An association between the dependent and independent variable may be explained by the extraneous confounder variable and thus create a false-positive finding of outcome for a study.

Summative Essay Question

Ms. Lola Wake is a 35-year-old physician who presents to a sleep physician with complaints of difficulty falling asleep. She is an emergency physician and rotates between day and night shifts frequently. She reports a sleep latency of 2–3 h and often is lying in bed watching TV while trying to fall asleep. She endorses "creepy crawly" feelings in her legs just prior to sleeping at night, which are only relieved with walking. She reports being a "night owl" and reports her ideal sleep time is 3 a.m. to 10 a.m. She drinks coffee throughout the day, and during her work shifts, to keep herself awake.

Her past medical history includes depression and ADHD, for which she takes fluoxetine and Ritalin. On physical examination, she is a thin, physically fit woman. Her vital signs are normal except a blood pressure 148/90. Her Mallampati score is 1, with no visible tonsils and with normal tongue and dentition. The rest of her physical examination is unremarkable.

Her sleep physician identifies the following problem list: (1) poor sleep hygiene, (2) probable restless legs syndrome (RLS), (3) possible shift work disorder, (4) delayed sleep phase disorder, (5) insomnia due to medication effects.

Part 1 Restless Legs Syndrome

Questions

1. The patient inquires about a recent Cochrane Database Review on iron therapy for restless legs syndrome, which concluded that there was insufficient evidence to determine whether iron therapy is beneficial for the treatment of RLS [6]. What features of the meta-analysis should be examined to determine the strength of the evidence?
2. The question of the association between RLS and antidepressant use is raised. The patient presents a study from 2005, which explores the topic [7]. In this retrospective review, 200 consecutive patients presenting with insomnia were studied for use of antidepressants.

   (a) What are potential confounders in this study?
   (b) The study reported 124 patients did not use antidepressants and 76 used antidepressants. Of those who did not use antidepressants, 66 had RLS, and of those who did use antidepressants, 39 had RLS.

      (i) What are the odds of RLS among those who used antidepressants?
      (ii) What are the odds of RLS among those who did not use antidepressants?
      (iii) What is the odds ratio for RLS among those who use versus those who don't use antidepressants?

Ideal Answers

1. A meta-analysis is a study that combines results from different studies to pool the data to determine a common measure of effect size. Some features of a meta-analysis to consider when determining the quality of the study include:

   (a) Publication bias – a meta-analysis may only rely on published data, which in general usually are only positive results. The authors should search for unpublished data (from investigators, from abstracts at conferences) that present negative results as well.
   (b) Base rate fallacy – if a result has already been published, then the likelihood of another study showing the same results being published is less. Again, the authors should search for unpublished data, either directly from authors or from abstracts at conferences.
   (c) Quality of the studies – well-done RCTs should be weighted more than observational or retrospective studies. Depending on the topic, there may be differences in the availability of quality studies.
   (d) Simpson's paradox – two smaller studies may point in one direction, and the combination study in the opposite direction. The consistency of the results of the original studies and the final effect size is considered a strength of a meta-analysis.

2a. Possible confounders may include age (depression (and therefore antidepressant use) and RLS are more common in older patients), iron deficiency, use of other medications that may worsen RLS (diphenhydramine, antipsychotics), use of other medications that may improve RLS (benzodiazepines, narcotics, gabapentin), and comorbidities associated with RLS (renal failure, neuropathy).

2bi. Odds of RLS among those who used antidepressants: 39/37 = 1.05

2bii. Odds of RLS among those who did not use antidepressants: 66/58 = 1.14

2biii. Odds ratio of RLS among those who did versus those who did not use antidepressants: 1.05/1.14 = 0.92

If the 95 % confidence interval crosses 1, then the association of RLS and antidepressant use would not be supported by this data.

Part 2 Circadian Rhythm Disorders

Questions

1. The patient brings a screening questionnaire for shift work disorder (SWD). In a recent publication, the test characteristics of the questionnaire were studied in a population of random shift workers (recruited from the general public and also from a sleep clinic where they were being seen for other sleep disorders).[1]

	Has SWD	No SWD	Totals
Questionnaire (+) for SWD	86	10	96
Questionnaire (–) for SWD	36	53	89
Totals	122	63	185

(a) What is the sensitivity and specificity of the questionnaire to diagnose SWD?
(b) What is the false-positive and false-negative rate for the questionnaire to diagnose SWD?
(c) What is the positive and negative predictive value of the questionnaire to diagnose SWD?
(d) How would you interpret the test characteristics in terms of the utility of the questionnaire as a screening tool for SWD?

2. The patient inquires about using the novel drug, Softkitty, which is already FDA approved for delayed sleep phase disorder, to help with her insomnia. There are no studies to date testing Softkitty for insomnia related to shift work disorder. Design a study to test the effects of Softkitty on insomnia related to shift work disorder. Explain the inclusion/exclusion criteria, the study design, the data to be collected, and the primary and secondary outcomes.

Ideal Answers

1a. $$Sensitivity = \frac{86}{(86+36)} = 0.70 = 70\%$$

$$Specificity = \frac{53}{(53+10)} = 0.84 = 84\%$$

1b. $$False\ Positive\ Rate = \frac{10}{(86+10)} = 0.10 = 10\%$$

$$False\ Negative\ Rate = \frac{36}{(36+53)} = 0.40 = 40\%$$

1c. $$Positive\ Predictive\ Value = 1 - False\ Positive\ Rate = 1 - 0.1 = 0.90 = 90\%$$
$$Negative\ Predictive\ Value = 1 - False\ Negative\ Rate = 1 - 0.4 = 0.6 = 60\%$$

1d. The consequences of having a false screening test should be considered when determining the value of a test. If the cost of missing the diagnosis is high, then a high sensitivity should be sought. If the cost of falsely labeling someone with a diagnosis is high, then a high specificity should be sought. For the diagnosis of SWD, you would want both sensitivity and specificity to be reasonable (>80 %). The sensitivity of this test is low, so one should expect that with screening in a similar population (general population, or patients in a sleep clinic), there will be 29 % of patients (100–71 %) who will have SWD, but not picked up by this test, which is somewhat high.

2. An RCT is likely the best way to approach the study of the new drug Softkitty. Inclusion and exclusion criteria would include the following: (1) ages 18 years and older; (2) nonpregnant; (3) employed in SWD for at least 1 year, with clear definition of number of 2nd and 3rd shifts required to be considered as "shift work"; (4) not on other sleeping aids (with a washout period of 2 weeks); and (5) not on stimulant medications (with washout period of 2 weeks).

   Subjects would be randomized to Softkitty versus placebo medication. The primary outcome would be a measure of daytime function – a QOL survey. Secondary outcomes may include number of car accidents, or Epworth Sleepiness Scale.

IQ Case for Student

Goal: To comprehend and be able to calculate the risk of obstructive sleep apnea in a patient presenting with various risk factors and how the risk changes based on results of a polysomnogram.

Case Vignette

A 52-year-old morbidly obese (BMI 45) woman visits you for evaluation of daily morning headaches. She has been told that she snores every night and is loud enough to be heard from other rooms. She notes difficulty waking in the morning and is sleepy throughout the day.

PMH: diabetes, uncontrolled hypertension, gastroesophageal reflux disease

Social: drinks three cups of coffee each morning. Tobacco use 1 pack per day × 30 years. Social alcohol use, with occasional binge drinking

Physical examination:

VS BP 170/100 HR 80 RR 12
Morbid obesity, with no acute distress
Oropharynx: modified Mallampati 3, 3+ tonsils, scalloped tongue
CV: RRR, no murmurs
Lungs: CTA bilaterally
No lower extremity edema

Objective data:

Berlin questionnaire score = high risk for obstructive sleep apnea
Labs: HCO3 22; Cr 1.0
Echo: normal LVEF; estimated PASP 30 mmHg
PFTs: moderate obstructive ventilatory defect

You pull the following article from your online library: Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131:485–91 [10]. You use Table 4 from that study (below) to determine the pretest probability of the patient having obstructive sleep apnea.

Respiratory disturbance index	Sensitivity	Specificity	Positive predictive value	Likelihood ratio
>5	0.86	0.77	0.89	3.79

The pretest odds of a diagnosis can be multiplied by the likelihood ratio to calculate the posttest odds (Bayes' theorem).

$$Positive\,Likelihood\,Ratio = \frac{Sensitivity}{1 - Specificity}$$

$$Negative\,Likelihood\,Ratio = \frac{1 - Sensitivity}{Specificity}$$

Diagnostic polysomnography revealed severe architecture abnormalities, with fragmented sleep, no slow-wave sleep, and no REM sleep. Apnea hypopnea index was 82/h, primarily obstructive apneas.

The patient undergoes a titration polysomnogram, and optimal control of sleep apnea is achieved with continuous positive airway pressure of 16 cm H_2O. However, in a follow-up clinic visit, the patient is hesitant to initiate CPAP and tells you that family members have told her that oxygen will be just as effective but much easier to use than CPAP.

IQ Case for Facilitator

Goal: To comprehend and be able to calculate the risk of obstructive sleep apnea in a patient presenting with various risk factors and how the risk changes based on results of a polysomnogram.

Case Vignette

A 52-year-old morbidly obese (BMI 45) woman visits you for evaluation of daily morning headaches. She has been told that she snores every night and is loud enough to be heard from other rooms. She notes difficulty waking in the morning and is sleepy throughout the day.
Past Medical History: diabetes, uncontrolled hypertension, gastroesophageal reflux disease
Social: Drinks three cups of coffee each morning. Tobacco use 1 pack per day × 30 years. Social alcohol use, with occasional binge drinking

Physical examination:

VS BP 170/100 HR 80 RR 12
Morbid obesity, with no acute distress
Oropharynx: modified Mallampati 3, 3+ tonsils, scalloped tongue
CV: RRR, no murmurs
Lungs: CTA bilaterally
No lower extremity edema

Objective data:

Berlin questionnaire score = high risk for obstructive sleep apnea
Labs: HCO3 22; Cr 1.0
Echo: normal LVEF; estimated PASP 30 mmHg
PFTs: moderate obstructive ventilatory defect

You pull the following article from your online library: Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131:485–91 [10]. You use Table 4 from that study (below) to determine the pretest probability of the patient having obstructive sleep apnea.

Respiratory disturbance index	Sensitivity	Specificity	Positive predictive value	Likelihood ratio
>5	0.86	0.77	0.89	3.79

Question

What is the likelihood that the patient has obstructive sleep apnea?

Answer

The patient is determined to be at high risk for obstructive sleep apnea given her response to the Berlin questionnaire. She has an 89 % chance of having OSA given the positive test. The positive likelihood ratio >1 means that we can have a high pretest (or pre-polysomnography) probability of having OSA. The pretest odds of a diagnosis can be multiplied by the likelihood ratio to calculate the posttest odds (Bayes' theorem).

$$Positive\,Likelihood\,Ratio = \frac{Sensitivity}{1 - Specificity}$$

$$Negative\,Likelihood\,Ratio = \frac{1 - Sensitivity}{Specificity}$$

Diagnostic polysomnography revealed severe architecture abnormalities, with fragmented sleep, no slow-wave sleep, and no REM sleep. Apnea hypopnea index was 82/h, primarily obstructive apneas.

Question

What comorbid disorders are attributable to or exacerbating the patient's sleep apnea?

Answer

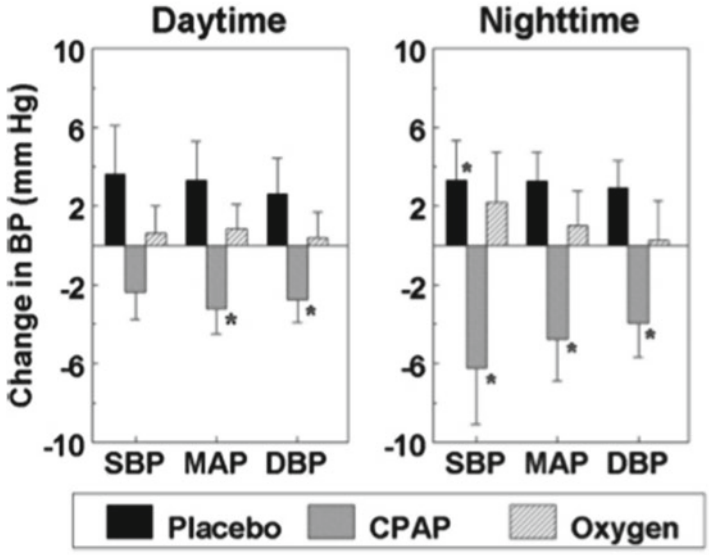
Comorbid conditions that are associated with the patient's sleep apnea include:

1. Obesity
2. Headaches
3. Snoring
4. Diabetes
5. Hypertension
6. GERD
7. Tobacco use
8. Alcohol use
9. COPD
10. Enlarged tonsils

The patient undergoes a titration polysomnogram, and optimal control of sleep apnea is achieved with continuous positive airway pressure of 16 cm H_2O. However, in a follow-up clinic visit, the patient is hesitant to initiate CPAP and tells you that family members have told her that oxygen will be just as effective but much easier to use than CPAP.

Questions

1. After a quick search on PubMed, you find a report of a randomized controlled trial comparing CPAP to sham-CPAP and oxygen in patients with OSA and hypertension [9]. What findings from the outcomes figure (see below) will you share with her to help her decide optimal treatment for her OSA and hypertension?



Change in 24-hour ABPM in each of the 3 treatment groups after 2 weeks of therapy. Daytime BP was measured from 6:00 AM to 10:00 PM. Nighttime BP values were measured from 10:00 PM to 6:00 AM. Change is measured from mean pretreatment minus post-treatment values. Bars represent mean±SE.
*Significant changes over time ($P<0.05$).

2. What factors may improve adherence to therapy, and to what extent?
3. Can you design a quality assurance project to ensure that patients with sleep apnea are receiving adequate follow-up for treatment of their disorder?

Answers

1. The figure demonstrates a significant improvement in daytime mean arterial and diastolic blood pressure during daytime among patients who used CPAP for 2 weeks compared to sham-CPAP and oxygen. During nighttime, CPAP patients

had significant improvement in systolic, mean arterial, and diastolic blood pressure compared to sham-CPAP and oxygen. Patients who used oxygen for 2 weeks had increases in all blood pressure measurements during the day and night.

2. Some of the factors that confer benefit in adherence to therapy include:

   (a) Pretreatment symptoms and symptom resolution with CPAP therapy. The more bothersome the perceived symptoms, the more positive feedback is given for the patient with treatment of the OSA.
   (b) Treatment of side effects of treatment. For CPAP therapy, 30–70 % of patients report side effects, including mask-fit problems, airway dryness, nasal congestion, and awakenings due to noise. Addressing these problems can improve adherence.
   (c) Psychological acceptance. Addressing reasons for apprehension for treatment early in the course of therapy is essential.
   (d) Early experience, education, and support. Positive CPAP experience in the first 2–4 weeks can improve CPAP adherence.
   (e) New technology. Heat and humidification have been shown to improve adherence. Other comfort factors for CPAP have incremental benefit, but at the cost of high price.

   The extent of benefit of each of these interventions will depend on the individual patient, the factors present prior to treatment, and the factors that develop with treatment.

3. A quality assurance project should be focused on understanding and addressing the unique barrier to optimal CPAP therapy among participating patients. It will be important to focus on systemic, provider, and patient barriers. Having representatives from all involved groups will be helpful. A plan-do-study-act cycle may be used to develop and implement an effective intervention.

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Chapter 7
Clinical Evaluations of the Patient

Rory Ramsey, Amit Khanna, and Motoo Yamauchi

Introduction

The clinical evaluation involves elicitation of a general sleep history with a focused follow-up on features relevant to other conditions, physical examination, review of prior notes and tests, and interpretation of the verbal and nonverbal communication that passes between physician and patient. It is a data gathering and utilization process aimed to align what becomes known with decisions designed to achieve the best overall subjective and objective outcome for the patient. Important components of this data gathering and decision-making process include utilization of history and physical examination to generate a differential diagnosis with associated pretest probabilities, assessment of potential benefits and risks of different pathways, and appreciation of important patient-centered factors, e.g., preference for particular management pathways, motivation, and cost.

The sleep clinical evaluation differs from other specialty organ system evaluations in one important way. It is a multiorgan system. The clinical evaluation and pathologies tied to the traditional organ systems (e.g., pulmonology, neurology) center around the organ of interest. Not having an organ system of its own sleep

R. Ramsey, M.D.
Sleep Medicine Specialist, Private Practice, Boise, ID, USA

A. Khanna, M.D.
Lawrence + Memorial Hospital Sleep Center,
224 Gold Star Highway, Groton, CT, USA
e-mail: khanna_amit@hotmail.com

M. Yamauchi, M.D., Ph.D. (✉)
Department of Respiratory Medicine, Nara Medical University,
840 Shijo-cho, Kashihara, Nara, 634-8522, Japan
e-mail: mountain@pastel.ocn.ne.jp

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medicine cannot do this. Instead it cuts a swath through many of the traditional organ systems and finds itself grouped into categories of disease (e.g., sleep-related breathing disorders, insomnia, movement disorders) that either focus on different organs or cross over into multiple organ systems. This unique starting point and built-in integration of many of the traditional organ systems introduces a level of complexity and richness not seen in other specialties. Practically speaking, it implies that more detailed probing into other organ systems is built into the core of its clinical evaluation.

This chapter is designed to provide tools for evaluating the sleep clinical evaluation. These tools were developed through interaction with sleep medicine physicians and review of existing literature on the subject. The instruments designed were history and physical examination checklist, recall matching answer sets, essay questions, summative essay questions, IQ case discussion, and lecture. They are by no means exhaustive, but the knowledge content intends to cover much of the essential information, and the different presentation formats are designed to provide a scaffolding for development of further materials.

The history and physical examination checklist details specific data expected to be collected but more commonly categories to be explored in varying details depending on the answer given. This highlights the two components of history and physical examination gathering. First, there is a fairly generic essential data gathering process that is relatively easy to test. Second, there is another feature akin to skill that is much harder to test and score. While this may, on occasion, involve the collection of otherwise missed data that ties the story together, it will more regularly manifest itself in data utilization. Testing one's ability to use data can incorporate how one directs the sequential questioning, the amount of data that is collected (more isn't necessarily better), one's relationship with and understanding of the patient, and the final decision making. All this introduces subjectivity to the testing process. As such the scoring is left relatively open.

The other instruments used in this chapter – recall matching answer sets, essay question, summative essay question, IQ case discussion, jeopardy answers and questions, and lecture – have been designed to test the subject knowledge and to some extent use of information that is considered broadly applicable to any sleep clinical encounter. This includes the body of data that makes up the standard history and physical examination and the latent knowledge that underpins the ability to use it, an understanding of scales and their utility, and an ability to apply some of the basic principles behind diagnostic testing, e.g., Bayes theorem.

Just as mapping a journey is different from actually taking one; thus, these exercises are quite different from "real-life" clinical encounters. Thus, they understandably fall short of testing everything needed to evaluate skill in clinical examination. This "real-life" component is many things and includes an ability to relate to a patient and navigate their personality empathetically while giving direction and finally putting together all of the information into a grand plan aimed to optimize patient outcomes.

Table 7.1 Cognitive Map of the Content Domains Relevant to the Physical Examination

		Knowledge	Skills	ACGME competency
I	*Epidemiology*	Yes	No	B, F
	Age			
	Risk factors			
	Special populations			
II	*Mechanisms of health and disease*	Yes	No	A, B
	Endocrine			
	Upper airway			
	Neurological			
III	*Risk factors*	Yes	No	A, B
	Environmental			
	Genetic			
	Age-related			
IV	*Patient assessments*	Yes	Yes	A, C, D, E
V	*Diagnostic measures and interpretation*	Yes	Yes	A, C, F
	Clinical decisions			
	Pretest probability			A, B, C
	Patient-based testing			A, B, F
VI	*Disease management*	Yes	Yes	
	Presentation of therapeutic options			A, D, E, F
	Follow-up			A, F
VII	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Code for ACGME competencies			
	A. Patient care		D. Interpersonal skills	
	B. Medical knowledge		E. Professionalism	
	C. Practice-based learning and improvement		F. System-based practice	

Table 7.2 Examples of Topics with Educational Objectives

Item I. Mechanisms

- Draw the essential elements of the upper airway in sagittal section
- List common collections of symptoms and signs for obstructive sleep apnea, restless leg symptoms, narcolepsy, and insomnia
- Describe and compare the questionnaires used to assess patients in the outpatient arena

Item II. Assessments

- List an approach to the neurologic examination in the patient with narcolepsy and restless leg symptoms
- Discuss the elements of pre-and posttest probability in patients presenting to a sleep specialist

(continued)

(continued)

Item III. Diagnostic strategies
- Contrast the utility and practice of actigraphy to that of a sleep diary
- Describe clinical scenarios that in evidence-based reviews provide indications for level I, II, III, IV monitoring

Item IV. Practice-based management
- Compare and contrast teaching methods for diagnostic testing
- Describe the concept of a multidisciplinary follow-up program for sleep disorders

Item V. Health and disease management pathways
- Describe the principles for development of a quality assurance program for adherence to therapy
- Now that a patient has been prescribed therapy, list the steps for evaluation of therapy
- List patient expectations vs. physician objectives in terms of testing
- List the differences in expectations and assessments for patients with ALS vs. those with stable chronic neuromuscular disease
- List Pros/Cons for medication therapy options for RLS, narcolepsy, and insomnia

Item VI. Practice-based learning and improvement
- Devise a program to optimize patient instruction prior to a test
- Formulate a checklist for assessment of a fellow and compare it to that for a faculty member

Item VII. Interpersonal and communication skills
- Describe motivational interviewing techniques for follow-up of patients being treated for a sleep disorder
- Create a checklist for assessment of such skills in a busy practice

Item VIII. Professionalism
- Fabricate a fair presentation of treatment choices for patients of different ages and genders
- Identify conflicts in the payment structures for assessments and education of patients

Item IX. System-based practice
- Diagnostic pathways
  - Develop a concept map to manage narcolepsy
  - Develop a reimbursement-based plan for a patient
- Evaluate inpatient assessments to that performed in the outpatient setting

Matching Test

Questions

Specific, not sensitive finding. ☐
Breath holding and glottis closure. ☐
Medication associated with RBD. ☐
Risk factor for central sleep apnea. ☐
Midfacial hypoplasia. ☐
A cause of pseudo-RBD. ☐
A potential cause of RLS. ☐
Anticholinergics precipitate this. ☐

Sleeping condition with eyes open. ☐
Secondary narcolepsy with cataplexy. ☐
Sudden intense painless head feeling with flash of light sensation. ☐
Repetitive stereotyped and rhythmic motor behavior. ☐
Reduces efficacy of oral contraceptive pill. ☐
A feature of psychophysiologic Insomnia. ☐
Sensation of impending death and residual hoarseness. ☐
Large male predominance. ☐
Associated with sleep-related breathing disorder and primary hypersomnia. ☐
Most common sleep aid. ☐
Originally validated in surgical patients. ☐
Substance abuse evaluation. ☐
Varies with prevalence. ☐
Unhelpful test. ☐
Helpful in ruling out disease. ☐
Potential long-term emergent effects of dopamine agonists. ☐
Monitoring sleep logs or actigraphy for more than 7 days is preferred. ☐
Unable to diagnose before the age of 5 years. ☐
Persistent hypopneas revealed on a bi-level PAP device download. ☐

Answers

1. Apnea, sleep paralysis, leg kicks in sleep
2. Catathrenia, snoring, whistling
3. Venlafaxine, morphine, theophylline, zolpidem, mirtazapine
4. Stroke, smoking, PVD, amitriptyline
5. Crouzon syndrome, Down's syndrome, Mobius syndrome
6. OSA, idiopathic insomnia
7. Gastric ulcer, diabetes mellitus, SLE, lumbar disk disease
8. Sleep walking
9. Sleep walking, REM behavior disorder
10. Sarcoidosis affecting hypothalamus, myasthenia gravis, Alzheimer's
11. Exploding head syndrome, seizure, migraine, sleep-related headache
12. Body rocking, PLM
13. Modafinil, methylphenidate
14. Sleep better in sleep lab, psychosis, preference for later sleep time, underestimation of sleep time
15. Sleep-related laryngospasm
16. Cheyne Stokes
17. Myotonic dystrophy, hypothyroidism
18. ETOH, zolpidem, temazepam
19. STOP-BANG, SAQLI, CAGE, GAD-7, FOSQ
20. CAGE, SF-36, MMSE, FSS, AIS
21. ppv, sens, spec, LR, pretest prob
22. LR 0.95
23. LR 0.1, LR 15 sensitivity 90 % ppv 80 %
24. Condition with low FVC, low FEV1, normal ratio, low TLC, high RV/TLC, normal DLCO
25. Condition with normal FVC, low FEV1, low ratio, high TLC, high RV/TLC, normal DLCO
26. Condition with normal FVC, normal FEV1, normal ratio, normal TLC, normal RV/TLC, low DLCO
27. Impulsive behaviors (gambling, shopping, sexual, driving)
28. Circadian sleep disorder – free-running type (nonentrained type)
29. Sleep enuresis (primary or secondary)
30. Insufficient EPAP

Questions with Answers

A cause of pseudo-RBD. 6
A feature of psychophysiologic insomnia. 14
A potential cause of RLS. 7
Anticholinergics precipitate this. 8
Associated with sleep-related breathing disorder and primary hypersomnia. 17
Breath holding and glottis closure. 2
Helpful in ruling out disease. 23
Large male predominance. 16
Medication Associated with RBD. 3
Midfacial hypoplasia. 5
Most common sleep aid. 18
Originally validated in surgical patients. 19
Reduces efficacy of oral contraceptive pill. 13
Repetitive stereotyped and rhythmic motor behavior. 12
Risk factor for central sleep apnea. 4
Secondary narcolepsy with cataplexy. 10
Sensation of impending death and residual hoarseness. 15
Sleeping condition with eyes open. 9
Specific, not sensitive finding. 1
Substance abuse evaluation. 20
Sudden intense painless head feeling with flash of light sensation. 11
Unhelpful test. 22
Varies with prevalence. 21
Potential long-term emergent effects of dopamine agonists. 27
Monitoring sleep logs or actigraphy for more than 7 days is preferred. 28
Unable to diagnose before the age of 5 years. 29
Persistent hypopneas revealed on a bi-level PAP device download. 30

Essay Questions

Case Study 1

A 79-year-old woman with mild dementia who lives in an assisted living environment is referred to you for evaluation of sleep apnea.

Questions

1. What is the purpose of the physician patient encounter?
2. List features in the history and physical examination that increase sleep apnea pretest probability.
3. What is the standard definition of sleep apnea? Why this 2-tier diagnosis?
4. What are common difficulties with the diagnosis of sleep apnea?
5. How do you quantify disease severity?
6. What are reasons for a patient to have minimal to no symptomatic benefit on otherwise well-controlled sleep apnea?
7. What features predict compliance with CPAP?

Ideal Answers

1. The physician patient encounter is designed to generate a differential diagnosis with associated disease pretest probabilities, an estimation of relative harm vs. benefits of different management pathways, and an understanding of patient preference for the above. This understanding is then marshaled into a decision designed to maximize patient benefit and minimize harm.
2. Features that contribute to increasing probability of sleep apnea include excessive daytime sleepiness, snoring, witnessed apneas, hypertension, coronary artery disease, heart failure, obesity, positive family history of sleep apnea, nasal obstruction, high Mallampati score, tonsillar enlargement, lateral narrowing of pharyngeal walls, age, and inferred post-menopausal status. Several features are often combined into models or rules for predicting sleep apnea, e.g., sleep apnea clinical score and Berlin Questionnaire.
3. Sleep apnea is a disorder of sleep fragmentation and intermittent hypoxemia that has diverse effects in different individuals. Some of these effects are excessive daytime fatigue and sleepiness, headaches, nocturia, edema, pulmonary hypertension, systemic hypertension, and increased risk for cardiovascular disease. One is considered to have sleep apnea if the AHI >5 and symptoms(s) are present or if the AHI >15 regardless of symptoms. This definition tries to incorporate the idea that people have different thresholds at which they become symptomatic and that there is a level at which it causes problems regardless of an individual's ability to recognize it.
4. Common difficulties include:

    (a) Different people have different thresholds for experiencing symptoms from sleep apnea and therefore the definition is a moving target.

(b) Different manifestations of disease in different people.
(c) The symptoms that are most commonly responsible for presentation to a physician (sleepiness and fatigue) are often vague, hard to measure, and particularly hard to identify in many personalities.
(d) Night to night variability in AHI as measured by polysomnography.
(e) Poor correlation between AHI and symptoms.

5. Most commonly by AHI or by its effects, e.g., degree of fatigue or sleepiness or pulmonary hypertension.
6. Reasons include symptoms were not due to sleep apnea, hypoxic damage to brain, history of heart failure, and idiopathic.
7. Predictors of long-term CPAP use are elevated AHI and subjective sleepiness (increased ESS).

Case Study 2

Sarah D. is a 49-year-old woman complaining of worsening sleep onset insomnia and excessive daytime fatigue over years. Her difficulty initiating sleep onset started in her early 20s soon after finishing college and having her first baby. Her Epworth score is 4. The fatigue severity score is 46.

Her husband verifies that she doesn't snore and he has never noticed her stop breathing at night. There is no family history of sleep apnea though her mother has had insomnia much of her life. The Berlin Questionnaire had her positive in only one category.

Sarah D. goes to bed with her husband around 11:30 p.m. and will typically take 2–3 h to fall asleep. She sometimes watches television in bed. She feels frustrated, often mulls over the day's events and anxieties and describes her mind as racing. She will read in bed and sometimes get up to go downstairs for a snack. She wakes up 0–2 times per night and regularly has difficulty getting back to sleep. She wakes up at 7:30 a.m. feeling exhausted so that she can go to her job as a librarian. She estimates 4–5 h of sleep nightly. She regularly feels like napping, but whenever she tries to nap she finds herself unable to fall asleep. She is a lifelong nonsmoker and only drinks 1–2 alcoholic beverages per month. She drinks 4–5 caffeinated beverages daily but none after 6 p.m. The Morningness-Eveningness Questionnaire shows an evening preference. The insomnia severity index score is 21.

She has a history of depression that dates back to the birth of her second (and last) child almost 25 years ago. She considers it well controlled and takes fluoxetine every morning. Becks depression index is 11. She experiences chronic low back pain from a slipped disk for which she takes oxycodone nightly. This has helped with the antsy feeling she gets in her legs at night that historically made it more difficult to fall asleep. No history of head injuries and no recent laboratory evidence for diabetes or thyroid disease.

Physical examination is mostly remarkable for obesity (BMI 33). Mallampati score is 3. Full pulmonary, cardiac and neurologic examinations are normal. The sleep apnea clinical score is 6.

Overnight oximetry was performed by a primary doctor as a "screening" tool. Numeric summary shows a total recording time of 7 h 22 min. A total of 4 % recording time was spent below an SpO 2 90 %. The oxygen desaturation index (4 % desaturations) was 1.5 events per hour. Visual inspection of arterial oxygen saturation waveforms identified minimal sawtoothing. When patient was asked, she said she felt she barely slept that night.

Patient has also asked about doing a home study for sleep apnea.

Part 1

Questions

1. What is the differential diagnosis for sleep onset and maintenance insomnia in this patient?
2. What features are supportive of and what further questions and tests might you ask to pursue each of the potential diagnoses above?

Ideal Answers

1. The differential diagnosis for this patient includes psychophysiologic insomnia, delayed sleep phase syndrome, poor sleep hygiene, mental disorders, medication effect, idiopathic, RLS, sleep apnea, and paradoxical insomnia. Like most cases of insomnia, the cause is likely multifactorial with contributions from several of the above.
2. Features and further questions could include:

   (a) Psychophysiologic insomnia: Supportive data includes description of mind racing and mulling over of the day's anxieties. Additionally, almost anyone who has had chronic insomnia has a component of this.
   (b) Delayed sleep phase syndrome: Supportive features include family history, insomnia started after patient left confines of college and an evening preference noted from Morningness-Eveningness Questionnaire. Probing into sleep schedule during vacations (without kids!), prior to insomnia onset would be very helpful.
   (c) Poor sleep hygiene: Spending too much time in bed, watching TV in bed, and drinking caffeine in the evening are supportive issues. Exploration of other known features such as exercise, working in bedroom, light exposure, sleeping with pets, and environmental noise could be explored further.
   (d) Mental disorders: Becks depression inventory suggest mild disease. She also describes anxiety.
   (e) Medication effect: Fluoxetine contributes to insomnia in some people. A history of previous antidepressants and any relationship to improving or worsening

insomnia should be elicited. She drinks caffeine up to 6 p.m. and this is likely too late to be drinking it for her.

(f) Idiopathic: Supportive data include a family history. To some extent nearly everyone with chronic insomnia has some component of this in the sense that it represents a biologic propensity for insomnia. Formally, though this diagnosis is given to people with insomnia in the absence of other causes.

(g) RLS: The patient appears to have a mild degree of RLS at this point, but further exploration in terms of onset, previous severity, frequency, and temporal relationship with insomnia severity would be important. Detailing the nature of her RLS before opioid use would better illicit her baseline status. The restless leg symptoms quality of life questionnaire could be employed to measure severity.

(h) Sleep apnea: The pretest probability can be estimated by the absence of snoring and apnea, a low sleep apnea clinical score, the Berlin Questionnaire score, the presence of excessive daytime fatigue and obesity, use of oxycodone, and to some extent the results of the overnight oximetry. Overall her probability is on the lower side, but other features that could be elicited to round this out more include a history of hypertension or heart disease.

(i) Paradoxical insomnia: A component of this is suggested by the fact that she estimates only 4–5 h nightly and yet does not have definite sleepiness (though she has profound fatigue). A sleep log and actigraphy could help resolve this issue.

Part 2

Questions

1. What is a scale? Give two examples of scales commonly used in sleep medicine.
2. A good scale is reliable, generalizable, and valid. Define these terms.
3. What is an index? Give an example.
4. Define internal and external validity, construct validity, content validity, and others?

Ideal Answers

1. A scale is an instrument that measures intensity or quantity. Examples of two commonly used scales in sleep practice and/or research are the Epworth Sleepiness Scale and the Fatigue Severity Scale.
2. Reliability is the extent to which a scale is reproducible. Generalizability is the ability to extrapolate from a sample to a larger population. Validity refers to the extent to which a measurement or scale accurately measures that which it is meant to measure.
3. An index is a ratio or other number derived from a series of observations and used as an indicator or measure (as of a condition, property, or phenomenon). -JAMA.

Examples include the insomnia severity index, Apnea-hypopnea index, and Beck's depression index.

4. Internal validity is a property of scientific studies which reflects the extent to which a causal conclusion based on a study is warranted. Such warrant is constituted by the extent to which a study minimizes systematic error (or 'bias'). External validity is the validity of generalized (causal) inferences in scientific studies. It is the extent to which the outcome of a study can be generalized to other situations and to other people. Construct validity is the extent to which a scale measures that which it was meant to measure. Content validity refers to the extent to which a measure represents all facets of a given construct. An element of subjectivity exists in relation to determining content validity.

Part 3

Questions

1. What is screening? What are the features of a good screening test? What are the problems of overscreening?
2. What is case finding?
3. What is a clinical prediction rule?
4. Is overnight oximetry useful for screening or case finding? What are its limitations?

Ideal Answers

1. Screening is a strategy to detect a disease in people without signs or symptoms. A good screening test is easy and safe to administer, has good sensitivity and specificity, is inexpensive, leads to demonstrated improved outcomes, is widely available, and identifies a disease which is serious enough to warrant treatment and treatment is practical and readily available. Problems arise whenever any of the above conditions are not met. For example, if the test is not sensitive enough, it will miss the diagnosis and falsely assure and if the test is not specific enough it will over diagnose people and lead to further unnecessary testing.
2. Case finding is searching for disease in people based on the presence of a risk factor.
3. A clinical prediction rule is a model that combines history, examination, and test findings into a parsimonious equation designed to best predict a disease or outcome. Examples of two commonly used clinical prediction rules in sleep practice and/or research are the Berlin Questionnaire and the Sleep Apnea Clinical Score.
4. Overnight oximetry has been employed by some physicians as a self-reported "screening" instrument when in fact it is being used as a case-finding device. It is used to look for evidence of sleep apnea in those for whom there is some pretest suspicion of its presence. This test has not been sufficiently validated to perform this function and so runs the risks of increasing testing, delaying diagnosis, and falsely reassuring. Other problems with overnight oximetry include

the following: it cannot differentiate between obstructive apneas, central apneas, and hyponeas; it cannot differentiate between wake and sleep; there is little uniformity in their use and interpretation; and there are a variety of devices that record at different sampling rates and store and analyze data in different ways.

Part 4

Questions

1. What is test sensitivity? What is test specificity?
2. What are likelihood ratios?
3. Should a portable home study be employed to rule in or rule out sleep apnea in this case? Explain.

Ideal Answers

1. Test sensitivity is the probability of a positive test if the patient has the disease. If a test has high sensitivity, a negative test is used to rule out disease. Test specificity is the probability of a negative test given that the patient is ill. If a test has a high specificity, then a positive test will mean a high probability of disease.
2. Likelihood ratios are used to assess the value of a diagnostic test. They use sensitivity and specificity to determine whether a test usefully changes the probability of disease. A positive likelihood ratio is >1 and confirms that the test is associated with the disease. A negative likelihood ratio is <1 and confirms that the test is not associated with the disease. Generally, positive likelihood ratios (LR+) >5 are interpreted as usefully increasing disease probability. Negative likelihood ratios (LR-) <0.2 are interpreted as usefully decreasing disease probability.
3. The purpose of portable home testing for sleep apnea is to improve the overall diagnostic and management of sleep apnea. Measuring this capability is complex and factors in many variables including cost, compliance, amount of testing, test sensitivity and specificity, outcomes of interest, patient preference, safety, etc. The current state of the literature and the sleep medicine community consensus is potentially useful in patients with a high pretest probability (e.g., 80 %) with few to no significant comorbidities. The use of a test with a LR>5 in such would increase the probability of disease to about 95 %. Portable study use in these settings would likely decrease the issue of false assurances, need for subsequent diagnostic polysomnograms and the associated cost, inconvenience, and lost to follow-up problems. Given this, the patient described in the above case should not undergo a portable study as her probability of disease is too low.

IQ Case for Student

Goal: Navigate the history and physical examination in a patient with excessive daytime sleepiness. This entails utilizing supplied information to create a differential diagnosis with estimates of disease probability, understanding the significance of commonly encountered features on history and examination, and being able to smoothly interact with this sequentially added information by directed probing and adjustment of pretest probabilities.

Case Vignette

A 35-year-old man presented to the sleep clinic complaining of 3–4 years of worsening "tiredness." In his own words he feels "exhausted" all the time. ESS is 18.

He snores but has no definite history of witnessed apneas. He works as a daytime janitor and has a regular sleep schedule going to bed at 9 p.m. and waking at 6 a.m., sleeping a full 9 h nightly but still not feeling refreshed. He describes episodes of lightheadedness and feeling weak at the knees several times over the last 3 months. He has had 3–4 episodes of sleep paralysis in his life and gives no convincing descriptions for hypnagogic or hypnopompic hallucinations. He denies restless leg symptoms.

Patient reports being a restrained passenger in a head on collision 5 years ago. He experienced small, multicompartment intracranial hemorrhages and contusions but did not require intracranial surgery. He had some facial, long bone, and pelvis fractures but little else. He spent a total of 2 months in various health care facilities (acute care hospital and rehabilitation facility) before being discharged. He notes his short term memory hasn't been the same since. He left hospital on paroxetine and methylphenidate and discontinued the latter soon thereafter.

Patient reports being on paroxetine since discharge 5 years ago but is not sure why he is on it. He takes it in the morning. He is not sure if he is depressed. He occasionally gets flashbacks related to the accident and this sometimes wakes him up. His best friend was the driver and was killed.

Patient has taken morphine since the accident for low back pain. He is also a smoker and has been for > 15 years despite a family history of emphysema. He takes albuterol 3–4 times per day. He complains of regular shortness of breath that is worse on exertion but experiences little cough or wheeze. He has had type 1 diabetes since he was 15 years old for which he takes insulin glargine (Lantus) and insulin glulisine (Apidra).

PMH: asthma/COPD, diabetes mellitus, motor vehicle accident 5 years ago with traumatic brain injury (TBI), chronic low back pain
FH: cousin has narcolepsy, dad with asthma/emphysema
SH: smokes 1–2 packs per day, drinks six caffeinated beverages daily, married with three children at home

Medications: paroxetine, lisinopril/HCTZ, albuterol, oxycodone, morphine, insulin glargine, and insulin glulisine
A physical examination was performed.

GA: obese, AA
VS: P 88 bpm, BP 144/90 mmHg, RR 16 cpm, SpO2 93 % on RA
HEENT: EOMI, PERLA, Mallampati 3 tonsils 2+
NECK: thick, no JVD, no palpable cervical or supraclavicular lymphadenopathy
Chest: mildly decreased breath sounds without added sounds
Heart: RRR no murmurs
ABD: soft, NT, no masses
EXT: no cyanosis, edema or clubbing
Neuro: normal cranial nerve and peripheral nervous system examination

IQ Case for Facilitator

Goal: Navigate the history and physical examination in a patient with excessive daytime sleepiness. This entails utilizing supplied information to create a differential diagnosis with estimates of disease probability, understanding the significance of commonly encountered features on history and examination, and being able to smoothly interact with this sequentially added information by directed probing and adjustment of pretest probabilities.

Learning Objectives

A. Create a differential diagnosis for excessive daytime sleepiness.
B. Understand significance of historical and examination features as they relate to heightening or lowering disease probability in the context of a case with multiple potential etiologies.
C. Learn how some disorders cause excessive daytime sleepiness.
D. Learn how to efficiently probe further into potential etiologies for excessive daytime sleepiness.

Case Vignette

A 35-year-old man presented to the sleep clinic complaining of 3–4 years of worsening "tiredness." In his own words he feels "exhausted" all the time. ESS is 18.

Probing Questions

1. How do you measure sleepiness?
2. What is, and how do you differentiate between tiredness, fatigue and sleepiness?
3. How do you assess driving risk?

He snores but has no definite history of witnessed apneas. He works as a daytime janitor and has a regular sleep schedule going to bed at 9 p.m. and waking at 6 a.m., sleeping a full 9 h nightly but still not feeling refreshed. He describes episodes of lightheadedness and feeling weak at the knees several times over the last 3 months. He has had 3–4 episodes of sleep paralysis in his life and gives no convincing descriptions for hypnagogic or hypnopompic hallucinations. He denies restless leg symptoms.

Probing Questions

4. What is the differential diagnosis of cataplexy? What features help distinguish cataplexy from its mimics?
5. What is the sensitivity and specificity of cataplexy, sleep paralysis, and hypnagogic/hypnopompic hallucinations for narcolepsy?

Patient reports being a restrained passenger in a head on collision 5 years ago. He experienced small, multicompartment intracranial hemorrhages and contusions but did not require intracranial surgery. He had some facial, long bone, and pelvis fractures but little else. He spent a total of 2 months in various health care facilities

(acute care hospital and rehabilitation facility) before being discharged. He notes his short term memory hasn't been the same since. He left hospital on paroxetine and methylphenidate and discontinued the latter soon thereafter.

Probing Questions

6. What are the different ways TBI causes excessive daytime sleepiness?
7. What is the prevalence of sleep disorders in patient with TBI and excessive daytime sleepiness?
8. Is neurologic imaging indicated in this patient?

Patient reports being on paroxetine since discharge 5 years ago but is not sure why he is on it. He takes it in the morning. He is not sure if he is depressed. He occasionally gets flashbacks related to the accident and this sometimes wakes him up. His best friend was the driver and was killed.

Probing Questions

9. How do you measure depression?
10. What are the potential reasons for this patient being on an antidepressant?
11. How common is it for depression to be the primary cause of excessive daytime sleepiness?
12. Antidepressants as a group can cause insomnia and EDS in equal measure. Which ones tend to be more sedating?
13. What is posttraumatic stress disorder? How is it diagnosed? How does it affect sleep and daytime functioning?

Patient has taken morphine since the accident for low back pain. He is also a smoker and has been for >15 years despite a family history of emphysema. He takes albuterol 3–4 times per day. He complains of regular shortness of breath that is worse on exertion but experiences little cough or wheeze. He has had type 1 diabetes since he was 15 years old for which he takes insulin glargine (Lantus) and insulin glulisine (Apidra).

Probing Questions

14. What are two ways opioids can cause sleepiness?
15. In what condition will morphine accumulate?
16. How can asthma and COPD cause excessive daytime sleepiness? What are different ways of measuring severity and control of these common disorders?
17. How do you measure DM severity?

PMH: asthma/COPD, diabetes mellitus, motor vehicle accident 5 years ago with traumatic brain injury (TBI), chronic low back pain
FH: cousin has narcolepsy, dad with asthma/emphysema
SH: smokes 1–2 packs per day, drinks six caffeinated beverages daily, married with three children at home
Medications: paroxetine, lisinopril/HCTZ, albuterol, oxycodone, morphine, insulin glargine, insulin glulisine

Probing Question

18. What is the differential diagnosis of excessive daytime sleepiness is this case? Rank these diagnoses and provide supporting information.

A physical examination was performed.

GA: obese, AA
VS: P 88 bmp, BP 144/90 mmHg, RR 16 cpm, SpO2 93 % on RA
HEENT: EOMI, PERLA, Mallampati 3 tonsils 2+
NECK: thick, no JVD, no palpable cervical or supraclavicular lymphadenopathy
Chest: decent breath sounds without added sounds
Heart: RRR no murmurs
ABD: soft, NT, no masses
EXT: no cyanosis, edema, or clubbing
Neuro: normal cranial nerve and peripheral nervous system examination

Probing Question

19. What is the additional value (after history) of the physical examination in this patient?

Final Handout/Objectives

Goal: Navigate the history and physical examination in a patient with excessive daytime sleepiness. This entails utilizing supplied information to create a differential diagnosis with estimates of disease probability, understanding the significance of commonly encountered features on history and examination, and being able to smoothly interact with this sequentially added information by directed probing and adjustment of pretest probabilities.

Learning Objectives

A. Create a differential diagnosis for excessive daytime sleepiness.
B. Understand significance of historical and examination features as they relate to heightening or lowering disease probability in the context of a case with multiple potential etiologies.
C. Learn how some disorders cause excessive daytime sleepiness.
D. Learn how to efficiently probe further into potential etiologies for excessive daytime sleepiness.

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Chapter 8
Diagnostic Testing

Michael Decker and Kingman P. Strohl

Introduction

The fellowship program should provide formal instruction, experience, and demonstrated competence in procedures and technical skills relevant to the specialty of sleep medicine (IV.A.2.h: procedures and technical skills). Essential components include the presence of a sleep laboratory of sufficient volume to encounter common and much of the uncommon presentations in sleep medicine that require diagnostic testing or tools to define patient problems and progress. There is an emphasis on the technology used to monitor and record physiologic parameters, scoring, and analysis of those records. Increasingly the ACGME and medical systems are asking for programs to address questions regarding the utility of testing, the manner in which testing in general leads to treatment, and cost-effectiveness, not only of the basic tests but also of ancillary tests like thyroid or pulmonary function testing. The fellowship program existing within a clinical practice system is asked to be part of the solution as much as being seen as a problem of cost, access, and outcome.

Sleep medicine, with its diagnostic standards, evolved from neurophysiologic measures or brain activity. The electroencephalograph[1], first used to measure patterns of global neural activity, epilepsy, and neuromuscular disorders, was employed to describe sleep and sleep states. Shortly thereafter, additional electrophysiologic sensors were added to measure breathing, the ECG, and limb movements. Collectively, the array of electroencephalographic, respiratory, cardiac, and limb movement sensors provide insight into what was going on in patients with hypersomnolence and led to the recordings of sleep apnea and the therapeutic effects of

M. Decker, Ph.D., D.A.B.S.M., R.N., R.R.T. (✉)
Francis Payne Bolton School of Nursing, Case Western Reserve University,
10900 Euclia Avenue, Cleveland, OH 44106, USA
e-mail: MJDG@CASE.EDU

K.P. Strohl, M.D.
Case Western Reserve University, Cleveland, OH, USA

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tracheostomy. The term polysomnography (PSG) was invented in the early 1970s to explain to those without sleep knowledge, and to insurance companies, the complexity and time commitment of this common test in our specialty. In the early 1980s almost every patient referred for testing to one of a few centers in the USA and most in Europe underwent overnight sleep recording followed by a daytime multiple sleep latency test (MSLT) one patient at a time. During this early period in sleep medicine, existing laboratories performed less than 10 studies a month. Fast forward to today, sleep laboratories are common, possess larger numbers of beds, and equipped with digital technology for recording and display, which enhances efficiency of physician interpretation. In addition, we have other self-report measures (Epworth Sleepiness Scales, Stanford Sleepiness Scale, Beck's Depression Inventory, Fatigue Severity Scale, etc.), procedures (actigraphy and psychomotor vigilance testing), and appropriate referral (imaging, HLA testing, ferritin levels, pulmonary function testing, etc.). This era has pushed to the forefront the importance of patient selection and education about the manner and purpose of sleep diagnostic test and any other referral testing procedures.

This chapter is designed to address procedures used in sleep medicine. In addition to the usual subjective surveys and objective tests that sleep physicians interpret, we also include consideration of other tests that are performed by referral physicians, such as imaging or pulmonary function testing, that are performed and interpreted by other specialists often unfamiliar with the patient with sleep disorders.

This chapter is not intended to be a "how-to" manual. For this the reader should look to original literature on these tests. This chapter will not cover scoring rules, as they may change or new ones develop for determining numeric values reflecting sleep-disordered breathing and oxygenation, REM behavior disorders, motor movements during sleep, etc. relevant to outcomes.

In our program we have tried, implemented, and assessed several formats to introduce diagnostic procedures, scoring, and interpretation of data generated by procedures in sleep medicine. Personally we have found that a blend of formal lectures coupled with ongoing formal instruction has been the most successful. In contrast, a dependence on a "boot camp" in PSG scoring is almost always inadequate due to the individuality of EEG, the variety of PSG presentations seen in health and disease, artifacts, as well as variations among laboratories and individual technologists.

ACGME program instructions include "in-house" diagnostic procedures/tests which include polysomnography, MSLT, maintenance of wakefulness testing (MWT), psychological and psychometric testing, and other requested tests by the practitioner. Home-based or "unattended" diagnostics include cardiorespiratory monitoring and actigraphy. Personal skills should also include certification of cardiorespiratory resuscitation and relating to patients and their families, and other allied health care practitioners, with integrity and respect.

Some things are started but not finished in a 1-year program. With this in mind, we believe the most necessary information conferred is the need for a systematic approach to data collection. In this foundation there is a common theme; for any test there is consideration of need and cost, pre-test probability, patient instruction, and knowledge of how the test is properly (and improperly) done (see Chap. 6). Then there is the test itself, where the sleep physician should know who will administer/perform the test, the policy and procedures needed to do the test, the primary

collection of the data, and scoring of the test. This is followed by the interpretation of the test results. For this we may include considerations of potential variations in clinical language of the interpretation that may be needed depending upon the patient, referral source, and basis for the diagnostic code or for insurance reimbursement. Finally, consideration is needed in regard to how the test results are presented to the patient and other doctors and how these results impact on the health status of the patient. A cavalier diagnosis of sleep apnea remains with the patient and will influence subsequent applications for insurance, disability, or long-term care plans. On occasion a problem noted on testing may be clinically insignificant or not worth pursuing, and this clinical judgment is needed. Some of these skills should be assessed as a process of development (see Chap. 1).

The material presented here was developed through interactions among sleep medicine specialists in Cleveland region. The recall matching answer sets, essay question, and summative essay question are by no means exhaustive and demand the development of further materials.

Some content domains along with corresponding ACGME areas for general competencies are illustrated in Table 8.1. While not as comprehensive as one would find in a textbook devoted to those domains, these areas touch upon all aspects of practice as well as the basic issues found in sleep and neurologic disorders. Some of the areas like epidemiology are solely knowledge-based and relate to the clinical use of procedures.

Formal presentations on questionnaires, procedures, and testing should be stated in such a manner as to capture what specific knowledge, skills, and attitudes a fellow should be able to exhibit following instruction. Some examples for a given content area are presented in Table 8.2. Note that this list tries to focus on work-related, measurable, or verifiable outcomes.

There is some art to the interpretation of these clinical assessments, and individual styles may vary; however, here one should attempt to define trainee progression concerning primary and ancillary tests. An example of how to track a trainee based on the R.I.M.E. paradigm is presented in Table 8.3.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/diagnostic-testing.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 8.1 Content Domains Relevant to Diagnostic Measures and Interpretation

	Knowledge	Skills	ACGME competency
I. *Technology*			
Measurement methods	Yes		B
Monitoring types I–IV	Yes	Yes	B
MSLT/MWT	Yes	Yes	A, B
Actigraphy	Yes	Yes	A, B, F
Other (PVT, pupillometry)	Yes	Yes	A, B, F

(continued)

(continued)

	Knowledge	Skills	ACGME competency
II. *Diagnostic interpretation*			
Blood testing for sleep disorders	Yes		A, F
Imaging studies	Yes		A, F
Posttest probability	Yes	Yes	A, C, F
Ethics in referral pathways	Yes		E
III. *Titration management*	Yes	Yes	
Presentation of therapeutic options	Yes	Yes	A, B, D, F
Decisions during PSG	Yes	Yes	A, B, D, F
Follow-up	Yes	Yes	F
IV. *Clinical pathways*	Yes	Yes	A, C, F
Code for ACGME competencies			
A. Patient care		D. Interpersonal skills	
B. Medical knowledge		E. Professionalism	
C. Practice-based learning and improvement		F. System-based practice	

Table 8.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
- Contrast clinical diagnostic pathways in fee-for-service, managed care, and private pay. For example, clinical diagnostic pathways utilizing "in-house" PSG with unattended cardiorespiratory monitoring
- Compare interpretations of diagnostic testing among practitioners and its impact on care

Item II. Diagnostic technology
- Draw the EEG electrode placements using 10–20 coordinates and electrode references used for standard montage, extended montage, and seizure monitoring
- Describe and compare the preparation of equipment for cardiorespiratory monitoring in a standard polysomnogram to that in portable monitoring
- List the essential factors used in monitoring by pulse oximetry

Item III. Assessments
- List an approach to defining and detecting artifacts and common variants along with correction
- List an approach to define and detect distracting features – in EEG/EOG, oximetry, respiratory monitoring (e.g., EEG alpha activity, EEG activity on EOG channels)
- Contrast post-test probability of confirming a diagnosis in primary care patients to those presenting to a sleep clinic

Item IV. Diagnostic strategies
- Compare level I, II, III, IV monitors and explain the types of sensors each might have
- Contrast the utility and practice of actigraphy in adult and pediatric populations
- Describe clinical scenarios that in evidence-based reviews provide indications for MSLT vs. MWT

Item IV. Practice-based management
- Compare and contrast teaching methods to enhance sleep technologists' skills and quality of recorded/collected data
- Describe the concept of "kid friendly" diagnostic facilities
- How might diagnostic strategies differ in the assessment of patients with spinal cord injury, amyotrophic lateral sclerosis, and developmental disability?

Item V. Health and disease management pathways
- Describe the principles for initiation and titration management during a sleep study (CPAP, bi-level, ASV, etc.)
- Once a patient has responded to therapy during an in-house study, list the necessary steps involved with instructions for long-term therapy
- List patient expectations vs. physician objectives in terms of patient testing

(continued)

(continued)

Item VI. Practice-based learning and improvement
- Devise a quality improvement program for patient instruction prior to a test
- Formulate a checklist for optimizing an interpretation

Interpersonal and communication skills
- Demonstrate and apply motivational interviewing techniques for technologist training
- Evaluate each other's interpretations for content and outcome

Professionalism
- Fabricate a fair presentation of testing needs to the patient and the objective criteria necessary justify the procedure to his/her health insurance company
- Identify ethical conflicts in the conduct of sleep testing

System-based practice
- Diagnostic pathways
  - Develop a concept map plan to manage pressure therapy (CPAP, bi-level, ASV, etc.) for sleep apnea
  - Develop a reimbursement-based plan for actigraphy in the practice of sleep medicine
- Evaluate inpatient testing for indications, outcome, and cost-effectiveness

Table 8.3 Diagnostic Procedures and Interpretation. Evaluation of Progression During a Sleep Medicine Fellowship

Reporter (3–6 months)
- Obtains and reports basic information for the procedure
- Has basic knowledge to know what to look for in the primary tests in sleep medicine
- Has the ability to recognize normal from abnormal and confidence to label a new problem
- Reliable in the context of a rotation for interpretation
- Laboratory staff exhibiting solid professional qualities

Interpreter (4–8 months)
- Good working fund of knowledge
- Consistently prepared for attending input
- Consistently able to interpret data: can identify and prioritize new problems
- Can offer reasonable possibilities for new problems or outcomes and cite reasons they may apply to this patient
- Not always correct, but has a higher level of knowledge, more skill
- Answers the *"how and why"* questions about polysomnography, actigraphy, and MSLT/MWT

Manager (8–12 months)
- Excellent general fund of knowledge
- Broad/deep knowledge of the testing
- Actively suggests management options, answers *"what's next"*
- Is proactive rather than reactive, actively suggests management options
- Confidence/willingness to state own preferences
- Diagnostic plans include more than one appropriate treatment option, and considers reasonable therapies

Educator (10–12 months)
- Can cite evidence citing pros and cons of testing and interpretations
- Takes an active role in educating themselves, colleagues, and patients
- Skilled in identifying questions that can't be answered from textbooks
- Superior fund of knowledge
- Consistently possesses superior knowledge and skill and can tailor management pathways for patients and for hospital systems

Adapted from Emory University School of Medicine & Pangaro LN. Academic Medicine 1999; 74:1203–7

Matching Test

Questions

Used to record physiological parameters of high frequency. ☐
Used to record slower moving potentials such as pH. ☐
Subjective scale for how sleepy you are right now. ☐
Has a 20- and a 40-min version. ☐
Proposed recording and staging for Sleep in 1936. ☐
1968 Rechtschaffen and Kales manual. ☐
Derived normal values for sleep in 1959. ☐
N1, N2, N3, and REM staging. ☐
Characterized by three types of A and one B phases. ☐
Creates the most controversy in the determination of AHI. ☐
AASM classification system for recording techniques and devices. ☐
1999 descriptor for events where there are arousals without hypoxemia but caused by ventilatory effort. ☐
Metric for sleep recording more likely to be lower than AHI. ☐
Metric for sleep recording more likely to be higher than AHI. ☐
The most direct measure of respiratory effort. ☐
Based on the two-compartment model for the estimation of tidal volume. ☐
Mislabeled because it is an appearance of respiratory-related EMG activity in the submental electrodes. ☐
Bursts of spiky transients followed by a slower component, lasting often <2 s. ☐
Best defense against artifact. ☐
A burst of rhythmic slowing seen in 10 % of normal children. ☐
A short circuit of deadly potential whose danger is mitigated by a three-pronged plug on the recording equipment. ☐
Estimation of human rest/activity cycles. ☐
Reaction time that is sensitive to sleepiness. ☐
Instability of this measure correlates with somnolence. ☐

Answers

1. Alternating current amplifiers
2. Direct current amplifiers
3. Impedance testing
4. Nasion
5. Inion
6. Stanford Sleepiness Scale
7. Epworth Sleepiness Scale
8. Beck's Scale
9. Fatigue Severity Scale
10. Orexin levels
11. MSLT
12. MWT
13. Alpha
14. Theta
15. Delta
16. Loomis
17. Dement-Kleitman
18. The Standard Manual
19. Sleep spindles
20. Williams and Karacan
21. AASM Scoring Manual
22. Cyclic alternating pattern (CAP)
23. PLMD
24. Hypopnea
25. Level I-IV devices
26. Apnea
27. RERA
28. ODI
29. RDI
30. Wake inhibition sleep preservation (WISP)
31. Impedance pneumography
32. Strain gauges
33. Magnetometers
34. Piezo sensors
35. Diaphragmatic electromyography
36. Konno-Mead analysis
37. Pacemaker artifact
38. Respiratory artifact
39. Myogenic movements
40. Sweating
41. Intravenous drip artifacts
42. Experienced technologist
43. Epileptiform discharges
44. Vertex waves
45. Hypnagogic hypersynchrony
46. K complexes
47. Asynchrony
48. Periodic lateralizing epileptiform discharges (PLED)
49. Alpha-delta sleep
50. Benign epileptiform transients of sleep (BETS)
51. Fault current
52. Analog-to-digital converter (ADC)
53. High-pass filter
54. Low-pass filter
55. International 10–20 system of EEG electrode placement
56. Preauricular points
57. Actigraphy
58. Psychomotor vigilance testing (PVT)
59. Pupillometry
60. Pedometer

Questions with Answers

Used to record physiological parameters of high frequency. 1
Used to record slower moving potentials such as pH. 2
Subjective scale for how sleepy you are right now. 6
Has a 20-and a 40-min version. 12
Proposed recording and staging for Sleep in 1936. 16
1968 Rechtschaffen and Kales manual. 18
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N1, N2, N3 and REM staging. 21
Characterized by three types of A and one B phases. 22
Creates the most controversy in the determination of AHI. 24
AASM Classification System for Recording Techniques and Devices. 25
1999 descriptor for events where there are arousals without hypoxemia but caused by ventilatory effort. 27
Metric for sleep recording more likely to be lower than AHI. 28
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The most direct measure of respiratory effort. 35
Based on the two-compartment model for the estimation of tidal volume. 36
Mislabeled because it is an appearance of respiratory-related EMG activity in the submental electrodes. 38
Bursts of spiky transients followed by a slower component, lasting often <2 s.
Best defense against artifact. 42
A burst of rhythmic slowing seen in 10 % of normal children. 45
A short circuit of deadly potential whose danger is mitigated by a three-pronged plug on the recording equipment. 51
Estimation of human rest/activity cycles. 57
Reaction Time that is sensitive to sleepiness. 58
Instability of this measure correlates with somnolence. 59

Essay Questions

Question

After verification of electrode placement, what are three sources that can induce 60 Hz artifact?

Answer

One of the electrodes has become detached or is not attached to the patient.

Ground electrode is detached.

Uneven impedance between electrodes.

Environmental source for the 60 Hz (elevator or heater).

A 15-year-old male (BK) presents with sleepiness in school. He is notorious for falling asleep in class especially when it is in first or second form. He is awoken at 7 a.m. to go to school by his single mother who works in a 9 p.m. to 5 a.m. shift at the newspaper. His grandmother who stays with the family goes to sleep at 9:30 p.m. and awakens at 5 a.m. BK says that he goes to bed at 11 p.m. and does nothing until he falls asleep. He states that he likes to sleep in on the weekend and that he has no problem staying awake at night especially on the weekend. His mother says he is a typical boy, just like his father at that age. BK has not been known to snore or appear to sleep poorly (restless, move, or sleep walk). There is no report of syncope or evidence for drug use.

Questions

1. What test is the appropriate test for excessive daytime sleepiness?
2. What is the principle measure for the test?
3. In general this test is appropriate for what sleep disorders or interventions?

Answers

1. Actigraphy is useful for assessing daytime sleepiness in situations where a laboratory sleep latency test is not appropriate.
2. The unit itself is an electronic device which generally consists of a piezoelectric accelerometer, a low-pass filter which filters out everything except the 2–3 Hz band (so external vibrations like being in a car), a timing mechanism to start/stop the actigraph at specific times and to accumulate values for a specific time frame, a memory, and an interface, usually USB both to program the timer and to download the data from memory.
3. It is used to clinically evaluate insomnia, circadian rhythm sleep disorders, excessive sleepiness, and restless legs syndrome. It is also used in assessing the effectiveness of pharmacologic, behavioral, phototherapeutic, or chronotherapeutic treatments for such disorders.

Questions

4. What is the principle feature that forms the basis for oximetry?
5. Compare and contrast the MWT vs. MSLT in terms of its execution, purpose, and expected interpretation of results.

Answers

4. The fundamental physical property that permits the measurement of arterial oxygen saturation is that blood changes its light spectra with the binding of hemoglobin. A pulse oximeter permits the estimation of saturation at the height of pulsatile flow, the best moment to measure arterialized blood.

   Bonus: A sensor is placed on a thin part of the patient's body, usually a fingertip or earlobe, or in the case of an infant, across a foot. Light of two wavelengths is passed through the patient to a photodetector. The changing absorbance at each of the wavelengths is measured, allowing determination of the absorbances at the peak of a pulse, thus reducing the contribution of venous blood, skin, bone, muscle, fat, and (in most cases) nail polish. Reflectance pulse oximetry may be used as an alternative to transmissive pulse oximetery. This method is suited to more universal application such as the feet, forehead and chest. There are more artifacts with reflectance oximetry. Vasodilation and pooling of venous blood in the head due to compromised venous return to the heart can cause a combination of arterial and venous pulsations in the forehead region and lead to non-arterial measures of saturation.
5. Both are intended as measurement of sleep onset with altered instruction, patient circumstances, and body position. The conclusions concerning degrees of individual sleepiness are mixed, possibly because the MWT probes for the ability to withstand sleep and the MSLT probes for the ability to initiate sleep. The instructions in the *MWT are to stay awake* while those for *the MSLT are to try to go to sleep*. Some consider the MWT as extending the sensitive range of the MSLT in terms of sleepiness onset.

   The MSLT has the greater history of use, normative standards, and experience, especially in the detection of objective sleepiness and the presence of unusual transitions from sleep onset to REM onset. There is also a more general consensus of abnormal vs. normal in the initial assessment of a patient. The MWT is more sensitive to prior night's sleep and to interventions. Because it tests the ability to stay awake and fall asleep unintentionally, MWT probes for how quickly a person falls asleep under soporific conditions such as reading, sitting in a chair, or driving.

IQ Case

Diagnostic Procedures and Interpretation for Student

Case Vignette

A 64-year-old businessman presents to your office with a sheaf of papers and asks for a second opinion. He was in his previous state of good health until 6 months ago when he started to develop headaches that would awaken him at night. His wife said he had snored all his life, and might have been louder in the past year. He related to being sleepy during the day and attributed it to long working hours. He generally denied neurologic complaints, symptoms of RLS or narcolepsy, or prior head injury or trauma. He was taking Lipitor and aspirin for hypercholesterolemia.

The notes indicate that on presentation his ESS was 13/24, oxygen saturation 97 %, blood pressure 130/80, HR 88, and BMI 27. Examination was called "unremarkable".

A sleep study was then performed that showed 20 % N1 sleep, 50 % N2, 10 % N3, and 20 % REM sleep.

Sleep onset occurred in 19 min, with REM latency of 130 min. There was an arousal index of 28, and a PLM Index of 12. Respiratory monitoring showed an AHI of 18, and RDI of 26. The REM AHI was 25 with a supine AHI of 22. The oxygen saturation was >90 %–98 % of the time.

A second sleep study was a CPAP titration and showed that with 10 cm H_2O the AHI was 3.1 (REM AHI 4.0), and the patient was placed on CPAP at a fixed pressure of 10 cm H_2O.

Two weeks later, the patient returned with an ESS of 10 and a report of using the machine. The dull frontal headache was less frequent, his snoring did not bother his wife anymore, and he generally felt better. Adherence was 90 % of the time with >4 h/night.

Three months later, he presented with sleepiness. He did not report snoring, and his headache was the same. The ESS was 14/24. Adherence was 89 % of the time with >4 h/night, and an average of 6.8 h of use per night. He asked about what the next steps were.

A PSG with an MSLT was ordered. The PSG showed good control of respiratory events with an AHI of 3.8, and the MSLT showed a mean sleep latency of 9.9 min without any REM periods. The patient was placed on modafinil.

Modafanil (200 mg each morning) was subjectively helpful for about a month, but he remained tired and sleepy. Frustrated with his care, he comes to you for a second opinion.

On your examination, you find the patient's history and physical are similar to that described before. The wife recounts endorses sleepiness and in addition has noticed that his judgment in social relationships has slipped. The ESS is 17/24, and vital signs were similar. Examination revealed a normal pharynx and chest and heart examination. Neurological examination showed a droop in the corner of the left mouth, and hyperreflexia in the left leg. (The droop has been there for a year or so, according to his wife). Vision, smell, sensory and memory for three items at 3 min is within normal limits.

Your options at this time are to perform repeat sleep studies. As the prior studies were inconclusive, you opt for CT imaging. A representative image is shown in Fig. 8.1.

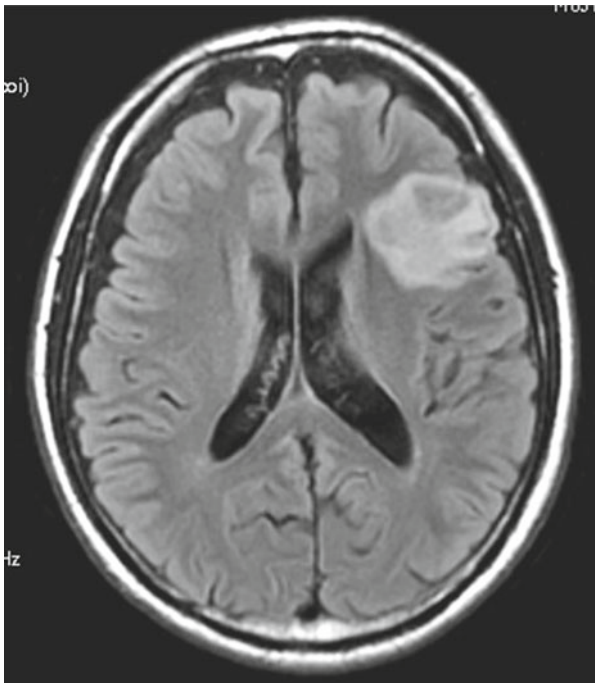

Fig. 8.1 The patient is referred for evaluation by neurosurgery and biopsy reveals a Grade 2 astrocytoma

Computed tomography (CT): A CT scan is a detailed X-ray. The CT imaging system is comprised of a motorized table that moves the patient through a circular opening and an X-ray machine that rotates around the patient as they move through. Detectors on the opposite side of the patient from where the X-ray entered record the radiation exiting that section of the patient's body, creating an X-ray "snapshot" at one position (angle). Many different "snapshots" are collected during one complete rotation of the X-ray machine. A computer then assembles the series of X-ray images into a cross section, or a picture of one small slice of the body. A CT scan is a series of these cross-sectional images.

CT scan is a less expensive test than MRI and provides good definition of extra-axial brain tumors, or brain tumors that are not located deep in the skull.

Magnetic resonance imaging (MRI): MRI is perhaps the most valuable test that doctors use to diagnose brain tumors. MRI uses a strong magnet and radiofrequency waves to produce an image of internal organs and structures. Under the influence of the strong magnet, the hydrogen atoms in the body line up like compass needles. Next, the patient is exposed to radio waves that cause the hydrogen atoms to momentarily change positions. In the process of returning to their orientation under the influence of the magnet, they emit a brief radio signal. The intensity of these radio waves reflects what type of tissue exists in that area of the body. The MRI system goes through the area of the body being imaged, point by point, collecting information from how the radio waves emit. A computer generates an image of organs and structures based on these radio wave recordings.

MRI is useful for diagnosing brain tumors because it provides accurate information on the following:

- Description of anatomy of the brain and shape of possible tumor tissue
- Definition of the extent of surrounding edema (swelling)

Positron emission tomography (PET): Unlike techniques that provide anatomical images, such as X-ray, CT, and MRI, PET scans show chemical and physiological changes related to metabolism. This is important because these functional changes often occur before structural changes in tissues. PET images may therefore show abnormalities long before they would be revealed by X-ray, CT, or MRI.

PET scans are often used after an anatomical scan, such as MRI or CT, has shown that an abnormal mass does exist. With a PET image that reflects the metabolic activity of the tumor, doctors are able to determine whether the tumor is benign or malignant. PET is also used to accurately determine the stage of the brain tumor.

Diagnostic Procedures and Interpretation for Facilitator

Goal: The common presentation of obstructive sleep apnea (OSA) and its treatment will require follow-up assessments of specific outcomes, targeted organ systems, and identification of unusual conditions that can potentially masquerade as sleep apnea or its sequela.

Learning Objectives

A. Evaluate a patient with suspected sleep-disordered breathing (SDB) and the indications for PSG.
B. List the risk factors for hypersomnolence following successful treatment of OSA.
C. Differentiate patients who need MSLT from those who need another approach to determine sleepiness or sleep-wake patterns.
D. Recount the differential diagnosis of hypersomnolence in the setting of a new neurological finding.
E. Provide the indications for imaging studies in the management of patients with sleep disorders.

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A 64-year-old businessman presents to your office with a sheaf of papers and asks for a second opinion. He was in his previous state of good health until 6 months ago when he started to develop headaches that would awaken him at night. His wife said he had snored all his life, and might have been louder in the past year. He related to being sleepy during the day and attributed it to long working hours. He generally denied neurologic complaints, symptoms of RLS or narcolepsy, or prior head injury or trauma. He was taking Lipitor and aspirin for hypercholesterolemia.

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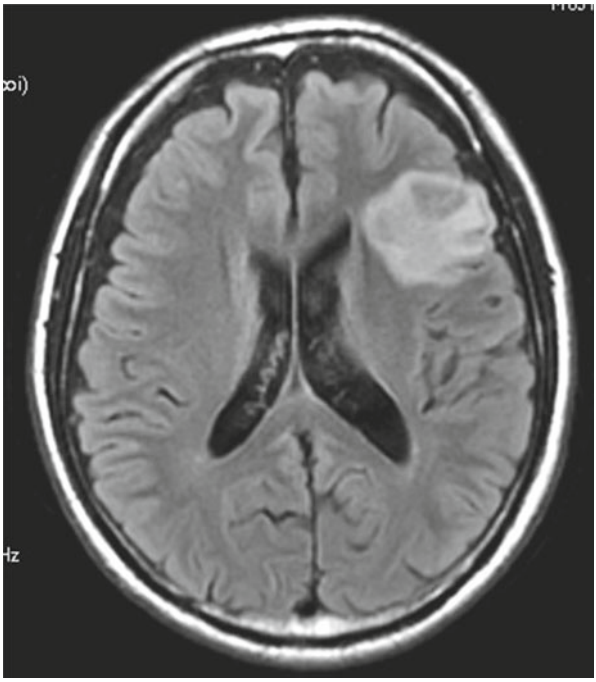

Fig. 8.2 The patient is referred for evaluation by neurosurgery and biopsy reveals a Grade 2 astrocytoma

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Diagnostic Procedures and Interpretation: Handout/Objectives

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E. Provide the indications for imaging studies in the management of patients with sleep disorders.

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Chapter 9
Insomnia

Harneet Walia

Introduction

Insomnia is a highly prevalent sleep problem in the industrialized world. Insomnia is often a persistent condition, with approximately 40 % of individuals reporting insomnia for a year or longer.

It has long been recognized that insomnia is often comorbid with other psychiatric and medical conditions. Not only that, insomnia is a risk factor for subsequent mental disorders such as depression and their persistence. Insomnia has also been demonstrated to be a risk factor for adverse outcomes in depression, such as suicidal ideation in adolescents with depression. The consequences of insomnia varies from impaired quality of life, increased health care costs and utilization and disability. It is as important to focus on the daytime consequences as the nighttime symptoms of insomnia.

The purpose of the following chapter is to serve as a foreground to direct a learning approach to the disorders of sleep onset and maintenance, insomnia upon which a specific skill and knowledge set can be developed in a sleep fellowship program. This may not be as comprehensive as is a textbook chapter; however, these areas touch upon all aspects of practice as well as the basic understanding for insomnia. Insomnia is listed under sleep medicine fellowship program as one of the knowledge-based competencies that the sleep medicine fellows should be well versed with. They should be able to see and evaluate these patients in the sleep clinic and able to determine the type of insomnia.

Treatment strategy for insomnia is based on the type of insomnia. They should be able to implement treatment approaches for insomnia, including cognitive behavioral therapy and pharmacologic therapy and be able to determine the progress of therapy.

H. Walia, M.D. (✉)
Cleveland Clinic Foundation, Sleep Disorders Center, Cleveland Clinic,
9500 Euclid Avenue, Cleveland, OH 44195, USA
e-mail: waliah@ccf.org

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This chapter is based on a competency-based approach. This chapter has various parts to it that will brainstorm the individual in various aspects of insomnia.

In this chapter there are a matching test, essay question, summative essay question, apnea IQ group exercise, case, facilitator guide, final handout, and answers.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/disorders-of-initiation-and-maintenance-of-sleep.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 9.1 Cognitive Map of the Content Domains Relevant to Disorders of Sleep and Maintenance

		Knowledge	Skills	ACGME competency
I.	*Epidemiology* Demographics Risk factors Special populations	Yes	No	B, F
II.	*Mechanisms* Somatic nervous system Autonomic nervous system	Yes	No	A, B
III.	*Risk factors* Psychiatric disorders Genetic Age related Gender	Yes	No	A, B
IV.	*Patient assessments* Adult Special populations	Yes	Yes	A, C, F
V.	*Diagnostic measures and interpretation* History and physical examination Self-administered questionnaires Patient-based testing	Yes	Yes	A, C, F
VI.	*Disease management* Decisions on therapy Type of therapy	Yes	Yes	A, E, D, F
VII.	*Health and disease clinical pathway* Psychiatric disorders Medical comorbidities	Yes	Yes	A, C, F
	Code for ACGME competencies A. Patient care B. Medical knowledge C. Practice-based learning and improvement			D. Interpersonal skills E. Professionalism F. System-based practice

Table 9.2 Examples of Topics with Educational Objectives

I.	*Epidemiology* • Define insomnia • Discuss the prevalence of insomnia • Define acute (adjustment) and chronic insomnia • Discuss the comorbidities that can be associated with insomnia
II.	*Mechanism of the disease* • Propose a mechanism by which hyperarousal leads to insomnia with increase in sympathetic nervous system • Discuss the Spielman model associated with insomnia • Discuss the polysomnography findings that can be seen in a patient with insomnia
III.	*Risk factors* • Discuss some of the genetic risk factors associated with insomnia • Discuss the relationship of the comorbid psychiatric disorders with insomnia
IV.	*Patient assessment* • List elements of the history and physical examination that are important for the diagnosis for insomnia • What is the role of the polysomnography in evaluating insomnia?
V.	*Diagnostic measures and interpretation* • What are the questionnaires that are used to assess the diagnosis and progress of insomnia?
VI.	*Disease management* • What is the mainstay of treatment for insomnia? • Name and explain some of the non-pharmacologic modes of treatment
VII.	*Health and disease clinical pathway* • What are the different classes of the drugs for the treatment of insomnia? Describe the mechanism of action. • What are the AASM guidelines for the treatment of insomnia? • What is the relationship of insomnia and hypertension? • What is the relationship of sleep duration and type 2 diabetes?
VIII.	*System-based practice* • Formulate a plan to enable the primary care physicians to evaluate for insomnia in a regular visit in your institution • Make a plan to implement a group session for treatment of insomnia in your institution

Matching Test

Questions

Therapy directing at unrealistic sleep expectations. ☐
Incongruence of subjective sleep symptoms with the objective evidence of sleep disturbance. ☐
Hypnotic having a short half-life of 1 h. ☐
Hypnotic associated with metallic tastes in the mouth. ☐
Therapy directing at excessive time in bed for insomnia. ☐
Therapy pointing to imprinting bed and bedroom as sleep stimulus. ☐

Insomnia associated with voluntary sleep practices that are inconsistent with good sleep quality and daytime alertness. ☐
Medication associated with decreased REM. ☐
Gene associated with fatal familial insomnia. ☐
Mutation of this gene is associated with circadian rhythm disturbance. ☐
This drug can be associated with priapism. ☐
The essential features of this disorder are heightened arousal and learned sleep-preventing associations. ☐
Hypnotic with anticholinergic side effects. ☐
Drug associated with decreased serum testosterone. ☐
Common cause of insomnia during menopause. ☐
Medication to be considered during insomnia due to menopause. ☐
This questionnaire may be used for screening and to monitor the treatment response. ☐
This can be found in sleep study of insomnia patient. ☐
Antidepressant less likely to increase periodic limb movements. ☐

Answers

1. Psychophysiological insomnia
2. Hyperarousal theory for insomnia
3. Mood disorders
4. Cognitive therapy for insomnia
5. Zaleplon
6. Antihistaminics
7. Ramelteon
8. Sleep restriction
9. Stimulus control
10. Inadequate sleep hygiene
11. Zolpidem
12. Alprazolam
13. Paradoxical intention
14. Insomnia due to medical disorder
15. Per 3 gene
16. BDB9
17. Eszopiclone
18. Chronotherapy
19. Biofeedback
20. Temazepam
21. Diphenhydramine
22. Actigrapy
23. Sleep logs
24. Trazodone
25. Dysfunctional beliefs and attitudes about sleep questionnaire
26. Fatigue Severity Scale
27. Melatonin
28. Restless legs syndrome
29. Advanced sleep phase syndrome
30. Free-running type
31. Pittsburgh Sleep Quality Index
32. Decreased delta EEG activity
33. Ramelteon
34. Flurazepam
35. Behavioral insomnia of childhood
36. Paradoxical insomnia
37. Idiopathic insomnia
38. Hot flashes
39. Selective serotonin reuptake inhibtors
40. Mutation at codon 178 of the prion protein gene
41. Bupropion

Questions with Answers

Therapy directing at unrealistic sleep expectations. 4
Incongruence of subjective sleep symptoms with the objective evidence of sleep disturbance. 36
Hypnotic having a short half-life of 1 h. 5
Hypnotic associated with metallic tastes in the mouth. 17
Therapy directing at excessive time in bed for insomnia. 8
Therapy pointing to imprinting bed and bedroom as sleep stimulus. 9
Insomnia associated with voluntary sleep practices that are inconsistent with good sleep quality and daytime alertness. 10
Medication associated with decreased REM latency. 39
Gene associated with fatal familial insomnia. 40
Mutation of this gene is associated with circadian rhythm disturbance. 15
This drug can be associated with priapism. 24
The essential features of this disorder are heightened arousal and learned sleep-preventing associations. 1
Hypnotic with anticholinergic side effects. 21
Drug associated with decreased serum testosterone. 33
Common cause of insomnia during menopause. 38
Medication to be considered during insomnia due to menopause. 39
This questionnaire may be used for screening and to monitor the treatment response for insomnia. 31
This can be found in sleep study of insomnia patient. 32
Antidepressant less likely to increase periodic limb movements. 41

Essay Questions

Part 1

Joe is an 18-year-old Caucasian male brought in by his mom due to difficulty sleeping. His past medical history is consistent with ADHD, for which he is on adderall with a good control of symptoms. His mom is concerned that he is not able to sleep well; thereby his performance in school has been declining. This problem started about three years ago. He denies any snoring or pauses in breathing. He feels fatigued during the daytime. He denies any excessive daytime sleepiness. There are no symptoms suggestive of cataplexy, hypnagogic, and hypnopompic hallucinations. His sleep timing during the weekday is from 2 a.m. to 7 a.m. and on the weekends is from 2 a.m. to noon. He endorses difficulty falling asleep when he lies down to sleep at 11:00 p.m. It takes him about 2–3 h to fall asleep. He would lie there and when he is unable to sleep would start watching TV. He states that he feels better during the weekends than during the weekdays. His Epworth Sleepiness Scale is 10/24. On physical examination he is alert and oriented. He appears to be uninterested in the conversation. He does not seem to have a good rapport with his mom, and there were instances where mom and son had fallen into an argument as well.

On examination, his blood pressure was 110/78, and heart rate was 110. On his oral examination, he had 2 + tonsils, Mallampati of 2, and tongue appeared normal. His heart and lung exams are unremarkable. His neurologic exam is within normal range.

Questions

1. Based on the history and physical examination, create a differential diagnosis for the patient.
2. What would be the first step in the diagnosis of this patient?
3. What is the likelihood of finding the etiology with the polysomnogram?
4. What is the effect of adderall on sleep?

Answers

1. Differential diagnosis would be sleep-onset insomnia, inadequate sleep hygiene, irregular sleep-wake schedule, insomnia due to medical condition, and circadian rhythm disorder.
2. Insomnia is diagnosed with history and physical examination. According to the ICSD 2 criteria, difficulty sleeping should be associated with sequel. If the circadian rhythm disturbance is suspected such as in this case, one would start off with sleep logs or actigraphy.
3. Polysomnography will have a very low yield in this case. Polysomnography may be indicated when considering a diagnosis of a CRSD to exclude other potential causes for sleep-related complaints. For instance, if there was a high probability of sleep apnea by history and physical exam. If this occurs, PSG is indicated to evaluate and establish appropriate therapy for OSA.
4. Adderall is a dextroamphetamine that is used in ADHD and narcolepsy. Adderall has a stimulating effect and can have the side effect of insomnia.

Part 2

Diagnosis was made based on the sleep logs brought in by the patient. Treatment is recommended for the patient. Patient is agreeable to the treatment.

Questions

1. Describe delayed sleep phase disorder.
2. How would you treat such a patient?
3. What are some of the consequences of delayed sleep phase disorder?

Answers

1. Delayed Sleep Phase Disorder is characterized by sleep wake times being habitually delayed compared to conventional times. Individuals with Delayed Sleep Phase Disorder (DSPD) are often unable to fall asleep until the early morning hours and unable to awaken until late morning or early afternoon. During their preferred sleep schedules, sleep duration and quality are generally normal. However, sleep-onset insomnia and morning sleepiness occur if sleep and waking are attempted at an earlier time. The prevalence is about 7 % in teens and young adults.
2. Properly timed morning light exposure causes a phase advance of sleep-onset time and circadian rhythms and increases daytime alertness. Light therapy can vary from 2500–10,000 lux, 2–3 hours prior to or at the rise time.
3. Delayed sleep phase syndrome has been associated with severe social problems, depression, decreased concentration, and daytime fatigue also higher rate of psychiatric disorders.

Part 3

Questions

1. What are some of the other circadian rhythm disorders that you know of?
2. What is core body temperature minimum and what is its significance in the treatment of the circadian rhythm disorder?
3. What is melatonin? What is its role in the circadian rhythm disorder?

Answers

1. Shift work disorder, advanced sleep phase syndrome, delayed sleep phase syndrome, and jet lag disorder.
2. Core body temp minimum occurs 2–3 h before the habitual wake time. Light given after the core body temp min will advance the rhythm and light administered before the (CBT min) can delay the circadian rhythm.

3. Melatonin is a hormone produced by the pineal gland. Melatonin secretion is high after the onset of darkness and falls before the time of light onset. Melatonin when administered at afternoon or evening can shift the circadian rhythm to an earlier time in DSPD. It should be given 2–6 hours prior to the habitual sleep time.

Part 4

Question

What is chronotherapy?

Answer

Chronotherapy is a behavioral strategy that can be used in patients with circadian rhythm disorders. It refers to the intentional delay of sleep onset by 2–3 h on successive days until the desired bedtime has been achieved. After this, the patient strictly enforces this sleep-wake schedule. Chronotherapy requires close monitoring of schedules.

IQ Case

Insomnia for Student

Case Vignette

Circada Redim is a 39-year-old female referred by her oncologist, Dr. Hauri, for difficulty sleeping. It developed over the past 10 months, after initiation of therapy for breast cancer, and was accompanied by irritability, difficulty concentrating, and fatigue. She notes that it is more difficult to get to sleep and stay asleep than before.

At bedtime, the patient watches "Twilight" and then turns out the light at 11 p.m. but otherwise has no routine for going to bed. Sleep onset is described as taking 1.5 h to get to sleep and being difficult because of "the mind racing." Only occasionally does she have a "good night's sleep." Once asleep she awakens every 1–2 h, sometimes in a sweat, and often taking >30 min to fall back asleep. Her husband states that she does not snore but once a month will talk in her sleep. She awakens and gets up in the morning feeling unrefreshed at 7 a.m. to get the children off to school. She feels tired all day long and loses her concentration more quickly than before. Her ESS is 3/24 and she worries how her lack of sleep will affect her the next day. She feels helpless and cries occasionally by herself or when she talks to her mother about her illness and her life.

She states that as a young mother her sleep was short as she worked a job as well as managed a family and sometimes could not fall asleep if she went to be "early" at 11 p.m. She had read a story in Good Housekeeping about sleep hygiene and it helped her, but she no longer remembers its advice. She slept "well" as a child and in high school and college worked hard into the night. She has no history of exposure to traumatic experiences including sexual abuse nor to industrial waste. She does not smoke cigarettes. She has always drunk coffee and tea and now has increased her intake to "get going in the morning" and "keep going in the afternoon." On the weekends or on visiting her parents, she sleeps in until 10 a.m. and seems to get her "best sleep."

A physical exam was performed.

Vital signs: temp 37.2, RR 12, HR 84, BP 107/56, BMI 23.
Wears a wig to hide hair loss. Mallampati 0. No tonsillar hypertrophy. There is no cervical adenopathy or jugular venous distension on neck exam. The thyroid is palpable.
Normal cardiopulmonary examination.
There are no signs of arthritis nor peripheral edema, skin changes, cyanosis, or clubbing.
The neurologic examination is within normal limits.

On the basis of this history and physical examination, you decide not to order any testing but ask for a sleep diary over the next 2 weeks, and it is faxed to you by the patient. You eyeball the diary and show it to Dr. Broderick who says it looks like "delayed phase."

In the meantime, and at the urging of her husband, she tried Benadryl (50 mg and 100 mg) as well as Tylenol PM, but they "stopped working" after a few days and gave her dry eyes. At an office visit to the oncologist, she was prescribed trazodone (50 mg), and she stopped the drug after three nights as she felt "drugged up." She saw advertisements for a pill and a butterfly and then one for a pill with Abe Lincoln and a beaver. She contacted her primary care physician who sent her a sample and a prescription "to try" before she sees you again.

Ms. Redim returns to see you after 2 months of treatment with Lunesta (2 mg each night). She is taking the therapy as prescribed. The medication has helped her get to sleep, although the cost to her family is $240/month (her husband's insurance policy currently requires him to pay for this drug). She asks if she still needs the medication, but she tried stopping the medication and her sleep difficulties increased. She was told by a friend that she could get "hooked" on sleeping pills. She is asking your advice on improving her sleep without using drugs.

Insomnia for Facilitator

Goal: Identify risks, conditions, and mechanisms associated with abnormal sleep initiation and maintenance; describe its impact on behavior and mood; and list for better or worse the consequences of medical therapy.

Learning Objectives

A. Create a differential diagnosis for insomnia.
B. Name precipitating, perpetuating, and maintaining features for insomnia.
C. Relate the personal and societal cost of insomnia.
D. Correlate the neurophysiology of sleep and wakefulness with the sleep history.
E. Apply the concepts of behavioral therapy for insomnia to its management.
F. Draw relationships between the drugs that treat breast cancer and the development of insomnia.
G. List the consequences of insomnia in behavioral and psychiatric terms.
H. Describe the mechanisms of actions, benefits, and side effects of the following classes of drugs: benzodiazepines, antihistamines, melatonin and melatonin receptor agonists, and trazodone.

Case Vignette

Circada Redim is a 39-year-old female referred by her oncologist, Dr. Hauri, for difficulty sleeping. It developed over the past 10 months, after initiation of therapy for breast cancer, and was accompanied by irritability, difficulty concentrating, and fatigue. She notes that it is more difficult to get to sleep and stay asleep than before.

Executive Summary: This case is designed to introduce the fellow to the general topic of insomnia. It has features in it which relate to epidemiology and societal

impact, pathophysiology, personal impact of health and family, and management decisions. It is a model work-up with clinical issues that often occur. At the end of this session, the group should be able to recognize the generality of this presentation and utilize the approach described in the case vignette in a practice setting. There are two "twists." One is that this patient has breast cancer and with its treatment may be suddenly postmenopausal. The other is the implication that her sleep problems are that of circadian misalignment (delayed phase type).

1. Probing Questions

1. What are the risk factors for poor sleep in this patient?
2. Can sleep problems be classified (acute and chronic)? Does this mean something in regard to severity or prognosis?
3. What is the significance of the diagnosis of breast cancer or its therapy?

Ideal Answers

1. Female, night owl when younger, stress, poor sleep hygiene, and possibly postmenopausal.
2. <2 weeks is acute and >3 months is chronic. Acute is more often self-limiting. In chronic insomnia the model is that there is a predisposing factor, an initiating factor, and a perpetuating factor, and all need to be addressed.
3. Stress, chemotherapy makes the patient suddenly postmenopausal.

At bedtime, the patient watches "Twilight" and then turns out the light at 11 p.m. but otherwise has no routine for going to bed. Sleep onset is described as taking 1.5 h to get to sleep and being difficult because of "the mind racing." Only occasionally does she have a "good night's sleep." Once asleep she awakens every 1–2 h, sometimes in a sweat, and often taking >30 min to fall back asleep. Her husband states that she does not snore but once a month will talk in her sleep. She awakens and gets up in the morning feeling unrefreshed at 7 a.m. to get the children off to school. She feels tired all day long and loses her concentration more quickly than before. Her ESS is 3/24 and she worries how her lack of sleep will affect her the next day. She feels helpless and cries occasionally by herself or when she talks to her mother about her illness and her life.

2. Probing Questions

1. What are the potential environmental features for poor sleep in this case?
2. Why does she wake up in a sweat?
3. What biological changes can explain this?

Ideal Answers

1. TV in the room.
2. Could be postmenopausal, drug, or sleep apnea.
3. Chronic stress increases CRF and creates a neuroexcitatory state. Orexin levels may increase.

She states that as a young mother her sleep was short as she worked a job as well as managed a family and sometimes could not fall asleep if she went to bed "early" at 11 p.m. She had read a story in Good Housekeeping about sleep hygiene, and it helped her but she no longer remembers its advice. She slept "well" as a child and in high school and college worked hard into the night. She has no history of exposure to traumatic experiences including sexual abuse nor to industrial waste. She does not smoke cigarettes. She has always drunk coffee and tea and now has increased her intake to "get going in the morning" and "keep going in the afternoon." On the weekends or on visiting her parents, she sleeps in until 10 a.m. and seems to get her "best sleep."

3. Probing Questions

1. What is sleep hygiene?
2. Why is it important to ask about sleep habits and quality at a younger age? Predisposing factors: "night owl"?
3. What are the diagnostic features and differential diagnosis for insomnia according to ICSD-2 criteria?
4. What is the relationship of trauma to insomnia?
5. Can exposures to toxins induce or create insomnia?

Ideal Answers

1. Various factors that promote or inhibit sleep. Getting ready for sleep.
2. A night owl likes late night while a lark likes the early morning. These are preferences and are called such in the absence of expressed distress.
3. Difficulty in initiation and/or maintenance of sleep, poor sleep satisfaction, and distress about the symptoms of poor sleep.
4. May initiate and perpetuate insomnia and overlap with post-traumatic stress disorder.
5. Mercury and arsenic as toxins, but caffeine is the major culprit and its half-life increases as one gets older.

A physical exam was performed.

Vital signs: temp 37.2, RR 12, HR 84, BP 107/56, BMI 23.

Wears a wig to hide hair loss. Mallampati 0. No tonsillar hypertrophy. There is no cervical adenopathy or jugular venous distension on neck exam. The thyroid is palpable.

Normal cardiopulmonary examination.

There are no signs of arthritis nor peripheral edema, skin changes, cyanosis, or clubbing.

The neurologic examination is within normal limits.

4. Probing Question

Can you list abnormal findings on physical examination in insomnia and explain their pathophysiology?

Ideal Answer

There is evidence for chemotherapy and here it is the absence of physical findings, i.e., no signs for sleep apnea or neurologic disease.

On the basis of this history and physical examination, you decide not to order any testing but ask for a sleep diary over the next 2 weeks, and it is faxed to you by the patient. You eyeball the diary and show it to Dr. Broderick who says it looks like "delayed phase."

5. Probing Questions

1. What does a sleep diary look like that has a "delayed phase"?
2. What is its reliability? Could it define disease severity? What are alternatives to a sleep diary?

Ideal Answers

1. The person goes to bed early, has a long sleep latency, and sleeps in on the weekend feeling better.
2. Could use actigraphy but it is not covered by insurance. Really there are no severity criteria.

In the meantime, and at the urging of her husband, she tried Benadryl (50 mg and 100 mg) as well as Tylenol PM, but they "stopped working" after a few days and gave her dry eyes. At an office visit to the oncologist, she was prescribed trazodone (50 mg), and she stopped the drug after three nights as she felt "drugged up." She saw advertisements for a pill and a butterfly and then one for a pill with Abe Lincoln and a beaver. She contacted her primary care physician who sent her a sample and a prescription "to try" before she sees you again.

6. Probing Questions

1. Why should Benadryl work?
2. Why was trazodone prescribed?
3. What are the classes of drug advertized to the public?
4. What are the implications of samples in the management of insomnia?

Ideal Answers

1. Benadryl is an antihistamine whereas histamine is an alerting agent.
2. Possible depression.
3. Non-benzodiazepines (Ambien and Lunesta) or melatonin agonists (Remeron).
4. Usually the most expensive and newest medication and often not compared to existing therapy.

Ms. Redim returns to see you after 2 months of treatment with Lunesta (2 mg each night). She is taking the therapy as prescribed. The medication has helped her get to sleep, although the cost to her family is $240/month (her husband's insurance policy currently requires him to pay for this drug). She asks if she still needs the

medication, but she tried stopping the medication and her sleep difficulties increased. She was told by a friend that she could get "hooked" on sleeping pills. She asks your advice on improving her sleep without using drugs.

7. Probing Questions

1. What does it mean to "get hooked"? Are sleeping pills addictive? Do they produce withdrawal in a pharmacologic sense?
2. What are the non-pharmacologic approaches to insomnia?
3. What are the pharmacologic approaches to delayed phase insomnia?
4. How should they work on the neurophysiologic factors that produce insomnia in this case?

Ideal Answers

1. Addiction and withdrawal are not properties of sleeping pills in a strict pharmacologic sense, but there are some similarities. When one stops a pill, one gets the poor sleep back and usually one is distressed about the poor sleep and the original problem is amplified. In classic withdrawal there is autonomic excitation (increased heart rate, blood pressure, etc.); in stopping sleeping medications in use today, there is no withdrawal in a classic sense.
2. Cognitive behavioral approaches and sleep hygiene.
3. Melatonin.
4. Inform and create an optimal wake-up time, and use light therapy along with melatonin.

Insomnia: Handout/Objectives

Goal: Identify risks, conditions, and mechanisms associated with abnormal sleep initiation and maintenance; describe its impact on behavior and mood; and list for better or worse the consequences of medical therapy.

Learning Objectives

A. Create a differential diagnosis for insomnia.
B. Name precipitating, perpetuating, and maintaining features for insomnia.
C. Relate the personal and societal cost of insomnia.
D. Correlate the neurophysiology of sleep and wakefulness with the sleep history.
E. Apply the concepts of behavioral therapy for insomnia to its management.
F. Draw relationships between the drugs that treat breast cancer and the development of insomnia.
G. List the consequences of insomnia in behavioral and psychiatric terms.
H. Describe the mechanisms of actions, benefits, and side effects of the following classes of drugs: benzodiazepines, antihistamines, melatonin and melatonin receptor agonists, and trazodone.

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Chapter 10
Circadian Rhythm Sleep Disorders

Hrayr Attarian and Phyllis Zee

Introduction

With the discovery of clock genes and increased knowledge and understanding of how circadian rhythms affect physiological functions, particularly sleep, there has been increased awareness of circadian rhythm sleep disorders. This, in turn, has lead to an increased need for understanding the clinical features, the diagnostic modalities, and treatment approaches of these disorders. Fellowship training in sleep medicine must include an understanding of the circadian rhythm sleep disorders or disorders related to sleep-wake timing. The ACGME requirements for a sleep medicine state that trainees must demonstrate comprehensive knowledge of circadian rhythms, its basic mechanisms and its disorders. In addition trainees must also demonstrate clinical skills required in diagnosing by interpreting diagnostic tools and treating these disorders. In addition, 5 % of the content of ABIM Sleep Medicine Certification deals directly with circadian rhythm sleep disorders or disorders related to sleep-wake timing.

Although the suprachiasmatic nucleus acts as a master timekeeper or an internal clock, each organ and even each cell has its own unique circadian oscillation. Specific genes and the proteins they code for regulate cellular rhythms through a series of both negative and positive feedback loop. In addition to the complex genetics, there are basic physiological mechanisms that govern the circadian

H. Attarian, M.D. (✉)
Department of Neurology, Northwestern University, 710 N Lake Shore Drive, Abbott Hall Suite 1123, Chicago, IL 60611, USA
e-mail: h-attarian@northwestern.edu

P. Zee, M.D., Ph.D.
Center for Sleep and Circadian Biology, Northwestern University Institute for Neuroscience, Chicago, IL, USA

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pattern of sleep-wake cycles. The International Classification of Sleep Disorders, second edition, describes six distinct circadian rhythm sleep disorders with unique features and comorbid conditions. Although the diagnostic and therapeutic tools for these disorders are few and not as well studied, it is essential for a practicing sleep specialist to be familiar with them and know their utility and when and how to use them [1].

We attempt to make the material presented in this chapter compliant with both ACGME and ABIM requirements as both clearly mandate a comprehensive knowledge of these disorders and the mechanisms underlying them.

The chapter is not designed to be an all inclusive review of the literature in this field of study, but rather to highlight knowledge and skills expected to be part of sleep medicine practice and to provide some limited examples of how topics in this area could be taught and assessed. Table 10.1 provides content domains showing how subtopics may be related to the ACGME general competencies. Medical knowledge is the competency most applicable to the topic of disorders related to sleep-wake timing, though there are areas where sleep diaries and other technology, e.g., actigraphy, and patient care can be addressed and assessed. Table 10.2 lists examples of learning objectives that can be formulated and used as the basis for essay questions, journal club discussions, or a lecture.

Intertwined with the content delivery, as organized and discussed above, is the need to assess competency. The matching test is an example of traditional knowledge assessment tools utilizing matching tests to review factual knowledge of circadian rhythm sleep disorders. As more data becomes available in this field, these questions can be modified and additions can be made. Essay questions provide sample essay questions that attempt to assess a more comprehensive understanding of the issue posed. These can be provided as either closed or, if self-directed learning is the goal, open book written questions. However, the most useful method to gauge the learner's comprehension of the topic might be to pose these types of questions as open discussion questions in a one-on-one session. This allows the evaluator to change the direction of the discussion to assess particular subtopics as well as allows the evaluator to judge the learner's ability to "think on their feet."

The IQ cases require the learners to seek, evaluate, and discuss information that they believe will achieve the learning objectives of the case. Group discussions are helpful for the learners in that they can share knowledge and hopefully improve their learning techniques. The IQ cases are probably best used to obtain an overall assessment of where the group or program is in their training. There are inherent limitations to performing individual assessments with this tool.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/circadian-rhythm-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 10.1 Cognitive Map of the Content Domains Relevant to the Circadian Rhythm Sleep Disorders [2]

		Knowledge	Skills	ACGME competency
I.	*Epidemiology*	Yes	No	A, B, F
	Age			
	Risk factors			
	Special populations			
II.	*Mechanisms*	Yes	No	A, B
	Neurophysiology			
	Genetics			
	Psychology and behavior			
III.	*Risk factors*	Yes	No	A, B
	Environmental			
	Genetic			
	Neurodegenerative			
IV.	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatrics			
	Special populations			
V.	*Diagnostic measures and interpretation*	Yes	Yes	A, B, C, F
	Actigraphy			A, B, C
	Biomarkers: DLMO, core body temperature			A, B, C, F
VI.	*Disease management*	Yes	Yes	
	Presentation of therapeutic options			A, B, E, D, F
	Decisions on therapy			A, B, F
	Follow-up			A, D, F
VII.	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Dementia and institutionalized older adults			
	Blindness			
	Adolescent sleep medicine			
	Work environment assessment for shift workers			
	Travel medicine			
	Code for ACGME competencies			
	A. Patient care			D. Interpersonal skills
	B. Medical knowledge			E. Professionalism
	C. Practice-based learning and improvement			F. System-based practice

Table 10.2 Examples of Topics with Educational Objectives

Item I. Genetics
- Describe the genes involved in regulating circadian rhythms
- List the different proteins and their various roles in regulating the clock genes
- Understand the positive and negative feedback loops involved in the regulation at the molecular level
- Become familiar with the terms CLOCK/Bmal1, CRY/PER, CCG panel, casein kinase 1ε, and F-Box

Item II. Anatomy and physiology
- Describe the location and role of the pineal gland, retinohypothalamic tract, and suprachiasmatic nucleus
- Understand the utility of the melatonin and light phase response curves and how to use them to advance or delay the endogenous rhythm
- Understand the meaning of dim light melatonin onset (DLMO) and its clinical utility
- Understand the meaning of circadian time 0 and minimum core body temperature and how to use this knowledge in clinical management of circadian rhythm sleep disorders

Item III. Clinical syndromes
- Describe delayed sleep phase disorder
- Describe advanced sleep phase disorder
- Describe irregular sleep-wake rhythm
- Describe non-24 h sleep-wake disorder
- Describe jet lag disorder
- Describe shift work disorder

Item IV. Diagnostic measures
- Know how to take a circadian rhythm sleep disorder focused history
- Interpret sleep diaries
- Interpret actigraphy
- Know when and how to use salivary melatonin levels

Item V. Therapeutics
- Know the usage of full spectrum of blue wavelength light and the timing of exposure based on the disorder being treated
- Understand the basics of sleep hygiene and its importance in the treatment of these disorders
- Know the different dosages of melatonin and when to use them and their efficacy, short comings, and side effects
- Understand the basics of chronotherapy and how to use them with the different circadian rhythm sleep disorders

Item VI. Prognosis, complications, and comorbid conditions
- Discuss complications of untreated circadian rhythm sleep disorders
- Name the comorbid neurological conditions associated with these conditions
- Know the prognosis of both treated and untreated circadian rhythm sleep disorders
- Understand the limitations of treatment and what happens when treatment is discontinued

Matching Test

Questions

A disorder where the sleep-wake patterns follow a non-24-h period. ☐
The region in the anterior hypothalamus that serves as a circadian pacemaker. ☐
The time when the core body temperature is at its minimum. ☐
One of the primary proteins transcribed by the clock genes and is involved in the positive feedback loop. ☐
An accepted method of assessing for treatment efficacy in circadian rhythm sleep disorders. ☐
A sleep-wake cycle reflecting partial entrainment adopted by night shift workers on their days off to allow for improved alertness and less fatigue on both nights off and nights on. ☐
The primary pathway by which light entrains the sleep-wake cycles by suppressing melatonin secretion. ☐
A biomarker sometimes used in assessing the direction of the sleep phase in certain circadian rhythm sleep disorders. ☐
A subjective scale designed to assess the circadian tendency of the sleep and wake times of an individual. ☐
The primary therapeutic modality of most circadian rhythm sleep disorders. ☐
Where melatonin is secreted. ☐
External cues such as light, timing of meals, and certain sounds that entrain the circadian rhythms. ☐
The ability of a therapeutic agent to change the circadian phase of an individual. ☐
The primary melatonin receptor found in the suprachiasmatic nucleus. ☐
A wake-promoting agent often used as an adjunct therapeutic modality in shift work disorder ☐
When melatonin levels start rising in response to dim light, a measurement often used as a circadian phase marker. ☐
A melatonin receptor agonist approved as a sedative hypnotic but also possesses phase-shifting effect. ☐
One of the clock genes that regulate circadian rhythmicity at the cellular level. ☐
A therapeutic modality for circadian rhythm sleep disorders that involves delaying or advancing bedtime and risetime by an hour or two every day until desired times are achieved. ☐
A circadian rhythm sleep disorder caused by travelling across multiple time zones. ☐

Answers

1. 6-hydroxymelatonin sulfate
2. Actigraphy
3. Anterior hypothalamus
4. Armodafinil
5. BMAL1
6. Bright light therapy
7. Caffeine
8. Chronobiology
9. Chronotherapy
10. Chronotype
11. Circadian rhythm sleep disorder, irregular sleep-wake type
12. Circadian rhythm sleep disorder, advanced sleep phase type
13. Circadian rhythm sleep disorder, delayed sleep phase type
14. Circadian rhythm sleep disorder, jet lag type
15. Circadian rhythm sleep disorder, nonentrained type
16. Circadian rhythm sleep disorder, shift work type
17. Circadian time 0
18. Clock
19. Compromise phase position
20. Core body temperature
21. Cry
22. Daytime social activities
23. Dim light melatonin onset
24. Ganglion cell layer
26. Light phase response curve
25. Light phase response curve
27. Lux
28. Melanopsin
29. Melatonin
30. Melatonin receptor 1A
31. Melatonin receptor 1B
32. Misalignment of circadian rhythm
33. Modafinil
34. Morningness-Eveningness Questionnaire
35. Munich Chronotype Questionnaire
36. Pacemaker
37. PER
38. Phase-shifting effect
39. Phase response curve for melatonin
40. Pineal gland
41. Ramelteon
42. Retinohypothalamic tract
43. Sedative hypnotic
44. Sleep diaries
45. Superior cervical ganglion
46. Suprachiasmatic nucleus
47. Tau
48. TBBim
49. Vasoactive intestinal peptide
50. Vasopressin
51. Zeitgeber

Questions with Answers

A disorder where the sleep-wake patterns follow a non-24-h period. 15
The region in the anterior hypothalamus that serves as the circadian pacemaker. 45
The time when the core body temperature is at its minimum. 17
One of the primary proteins transcribed by the clock genes and is involved in the positive feedback loop. 5
An accepted method of assessing for treatment efficacy in circadian rhythm sleep disorders. 2
A sleep-wake cycle reflecting partial entrainment adopted by night shift workers on their days off to allow for improved alertness and less fatigue on both nights off and nights on. 19
The primary pathway by which light entrains the sleep-wake cycles by suppressing melatonin secretion. 41
A biomarker sometimes used in assessing the direction of the sleep phase in certain circadian rhythm sleep disorders. 20
A subjective scale designed to assess the circadian tendency of the sleep and wake times of an individual. 33
The primary therapeutic modality of most circadian rhythm sleep disorders. 6
Where melatonin is secreted. 39
External cues such as light, timing of meals, and certain sounds that entrain the circadian rhythms. 50
The ability of a therapeutic agent to change the circadian phase of an individual. 37
The primary melatonin receptor found in the suprachiasmatic nucleus. 29
A wake-promoting agent often used as an adjunct therapeutic modality in shift work disorder. 32
When melatonin levels start rising in response to dim light, a measurement often used as a circadian phase marker. 23
A melatonin receptor agonist approved as a sedative hypnotic but also possesses phase-shifting effect. 40
One of the clock genes that regulate circadian rhythmicity at the cellular level. 21
A therapeutic modality for circadian rhythm sleep disorders that involves delaying or advancing bedtime and risetime by an hour or two every day until desired times are achieved. 9
A circadian rhythm sleep disorder caused by travelling across multiple time zones. 14

Essay Questions

Case Study 1. Delayed Sleep Phase Disorder

An 18-year-old male presents with the complaint of nightly difficulty falling asleep that started 4 years ago but over the past 2 years has worsened. His bedtime on school days is 9:30–10:00 p.m. and he cannot fall asleep until around 2 a.m.; he gets up in the morning with extreme difficulty between 6:00 and 6:30 a.m. He has no problem staying asleep. He is unable to pay attention in morning classes and has been in trouble with the teachers for falling asleep in class. On weekends he goes to bed at 1:00–1:30 a.m. and it can take him up to ½ h to fall asleep; he tends to sleep in until about noon. He feels better after awakening on weekends and no longer falls asleep during the day. His Epworth Sleepiness Scale (ESS) score is 8 on Sunday and 16 on Friday (normal score is 0–10, and the range is 0–24).

Questions

1. What is the most likely diagnosis?
2. What time would bright light exposure be effective initially in advancing his phase?
3. When should melatonin (not FDA approved) be given?
4. What is the long-term effectiveness of exogenous melatonin?

Answers

1. Delayed sleep phase disorder: Patients with delayed sleep phase cannot fall asleep before 2 a.m. and if circumstances allow sleep in till late morning/early afternoon. Their biological rhythms and major sleep timing are all delayed, but they are in phase with each other much like healthy controls. They complain of sleep-onset insomnia and daytime sleepiness due to sleep deprivation only if they are forced to conform to societal schedules.
2. Around 9–10 a.m. shortly after his nadir of the circadian core body temperature rhythm. If done earlier than the nadir core body temperature, it may delay him further.
3. Melatonin 0.5–5 mg given 5–6.5 h prior to the individual DLMO results in the largest phase advance.
4. Exogenous melatonin has shown long-term sustained effectiveness in most DSPD subjects, but relapse occurs after discontinuation and can be immediate and severe in some cases.

Case Study 2. Shift Work

A 32-year-old nurse complains of fatigue and difficulty keeping up with her duties since starting her current job 4 months ago. She works 12-h nights (7 p.m.–7 a.m.)

for 3 consecutive days and has 4 days off. She has no problem falling asleep when she gets home at 8 a.m. but cannot sleep past 11 a.m. and then is dozing on and off till 1 p.m. She tries to nap at 5 p.m. but is not always successful in sleeping more than 15–20 min. When she gets to work, she feels sleepy and has decreased concentration, especially the last 4 h of the shift. She consumes large amounts of caffeine and sugar to help her stay awake at work. She describes malaise, anxiety, and decreased libido that persist even on her days off. On the first day she is off, she sleeps from 8 to 11 a.m. and then again from 8 p.m. to 6 a.m. The following days she sleeps according to her "old normal" schedule from 11 p.m. to 7 a.m. On the first day of her shift, she takes a brief nap around 4 p.m. She also has gained 20 lbs since taking this new position. She tried using over-the-counter sleep aids during the day to help her sleep, but they only worked for 2 days. She is also concerned about the risk of breast cancer that she has heard is high in women who work night shift.

Questions

1. Is there validity to her concern about breast cancer risk?
2. What is the proposed mechanism of the association of breast cancer risk and shift work?
3. How would taking melatonin supplements impact her symptoms and concerns?

Answers

1. Several studies have shown that the risk of breast cancer is elevated in women who work the night shift and is even more increased in those who primarily work night shift with an occasional day/night swing shifts. The longer the duration of night work, the higher is the risk as studies with nurses working over 30 years of night shift have demonstrated. Various studies have shown odds ratios (OR) of 1.5–2.2 with 95 % confidence interval (CI).
2. One proposed mechanism involves nighttime light exposure and decreases in melatonin, a circadian rhythmic hormone. Decreased melatonin leads to elevated levels of FSH and LH which in turn can impact breast cancer risk. Interestingly melatonin levels stay low even when a night shift worker sleeps at night.
3. There is no evidence yet that melatonin supplementation reverses the risk of breast cancer, and different doses of melatonin taken immediately before bed or 30 min before desired bedtime improved daytime sleep significantly, both in quality and duration, compared to placebo in some but not all subjects. They did not, however, have an impact on nighttime alertness

IQ Case

Evaluation of Circadian Rhythm Sleep Disorders for Student

Case Vignette

A 30-year-old man is self-referred to the sleep clinic because since age 23 he has been unable to fall asleep at the same time every night and wake up at the same time every morning. This irregular sleep pattern has made it difficult for him to hold a job. On some days he is able to fall asleep late evening and wake up 8–9 h later refreshed, but this lasts a short period of a few days before it becomes progressively more difficult for him to fall asleep when he needs to and subsequently get up when he needs to. There are days where he is sleeping during the daytime hours and awake at nighttime. He is currently somewhat tired and his Epworth Sleepiness Scale is 13 as he has been falling asleep 2–3 a.m. and waking up around 8–9 a.m. He is physically fit with no other medical problems or sleep-related symptoms except for mild snoring.

An overnight PSG is done and it is normal.

The patient is diagnosed with free-running-type circadian sleep disorder.

Treatment is initiated and the patient is doing reasonably well on it and is able to maintain employment.

Evaluation of Circadian Rhythm Sleep Disorders for Facilitator

Goal: Understand the tools available for the evaluation of circadian rhythm sleep disorders and how to interpret them.

Objectives

A. Describe the different circadian rhythm sleep disorders.
B. Interpret actigraphy.
C. Discuss the clinical presentation of different circadian rhythm sleep disorders.
D. Describe the impact of CRSD on the patient's quality of life.
E. Propose a diagnostic plan to properly assess the timing of circadian rhythms.

Case Vignette

A 30-year-old man is self-referred to the sleep clinic because since age 23 he has been unable to fall asleep at the same time every night and wake up at the same time every morning. This irregular sleep pattern has made it difficult for him to hold a job. On some days he is able to fall asleep late evening and wake up 8–9 h later refreshed, but this lasts a short period of a few days before it becomes progressively

more difficult for him to fall asleep when he needs to and subsequently get up when he needs to. There are days where he is sleeping during the daytime hours and awake at nighttime. He is currently somewhat tired and his Epworth Sleepiness Scale is 13 as he has been falling asleep 2–3 a.m. and waking up around 8–9 a.m. He is physically fit with no other medical problems or sleep-related symptoms except for mild but snoring.

Probing Questions

1. What kind of circadian rhythm sleep disorder is most likely?
2. What conditions may predispose to this disorder?
3. What complications may arise from this if left untreated?
4. How would you proceed with a diagnostic plan?

An overnight PSG is done and it is normal. His sleep logs and actigraphy results are given below.

Probing Questions

5. What do the actigraphy and sleep logs show?
6. What is your diagnosis based on the actigraphy and sleep logs?
7. What is the concordance between sleep logs and actigraphy?

The patient is diagnosed with free-running-type circadian sleep disorder.

Probing Questions

8. What can you tell the patient about the chance of his children developing this type of irregular sleep pattern?
9. What is the chance of successful treatment?
10. How can you reduce the chance of other sleep and psychiatric disorders from developing?

Treatment is initiated and the patient is doing reasonably well on it and is able to maintain employment.

Probing Questions

11. What is the long-term efficacy of treatment?
12. What other circadian rhythm sleep disorders can you name?

Evaluation of Circadian Rhythm Sleep Disorders: Handout/Objectives

Goal

Understand the tools available for the evaluation of circadian rhythm sleep disorders and how to interpret them.

Objectives

A. Describe the different circadian rhythm sleep disorders.
B. Interpret actigraphy.
C. Discuss the clinical presentation of different circadian rhythm sleep disorders.
D. Describe the impact of CRSD on the patient's quality of life.
E. Propose a diagnostic plan to properly assess the timing of circadian rhythms.

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Chapter 11
Hypersomnolence

Fang Han, Xiao Song Dong, and Han Yan

Introduction

Over the last 15–20 years, there has been rapid advancement in our understanding of sleep physiology and pathophysiology. The foundation is now in place such that training in Sleep Medicine must include an appreciation of disorders of excessive sleepiness, also called hypersomnia, in terms not only of epidemiology and clinical management but also of pathophysiology and pharmacology. In the ACGME requirements for the content of a Sleep Medicine Fellowship, this is most clearly stated in the medical knowledge competency, though elements of this topic can be found in other competencies as well. In addition, 8–10 % of the content of Sleep Medicine Certification examinations, regardless of the board offering the examination (i.e., http://www.abim.org/pdf/blueprint/sleep_cert.pdf: last accessed 2/22/12), deals directly with disorders of hypersomnolence.

Being "so sleepy that one can hardly keep their eyes open" is a common condition in everyday life, most often associated with sleep loss or deprivation. It is said that the countries with the "sleepiest" people are Japan, China, and Korea, and this is ascribed to behavioral factors, long commuting times, and acceptance of sleepiness. The subjective complaint is not linearly related to sleep loss but rather is attenuated by chronic sleep deprivation, so that some can report feeling "fully alert" only to be found to enter electrophysiologically defined slow-wave sleep some 30–45 s later. This mismatch between subjective and objective sleepiness not only leads to problems of fall-asleep moments but also confounds clinicians who find the patient relatively normal at the time of examination. Further the common knowledge that one can just recover with "extra sleep" is not the experience of those patients with intrinsic disorders of the sleep-wake cycle like those with narcolepsy. Hence, in the

F. Han, M.D. (✉) • X.S. Dong, M.D. • H. Yan, M.D.
Department of Pulmonary Medicine, Peking University People's Hospital, Beijing, China
e-mail: hanfang6812@163.com

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evaluation of the patients whose major complaint is excessive daytime sleepiness, features of average sleep time, chronicity, effectiveness of napping, etc. are important to document (see Chapter on Physical Examination, Chap. 7).

For this chapter, the competency examples using a list of objectives and the assessments were developed through review of existing literature in the fields of interest, discussion with faculty and fellows, and examination of the ACGME requirements. This chapter will focus on the primary and secondary hypersomnias with some idea on how patients are assessed [1].

The chapter will emphasize information expected to be part of a sleep practitioner's knowledge base. It will provide specific examples of how topics in this area could be taught and then assessed for competency. Table 11.1 provides a map of chapter content related to the ACGME general competencies for training in Sleep Medicine. Table 11.2 lists examples of content-specific questions from which learning objectives can be formulated. These are only examples, and perhaps for some programs, these examples do not have enough depth or breadth. Any topics could form the basis for development of essay questions, for identification of a journal club article, or for a lecture on the particular issue raised by the question. The goal is to provide standardized content from which the program can foster self-learning and formatively evaluate the learner's knowledge through follow-up on the topic.

This chapter provides specific examples of how this can be accomplished. The matching test is an example of traditional knowledge assessment tools utilizing matching tests to review factual knowledge. As more data becomes available in this field, questions can be modified and additions can be made. Again this is only an example.

Essay questions attempt to assess comprehensive understanding of an issue through a written response. These can be provided as in either a closed or, if self-directed learning is the goal, open book session. However, the most useful method to gauge the learner's comprehension of the topic might be to pose these types of questions as open discussion questions in a one-on-one session. This allows the evaluator to change the direction of the discussion to assess particular subtopics as well as allows the evaluator to judge the learner's ability to "think on their feet." If provided as true essay questions, besides content, the program can evaluate how well the trainee can put their thoughts on paper, including logic and grammar, and thus assess and develop some writing skills beyond that of a patient note and more general than an academic report.

The IQ case offers an example of group learning for fellows to seek and evaluate information that they believe will achieve the learning objectives of the case. These group discussions are helpful for the learners in that they can share knowledge and hopefully improve their learning techniques. There are inherent limitations to performing individual assessments of knowledge or skills with this tool; however, the purpose is to assess and hopefully encourage individual learning beyond the scheduled lecture environment.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/hypersomnolence.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 11.1 Content Domains Relevant to Disorders of Hypersomnolence

		Knowledge	Skills	ACGME competency
I.	*Epidemiology* Demographic Special populations	Yes	No	B, F
II.	*Mechanisms* Acquired Immunology Genetic	Yes	No	A, B
III.	*Risk factors* Trauma Gender Age related Medications	Yes	No	A, B
IV.	*Patient assessments* Adult Children Special populations	Yes	Yes	A, C, F
V.	*Diagnostic measures and interpretation* History and physical examination MSLT, MWT, actigraphy	Yes	Yes	A, C, F
VI.	*Disease management* Decisions on therapy Type of therapy	Yes	Yes	A, E, D, F
VII.	*Health and disease clinical pathway* Psychiatric disorders Medical conditions	Yes	Yes	A, C, F
Code for ACGME competencies				
A. Patient care		D. Interpersonal skills		
B. Medical knowledge		E. Professionalism		
C. Practice-based learning and improvement		F. System-based practice		

Table 11.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
- Compare the epidemiology of narcolepsy with that of Kleine-Levin syndrome
- Describe everyday factors in human behavior that lead to excessive daytime sleepiness in otherwise healthy subjects

Item II. Mechanisms of health and disease
- Suggest a pathophysiology for the induction of narcolepsy with cataplexy
- Draw the anatomy of the sleep-wake functions of the hypothalamus
- Describe how autonomic function is alerted by hypersomnolence in narcolepsy, sleep loss, and sleep apnea
- Discus factors that lead to cataplexy and its treatment
- Make a table of the actions of medications that treat hypersomnolence disorders

(continued)

Item III. Risk factors
- Give three examples of primary and three examples of secondary causes of hypersomnolence
- Describe how environmental factors play a role in the presentation of excessive daytime sleepiness
- Discuss how long-term severe sleep loss alters immune function in animal models

Item IV. Patient assessments
- Describe the effect of sleepiness on driving risk and its assessment in a patient
- Differentiate the effects on sleepiness of experimental sleep deprivation including selective sleep state loss (NREM vs. REM)

Item V. Diagnostic measures and interpretation
- Propose mechanisms for SOREMS in comparison to REM onset during a PSG
- Compare CNS areas of activity and inactivity in hypersomnolence
- Describe the appropriate use of MSLT and MWT
- Describe pretest probability and posttest uncertainty for MSLT in the assessment of excessive daytime sleepiness
- Discuss how you would utilize actigraphy to assess sleepiness in adolescents

Item VI. Disease management
- Discuss the impact of sleep stage progressions in recovery from chronic sleep loss to that of narcolepsy
- Describe the expected time course of improvement of sleepiness with CPAP therapy for OSA
- Compare and contrast the approaches for hypersomnia
  - Behavioral
  - Medical
  - Pharmacologic therapy
- Imagine novel approaches

Item VII. Health and disease clinical pathways
- Propose a collaboration pathway in managing Kleine-Levin syndrome with a general pediatrician
- Compare the effectiveness of stimulants in narcolepsy with narcolepsy without cataplexy
- Describe the principles in the initiation of stimulants for hypersomnia
- Now that a patient has responded to therapy, list the factors for management of narcolepsy as a chronic disease
- List patient expectations vs. physician objectives in terms of outcomes

Matching Test

Questions

Remitting and relapsing hypersomnolence. ☐

Serum markers for hypersomnolence and stupor more often found in association with liver disease. ☐

Hypersomnolence lasting >2 weeks associated with HCG levels. ☐

Hypersomnolence associated with head trauma ICSD-2 code. ☐
A need for >10 h of sleep/day. ☐
Refreshing sleep with recurrent hypersomnia within 1–2 h. ☐
Sleepiness associated with monthly cycles in women. ☐
Low CSF levels in those with hypersomnolence with cataplexy. ☐
A symptom to elicit in the setting of recurrent syncope. ☐
Salt of gamma-hydroxybutyrate (GBH) with a short half-life. ☐
Blocks monoamine uptake at doses lower than amphetamines. ☐
ICSD stands for. ☐
A common cause for secondary narcolepsy often presenting with fatigue. ☐
HLA marker associated with narcolepsy with cataplexy but present in ~30 % of the healthy population. ☐
Objective measure of sleep-wake and activity profiles over time. ☐
Elevated in the hypersomnolence with acute viral illness. ☐
Downregulated by the lack of orexin in narcolepsy with cataplexy. ☐
Medical disorder commonly found in adult narcoleptics. ☐
Described the first case of Kleine-Levin syndrome. ☐
Besides sleepiness, cataplexy, hypnagogic hallucinations, and sleep paralysis, the fifth feature in narcolepsy is…. ☐
Encephalitis lethargica or "sleepy sickness" was his observation. ☐
First to recognize the clinical syndromic nature of narcolepsy with cataplexy. ☐
Increases activity of the phosphoinositol cycle via an indirect release of dopamine and norepinephrine. ☐

Answers

1. Actigraphy
2. Automatic behavior
3. Bradykinin
4. Bradykinin
5. Brierre de Boismont
6. Cataplexy
7. Catathrenia
8. Central sleep apnea
9. Chronic fatigue syndrome
10. Chronic sleep deprivation
11. Coffin-Lowry syndrome
12. Constantin Freiherr von Economo
13. Depression
14. Dextroamphetamine
15. Diabetes type I
16. Diabetes type II
17. DQB1*0601
18. DQB1*0602
19. Endozepines
20. Epworth Sleepiness Scale
21. Fatigue
22. Fluoxetine
23. Hyperphagia
24. Hypersomnia of pregnancy
25. Hypersomnia secondary to medical condition, drug, or substance
26. Hypocretin/orexin
27. Hypothyroidism
28. Idiopathic hypersomnia with long sleep time
29. Idiopathic hypersomnia without long sleep time
30. Insomnia or difficulty in maintaining sleep
31. Insufficient sleep
32. Interleukin 6 (IL-6)
33. International classification of sleep disorders
34. Jean-Baptiste-Édouard Gélineau
35. Kleine-Levin syndrome
36. Maintenance of wakefulness test (MWT)
37. Max Levin
38. Menstruation-related hypersomnia
39. Metabolic rate
40. Methylphenidate
41. Myotonic dystrophy
42. Narcolepsy with cataplexy
43. Narcolepsy without cataplexy
44. Niemann-Pick type C
45. Obstructive sleep apnea
46. Parkinson's disease
47. Physiological (organic) hypersomnia, not otherwise specified
48. Polysomnogram followed by an MSLT
49. Prader-Willi syndrome
50. Psychomotor vigilance testing (PVT)
51. Sarcoidosis
52. Sleep diary
53. Sleep paralysis
54. Sodium oxybate
55. SOREM
56. Stanford Sleepiness Scale
57. Stroke
58. Tumor necrosis factor
59. Urinary drug screening
60. Venlafaxine
61. Willi Kleine

Questions with Answers

Remitting and relapsing hypersomnolence. 35
Serum markers for hypersomnolence and stupor more often found in association with liver disease. 19
Hypersomnolence lasting >2 weeks associated with HCG levels. 24
Hypersomnolence associated with head trauma ICSD-2 code. 25
A need for >10 h of sleep/day. 28
Refreshing sleep with recurrent hypersomnia within 1–2 h. 47
Sleepiness associated with monthly cycles in women. 38
Low CSF levels in those with hypersomnolence with cataplexy. 42
A symptom to elicit in the setting of recurrent syncope. 2
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ICSD stands for. 33
A common cause for secondary narcolepsy often presenting with fatigue. 51
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Besides sleepiness, cataplexy, hypnagogic hallucinations, and sleep paralysis, the fifth feature in narcolepsy is…. 30
Encephalitis lethargica or "sleepy sickness" was his observation. 12
First to recognize the clinical syndromic nature of narcolepsy with cataplexy. 34
Increases activity of the phosphoinositol cycle via an indirect release of dopamine and norepinephrine. 14

Essay Questions

Case Study #1

A 54-year-old milk truck driver has been managed by his primary care doctor and referred for residual sleepiness on therapy for sleep apnea. Two years ago he presented with moderate OSAHS (AHI 16/h with the percent time less than 90 % of 20 %) initially suspected because of snoring and excessive daytime sleepiness (ESS 16) and over the past 2 years has undergone 2 titration nights, leading to the conclusion that BiPaP 12/6 cm H_2O is appropriate and reduced the AHI to <5 and kept oxygen saturation >90 % in REM supine; he has excellent compliance. He has mild COPD (FVC 90 % and FEV1 66 % of predicted), but no other known neurological or medical disease. He takes no medications. He awakens for work at 3 a.m., and his workday finishes at 2 p.m. His usual bedtime is 9 p.m. (5.5 h of sleep at night and a nap of 2 h in the afternoon after a workday). The ESS now is 14/24. He has trouble later in the morning with drowsy driving and has to keep busy. There have been no crashes or near misses. According to his bed partner, he has no unusual behaviors while he is sleeping, including snoring or sleep talking or physically dreaming. On physical examination his blood pressure is 130/82, pulse 66, BMI 30, and baseline oximetry 93 %. The pharynx is crowded (Mallampati 3), but otherwise the physical examination including the neurological examination is normal.

A PSG and MSLT to objectively document sleepiness were performed and adjusted for the patient's usual bedtime and awakening. The results showed he slept from ~9 p.m. to 4 a.m. (~7 h) with all stages of sleep, a sleep latency of 8 min and a REM latency of 119 min. The AHI was 6/h on his therapeutic bilevel setting, and in the 5 naps the mean sleep latency was 9.5 min with one SOREM on nap 1.

Questions

1. Create a differential diagnosis for sleepiness in this patient and include pertinent negatives.
2. What are potential mechanisms that link residual sleepiness to prior sleep apnea and what might be the treatment?
3. What are the important features to note in the PSG prior an MSLT?
4. What would be the day times planned for a 5-nap MSLT in this patient?

Ideal Answers

1. In a patient referred for evaluation of sleepiness after treatment of OSA, sleepiness risks are evaluated in a manner much like another patient, provided there is strong evidence for adequate use of therapy. An exhaustive sleep history will be needed.
2. Studies in animal models have shown that severe episodic hypoxemia over time leads to frontal lobe damage that appears irreversible at 3 months. Studies suggest that ~35 % of patients have documented residual sleepiness despite acceptable

pressure therapy for sleep apnea and presumably adequate sleep. Double-blind controlled studies have shown that a class of stimulants (modafinil or armodafinil) will reduce sleepiness, and there is FDA approval for their use in sleep apnea.
3. The polysomnogram prior to an MSLT is to assure that there is sufficient sleep (arbitrarily set at 6 h) and a lack of "significant" sleep disturbances, such as an AHI >10 or PLMD arousal index >15, that might lead to an abnormal but false-negative result for an MSLT. In addition, the presence of a REM latency <40 min on the prior MSLT is another clue relevant to narcolepsy.
4. The first nap starts 2 h after awakening (6 a.m.) and then every 2 h for a maximum of 5 naps. If two or more SOREMS are present in the first 4 naps, a fifth nap can be cancelled. A pattern of a SOREM on the first nap is a clue to the presence of a delayed sleep phase syndrome or insufficient sleep.

Case Study #2

This 21-year-old male student has a 3-year history of daytime sleepiness, and the consult request is "rule out OSA." He snores but without witnessed apneas. He has occasional episodes of sleep paralysis in which he cannot move for about a minute after awakening. He typically goes to bed at 11:30 p.m. on weekdays and 1 a.m. on weekends. He has fitful sleep. He falls asleep easily, awakens around 7 a.m. on weekdays and 11 a.m. on weekends. He falls asleep in morning and evening classes. There are times when he gets home without remembering stopping at stoplights and times when he does the dishes without remembering how. His medical history includes a flu-like syndrome in the H1N1 epidemic of 2009, 4 years ago. He drinks caffeinated drinks all day long. Upon examination he has a BMI 29, a Mallampati of 2, and 2+ tonsillar hypertrophy.

Questions (2–3 Sentences for Each)

1. What is the most appropriate next step for this patient?
2. What is the most specific symptom to distinguish pathologic from physiological sleepiness?
3. What is the significance of eliciting a history of H1N1 infection?
4. When would you collect a CSF sample for orexin?

Ideal Answers

1. While one can consider thyroid function tests, sleep extension, and blood work, the symptoms are consistent with either sleep apnea or a hypersomnolence syndrome. A PSG is followed by an MSLT, if the patient has an AHI <10 during at least 6 h of sleep the prior night. At the same time there could be a drug screen, which is either done as part of a written, prior protocol for MSLT or after informing the patient of its need.

2. The most specific symptom is cataplexy. Sleep paralysis, automatic behavior, poor sleep (whatever that is), and excessive sleepiness can be seen in those with sleep restriction due to employment, shift work, or lifestyle.
3. H1N1 epidemics and some adjuvant virus vaccines have been associated with a spike in cases of narcolepsy with cataplexy. This and an association with HLA markers appear to indicate that narcolepsy has the features of an autoimmune disorder. The genetic risk of children getting the condition with a parent with narcolepsy is ~1 %.
4. 99% of narcolepsy with cataplexy and HLADQB1 *0602 positivity have very low (<20 pg/ml with normal being >110 pg/ml) levels of CSF orexin, so that if cataplexy is present there is no need. However, if the patient does not have cataplexy or cannot be taken off antidepressants or potentially has a secondary cause for narcolepsy without cataplexy, CSF orexin levels can be very helpful.

IQ Case

Hypersomnia for Student

Goal: Describe the required clinical history and risk factors, work-up, rationale for diagnostic testing, and long-term management of excessive daytime sleepiness in an adult patient.

Case Vignette

A 28-year-old woman from a rural community is referred to the sleep clinic from the rheumatology clinic. The patient was noted to fall asleep during the follow-up visits for suspected chronic fatigue syndrome even before starting a trial of Lyrica. Sleepiness has been present since age 18. When asked for details, the patient reported having drop attacks when she was a teenager and was evaluated for syncope by a cardiologist. She reports doing the dishes or washing clothes and not remembering how she did it. Asked about her most unusual experience, she stated that when she walked to her mother's house in the woods 1 day, a skunk surprised her and she fell down, unable to move, and watched the skunk come up to her and then walk away; she recovered fully in a minute or so.

The ESS is 17/24. The patient has been working 6–8 h/day in a dress shop where she can take frequent naps and drinking a lot of caffeine.

Her average sleep duration is 5–6 h per night, with frequent awakenings and annoying dreams. On 4–5 occasions she has awakened feeling that she cannot move, a sensation lasting 20 s or so. She denies witnessed apneas, RLS symptoms, and interference with her sleep by pets, children, or phone calls.

The patient has past history of one nonidentical twin pregnancy (one boy and one girl) during which the sleepiness became more severe, but no other medical diseases, social vices, or head trauma. The patient's family history is significant for a cousin with sleepiness who had to stop working because of drowsy accidents.

On examination, the vital signs are normal other than for a BMI of 24. The pulmonary and cardiovascular examinations are normal. The neurological examination reveals a normal affect, normal motor and sensory functions, and pupillary instability.

You contact the rheumatologist and you agree to stop the Lyrica for 2 weeks to permit testing of sleep and objective testing of sleepiness. The patient is sent for a PSG with the instructions to do an MSLT if in the PSG the AHI is <10/h. She is also instructed to keep a sleep diary for 2 weeks before the PSG and 1 week after.

The nocturnal PSG results showed she slept ~9:30p.m. to 6a.m with all stages of sleep, a sleep latency of 5 min, s REM latency of 49 min, and an AHI of 3/h.

For the MSLT, you calculate the mean sleep latency of 6 min with three SOREMs.

The patient returns to the clinic where you tell her that the testing is consistent for narcolepsy. Upon further questioning she remembers that she has to control herself from weakness attacks if someone tells a funny joke. She recalls that this

happens about once a week or so and consists of dropping a spoon or a droop of her head for 10–20 s.

The patient mentions to you that her father used to have sleepiness. He was a thin man. She asks if this disorder is one that can be passed along to her twins.

She asks for advice regarding treatment and how to talk to her employers about her condition.

You send your report to the referring physician (a rheumatologist) who still insists that the patient has chronic fatigue syndrome. He states that both CFS and narcolepsy are based on symptom reports and exclusionary and correlative data, rather than an objective measure of the disease. He asks why you are so sure. You state that one can measure CSF levels to be sure of the diagnosis, and you investigate that possibility.

The patient comes back 6 months later. She feels generally OK with her sleepiness on modafinil (200 mg BID) and can work. Based on your prior questions, she notices that "drop attacks" occur about 5–6 times a week and usually are not intense or controllable. You conclude that she has narcolepsy with cataplexy. She asks if there are options for treatment of this cataplexy.

She told her supervisor about her illness and feels as if she is being scrutinized more than others. For instance, she naps on her break 2–3 times a week, and now it is noticed. Others nap but they laugh it off as "insufficient sleep." She asks about her future with the disease and will it get better or worse. She seeks your advice about employment and asks whether she is disabled.

Hypersomnia for Facilitator

Goal: Describe the required clinical history and risk factors, work-up, rationale for diagnostic testing, and long-term management of excessive daytime sleepiness in an adult patient.

Objectives (Revealed at the End of the Session)

A. List the most common and specific symptoms for hypersomnolence not caused by sleep restriction or sleep apnea.
B. Recount the recommended steps needed for the optimal performance of an MSLT.
C. Explain the pharmacology of treatments for narcolepsy.
D. What pathophysiological markers are used to indicate the presence of narcolepsy with or without cataplexy?
E. Describe the societal and employment dimensions in a patient living with a diagnosis of narcolepsy.

Case Vignette

A 28-year-old woman from a rural community is referred to the sleep clinic from the rheumatology clinic. The patient was noted to fall asleep during the follow-up

visits for suspected chronic fatigue syndrome even before starting a trial of Lyrica. Sleepiness has been present since age 18. When asked for details, the patient reported having drop attacks when she was a teenager and was evaluated for syncope by a cardiologist. She reports doing the dishes or washing clothes and not remembering how she did it. Asked about her most unusual experience, she stated that when she walked to her mother's house in the woods 1 day, a skunk surprised her and she fell down, unable to move, and watched the skunk come up to her and then walk away; she recovered fully in a minute or so.

The ESS is 17/24. The patient has been working 6–8 h/day in a dress shop where she can take frequent naps and drinking a lot of caffeine.

Her average sleep duration is 5–6 h per night, with frequent awakenings and annoying dreams. On 4–5 occasions she has awakened feeling that she cannot move, a sensation lasting 20 s or so. She denies witnessed apneas, RLS symptoms, and interference with her sleep by pets, children, or phone calls.

The patient has past history of one nonidentical twin pregnancy (one boy and one girl) during which the sleepiness became more severe, but no other medical diseases, social vices, or head trauma. The patient's family history is significant for a cousin with sleepiness who had to stop working because of drowsy accidents.

On examination, the vital signs are normal other than for a BMI of 24. The pulmonary and cardiovascular examinations are normal. The neurological examination reveals a normal affect, normal motor and sensory functions, and pupillary instability.

Probing Questions

1. What is the difference between fatigue and sleepiness, and how does one ask questions to distinguish the two?
2. What is the significance of the physical examination?

You contact the rheumatologist and you agree to stop the Lyrica for 2 weeks to permit testing of sleep and objective testing of sleepiness. The patient is sent for a PSG with the instructions to do an MSLT if in the PSG the AHI is <10/h. She is also instructed to keep a sleep diary for 2 weeks before the PSG and 1 week after.

The results showed she slept from ~9:30 p.m. to 6 a.m. with all stages of sleep, a sleep latency of 5 min, a REM latency of 49 min, and an AHI of 3/h.

For the MSLT, you calculate the mean sleep latency of 6 min with three SOREMs.

The patient returns to the clinic where you tell her that the testing is consistent for narcolepsy. Upon further questioning she remembers that she has to control herself from weakness attacks if someone tells a funny joke. She recalls that this happens about once a week or so and consists of dropping a spoon or a droop of her head for 10–20 s.

The patient mentions to you that her father used to have sleepiness. He was a thin man. She asks if this disorder is one that can be passed along to her twins.

Probing Questions

3. What can you tell the patient about the significance of these "weakness attacks"?
4. What is the genetic risk in narcolepsy with cataplexy?
5. How can you reduce this patient's risk of fall-asleep accidents?

She asks for advice regarding treatment and how to talk to her employers about her condition.

You send your report to the referring physician (a rheumatologist) who still insists that the patient has chronic fatigue syndrome. He states that both CFS and narcolepsy are based on symptom reports and exclusionary and correlative data, rather than an objective measure of the disease. He asks why you are so sure. You state that one can measure CSF levels to be sure of the diagnosis, and you investigate that possibility.

The patient comes back 6 months later. She feels generally OK with her sleepiness on modafinil (200 mg BID) and can work. Based on your prior questions, she notices that "drop attacks" occur about 5–6 times a week and usually are not intense or controllable. You conclude that she has narcolepsy with cataplexy. She asks if there are options for treatment of this cataplexy.

She told her supervisor about her illness and feels as if she is being scrutinized more than others. For instance, she naps on her break 2–3 times a week, and now it is noticed. Others nap but they laugh it off as "insufficient sleep." She asks about her future with the disease and will it get better or worse. She seeks your advice about employment and asks whether she is disabled.

Probing Questions

6. What is the sensitivity and specificity of CSF orexin levels?
7. What is the literature on employment and disability in narcolepsy?

Hypersomnia: Handout/Objectives

Goal: Describe the required clinical history and risk factors, work-up, rationale for diagnostic testing, and long-term management of excessive daytime sleepiness in an adult patient.

Objectives (Revealed at the End of the Session)

A. List the most common and specific symptoms for hypersomnolence not caused by sleep restriction or sleep apnea.
B. Recount the recommended steps needed for the optimal performance of an MSLT.
C. Explain the pharmacology of treatments for narcolepsy.
D. What pathophysiological markers are used to indicate the presence of narcolepsy with or without cataplexy?
E. Describe the societal and employment dimensions in a patient living with a diagnosis of narcolepsy.

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Chapter 12
Sleep-Related Movement Disorders and Parasomnias

Brian B. Koo

Introduction

Movement, under normal circumstances, is relatively suppressed during sleep to the extent that the person lying down will be more often assumed as being asleep than just resting. Yet individuals present to the sleep specialist with abnormal movements during sleep. Some may be disturbing to the individual while others are disturbing only to bed partners or observers. Some may be associated with known neurologic disorders, while others like REM behavior disorder could be the initial manifestation of disease. All these fall into the realm of the sleep-related movement disorders.

For this chapter, sleep-related movement disorders are considered as repetitive, nonepileptic, purposeless movements which are automatic and likely out of the control of higher cortical centers. Examples of sleep-related movement disorders include the hypnic jerk, hypnagogic foot tremor, and periodic limb movements during sleep. Although not per se a movement disorder, the restless legs syndrome which presents with symptoms related to sleep is often considered among this case of disorders because it responds to dopaminergic medications which have traditionally been used by movement disorder specialists. In addition, periodic limb movements both during sleep and wakefulness often accompany the restless legs syndrome.

Knowledge and skill in the clinical assessment and treatment of the sleep-related movement disorders is of paramount importance to the practicing sleep specialist. The purpose of the following chapter is to serve as a framework to direct an approach to the sleep-related movement disorders upon which a specific skill and knowledge set can be developed in a training sleep clinician. To do this, the chapter will take on a competency-based approach by presenting patient care, medical knowledge, practice-based, and systems-based cores to form curricula that could be used as a

B.B. Koo, M.D. (✉)
Department of Neurology, University Hospitals; Case Western Reserve University School of Medicine, 11100 Euclid Ave, Cleveland, OH 44106, USA
e-mail: koobri@gmail.com

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template for use by training programs. As part of this chapter, specific exercises will be incorporated to enrich development including examples of matching tests, essay questions, and a sample IQ group session.

A differential diagnosis for sleep-related movements can include seizures during sleep, and for this history taking is a key skill. More often knowledge and skills for this class of disorders involves a basic understanding of motor control during sleep, and the neurologic examination and its normal features, to uncover clues to the presence or absence of an underlying neurologic or cardiovascular disease. These include an ability of the sleep consultant to distinguish sleep disorders from neuropathy, vasculopathy, spinal cord disorders, stroke, and pharmacologic actions or mischief. Also unique to this class is that management may not require polysomnography or other specialized testing, so that in this instance the sleep consultant becomes a gatekeeper in preventing inappropriate testing.

This chapter does not aim to take the place of a comprehensive text on the sleep-related movement disorders but more guide an approach to the introduction to and learning of these disorders in the context of a fellowship program.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/parasomnias-and-movement-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the Essay Questions or IQ case.

Table 12.1 Map of Content Areas Relevant to Sleep-Related Movement Disorders and to ACGME Competencies

		Knowledge	Skills	ACGME competency
I.	*Epidemiology*	Yes	No	B, F
	Prevalence			
	Gender			
	Age			
	Comorbidity			
II.	*Mechanisms*	Yes	No	B, F
	Neurochemistry			
	Neuroanatomy			
	Periodic limb movements during sleep			
III.	*Risk factors*	Yes	No	A, B, C
	Environmental			
	Genetic			
	Comorbidity			
IV.	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatrics			
	Special populations			
V.	*Diagnostic measures*	Yes	Yes	A, B, C, D, E, F
	Clinical history			A, C, D, E
	Ancillary studies			A, B, C, F

(continued)

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VI. *Disease management*	Yes	Yes	A, E, D, F
Presentation of therapeutic options			
Decisions on therapy			A, F
Follow-up			A, F
VII. *Health and disease clinical pathways*	Yes	Yes	A, B, C, F
Quality of life			
Neuropsychiatric aspects			
Sleep-related complaints			
Cardiovascular associations			
Code for ACGME competencies			
A. Patient care	D. Interpersonal skills		
B. Medical knowledge	E. Professionalism		
C. Practice-based learning and improvement	F. System-based practice		

Table 12.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
- Describe the prevalence of restless legs syndrome (RLS) in North America, Europe, and Asia
- Describe the effects of age and gender on restless legs prevalence and severity

Item II. Mechanisms of health and disease
- Propose a mechanism by which RLS leads to increased cardiovascular risk through changes in the sympathetic nervous system. Outline some potential molecular substrates that could confer increased cardiovascular risk
- Outline higher cortical control on movement and describe how sleep might effect this control taking into account different parts of the nervous system including spinal cord, peripheral nerves, and muscle
- Propose different mechanisms, either biochemical, physiologic, or psychosocial, that could relate RLS to depression
- Describe physiologic changes during pregnancy that might associate with RLS expression

Item III. Risk factors
- Locate key structures in the brain which are involved in depression
- Describe environmental and behavioral factors that could influence the expression of periodic limb movements during sleep
- Describe how common lesions in the nervous system like spinal canal stenosis and peripheral neuropathy could relate to RLS, sleep myoclonus, and periodic limb movements during sleep (PLMS)

Item IV. Patient assessments
- Describe the effect of sleep deprivation on normal motor activity
- Recount an approach to a patient presenting with complaints of fatigue and periodic limb movements during sleep
- Describe your approach to the psychiatric history in a patient with severe restless legs syndrome, affecting quality of life. Describe how some of the below factors may play a role in this approach
  - Gender
  - Age
  - Ethnicity
  - Work history
  - Alcohol/drug history

(continued)

(continued)

Item V. Diagnostic measures and interpretation
- Describe key components of RLS symptomatology that determine overall RLS severity, referring to the International RLS Severity Scale
- Describe the muscular activation pattern in an individual movement among a PLMS cluster
- Outline the frequency of PLMS by age in persons with RLS
- Consider the sensitivity and specificity of RLS diagnosis using the four essential RLS diagnostic criteria. Describe how your approach to getting this history could affect sensitivity and specificity (i.e., the use of open-ended questions or rephrasing and repeating a question)

Item VI. Disease management
- Discuss the effect of hypnotic agents on sleep myoclonus and rhythmic movement disorder
- Describe behavioral measures that can be used to treat RLS. Consider why these may work
- Advise a patient with pregnancy and severe RLS on her options and what she might expect in subsequent pregnancies
- Describe the relationship between sleep apnea and RLS

Item VII. Health and disease clinical pathways
- Advise a patient that asks if they will need lifelong therapy for severe RLS
- List patient expectations vs. physician objectives in terms of outcomes
- A young woman with severe RLS is planning to have a child and asks what the likelihood that her child will also have severe RLS is. Outline your answer

Matching Test

Questions

A response to this drug or class of drug suggests a diagnosis of RLS. ☐
Examination in the lower extremities of primary RLS may reveal this. ☐
If administered with iron, increases its absorption. ☐
Movements most specific for RLS. ☐
A test best carried out in the evening when severity is at its highest. ☐
Movements which are seen in 80–90 % of RLS sufferers but can be seen in the normal elderly as well. ☐
Sensory test which measures the integrity of small nonmyelinated nerve fibers (Aδ and C fibers). ☐
Preparation of iron most well tolerated intravenously. ☐
A common description of RLS perhaps from persons growing up in the 1950s and 1960s, referring to a music icon. ☐
A substance that contains the drug whose use was banned by the FDA for leg cramps for commonly causing cardiac arrhythmia. ☐
Jerking movement often of the torso which may be seen in RLS. ☐
A decrease in periodic limb movements is often seen in this stage of sleep. ☐
Most recently accepted name for RLS. ☐
An entity which fulfills RLS diagnostic criteria but does not represent RLS. ☐
PLMS is often seen along with this entity. ☐

Levels of this iron-related protein are often increased in RLS. ☐
This gene was discovered in an RLS cohort in Iceland. ☐
Sleep start. ☐
Benign variant of movement in sleep. ☐
This scale measures frequency of RLS, degree to which movement relieves symptoms and consists of 10 questions. ☐
This muscle is most commonly activated in PLMS. ☐
A substance in brain which shows low ferritin. ☐
PLMS is associated with this entity especially when occurring with arousal. ☐
PLMS rhythmicity is thought to result from this. ☐
This type of RLS most often occurs in women. ☐
An instrument to measure PLMS. ☐
Jactatio capitis. ☐
This sensory modality is subserved by small diameter unmyelinated nerve fibers.
A sudden spreading of RLS symptoms to other prior uninvolved body parts, may constitute. ☐

Answers

1. Myoclonus
2. Hypnagogic foot tremor
3. Periodic limb movements during sleep (PLMS)
4. Periodic limb movements (PLMs)
5. Suggested immobilization test
6. Hypnic jerk
7. BTBD9
8. Head banging
9. Ropinirole
10. Karl Ekbom
11. Secondary RLS
12. Willis-Ekbom disease
13. Propriospinal myoclonus
14. Fragmentary myoclonus
15. Alternating leg muscle activation
16. Quinine
17. Periodic limb movement arousal index
18. International RLS Severity Scale
19. Ferritin
20. RLS mimic
21. Augmentation
22. Periodic limb movement disorder
23. Neuromelanin
24. Transferrin
25. Tremor
26. Gastrocnemius
27. Anterior tibialis
28. Sympathetic hyperactivity
29. Circadian rhythmicity
30. Insomnia
31. Periodic limb movements during wakefulness
32. RLS Quality of Life Scale
33. Substantia nigra
34. Dopamine A-11 neurons
35. Pro-opiomelanocortin
36. Spinal cord generator
37. Electromyography
38. Accelerometer
39. REM sleep
40. Narcolepsy
41. Primary RLS
42. Tonic water
43. Jimmy legs
44. Soap under the mattress
45. Vitamin C
46. Ferrous gluconate
47. Peripheral neuropathy
48. Myelopathy
49. Hemoglobin A1c
50. Pinprick
51. Cold feet
52. Ferrous sulfate
53. NREM sleep
54. MAP2K5
55. Joint position
56. Pain

Questions with Answers

A response to this drug or class of drug suggests a diagnosis of RLS. 9
Examination in the lower extremities of primary RLS may reveal this. 51
If administered with iron, increases its absorption. 45
Movements most specific for RLS. 31
A test best carried out in the evening when severity is at its highest. 5
Movements which are seen in 80–90% of RLS sufferers but can be seen in the normal elderly as well. 3
Sensory test which measures the integrity of small nonmyelinated nerve fibers (Aδ and C fibers). 50
Preparation of iron most well tolerated intravenously. 46
A common description of RLS perhaps from persons growing up in the 1950s and 1960s, referring to a music icon. 43
A substance that contains the drug whose use was banned by the FDA for leg cramps for commonly causing cardiac arrhythmia. 16
Jerking movement often of the torso which may be seen in RLS. 13
A decrease in periodic limb movements is often seen in this stage of sleep. 39
Most recently accepted name for RLS. 12
An entity which fulfills RLS diagnostic criteria but does not represent RLS. 20
PLMS is often seen along with this entity. 40
Levels of this iron-related protein are often increased in RLS. 24
This gene was discovered in an RLS cohort in Iceland. 7
Sleep start. 6
Benign variant of movement in sleep. 15
This scale measures frequency of RLS, degree to which movement relieves symptoms and consists of 10 questions. 18
This muscle is most commonly activated in PLMS. 27
A substance in brain which shows low ferritin. 23
PLMS is associated with this entity especially when occurring with arousal. 22
PLMS rhythmicity is thought to result from this. 36
This type of RLS most often occurs in women. 41
An instrument to measure PLMS. 38
Jactatio capitis. 8
This sensory modality is subserved by small diameter unmyelinated nerve fibers. 56
A sudden spreading of RLS symptoms to other prior uninvolved body parts, may constitute. 21

Essay Questions

Question 1

1. Name at least three sleep-related movement disorders that likely represent benign variants and describe these entities.

   Hypnic jerk. Sudden, brief myoclonic contractions of the body (often torso) or extremity (ies) which occurs with sleep onset.
   Hypnagogic foot tremor. Rhythmic movement of the feet and, in particular, the toes, which occurs most frequently at sleep onset.
   Propriospinal myoclonus. Sudden flexion movement involving abdominal and trunk muscles initially, then spreading to the neck and proximal extremities

2. What might one see on the EMG and EEG portions of polysomnography when each of these movements occurs?

   Hypnic jerk. On EMG, brief isolated events (less than 250 msec) which consist of muscle potentials occurring either simultaneously or in rapid succession. EEG shows stage N1 sleep or drowsiness and the jerk is often coincident with a vertex sharp wave.
   Hypnagogic foot tremor. On EMG, the bursts typically are 250–1,000 msec in duration, occurring at a frequency of 1–2 Hz with trains of 4 or more bursts, lasting for about 15 s.
   Propriospinal myoclonus. EEG shows alpha rhythm. On EMG, there is activation of abdominal and truncal muscles with subsequent rostral and caudal propagation into neck and extremity muscles.

3. For each of these movements what might constitute it being called a sleep-related movement disorder?
   For each of these entities, excessive amounts or repetitive occurrence with concomitant sleep disruption constitutes categorization into one of the movement disorders. Additionally if the abnormal movements are enough to cause distress, then a sleep-related movement disorders classification would be warranted.

4. Include parts of the neurologic exam which are important to perform and why.
   It is most important to focus on the motor and sensory exams as myelopathy and neuropathy can both precipitate any of these phenomena or at least movements that can mimic these phenomena. Myelopathy rather than neuropathy is more likely to cause these abnormal movements. Muscular weakness in a central pattern such as arm extensors more than flexors and knee flexion more than extension suggests a central process, possibly in the spine. Decreased sensation to pinprick and/or vibration in a stocking and/or glove pattern suggests neuropathy. Of course, hyperreflexia is seen in an upper motor neuron lesion while decreased reflexes are seen in peripheral nerve lesions.

Question 2

1. List the four essential diagnostic criteria for restless legs syndrome.
2. List other features that can be used to support a diagnosis of RLS if there is ambiguity.
3. Define primary and secondary RLS and give examples of the latter.
4. Name and describe RLS mimics and point out features that can be used to distinguish these mimics from RLS.

Answers

1. (a) Urge to move often associated with sensory discomfort
   (b) Worsening of symptoms in the evening or nighttime
   (c) Temporary relief at least partially with movement
   (d) Worsening of symptoms at rest or with inactivity
2. (a) Family history of RLS
   (b) Presence of periodic limb movements during sleep
   (c) Response to dopaminergic medications
3. Primary RLS refers to idiopathic RLS which occurs in the absence of entities that can precipitate RLS. Secondary RLS refers to RLS which occurs in the setting of something which precipitates the symptoms of RLS. Examples of diseases or states which are associated with secondary RLS include pregnancy, iron deficiency, peripheral neuropathy, myelopathy, Parkinson's disease, multiple sclerosis, and end stage renal disease.
4. Nocturnal leg cramps. Leg cramps are very common and often can fulfill each of the RLS diagnostic criteria. Leg cramps are often described as quite painful and the sufferer can often pinpoint the muscle which is affected which most commonly includes the small muscles of the feet or the gastrocnemius muscles.

Peripheral neuropathy. Neuropathy is more often described as a burning pain but also a tingling which can be confused with RLS. Neuropathic symptoms can have predilection to the nighttime but not uncommonly symptoms occur all day. The neurologic examination is of utmost important here, being normal in RLS and often showing abnormalities in the sensory exam in neuropathy.

Vascular claudication. This symptom is typically described as an aching but unlike RLS is exacerbated by activity and relieved with rest.

Question

5. What is periodic limb movement disorder (PLMD)? How does this differ from RLS? Can you have both PLMD and RLS?

Answer

5. By definition, PLMD and RLS cannot co-occur. PLMD is an entity which consists of frequent periodic limb movements during sleep (PLMS) most often of the lower extremities. These movements cause frequent arousal and sleep fragmentation and often a subjective feeling of unrefreshing sleep. Frank daytime

hypersomnolence or inanition may also result. It is important to note that the majority of patients with RLS will have PLMS but if RLS is associated with PLMS and sleep fragmentation, the diagnosis is RLS with PLMS and not PLMD.

Question 3

1. What does PLMS stand for? Describe what PLMS is semantically, including what the actual movements are (muscle groups, etc.) and describe polysomnographic features that are used to define them.
2. Describe the autonomic changes associated with PLMS.
3. By what indices are PLMS severity measured on polysomnography and what is the clinical significance of these values giving cutoff values?
4. In what percentage of RLS sufferers are PLMS seen? Name conditions other than RLS in which PLMS are seen.

Answers

1. PLMS: periodic limb movements during sleep

   PLMs: periodic limb movements
   PLMS are muscular activations often in the legs which occur approximately every 30 s and most often during NREM sleep. Polysomnographically, limb movements can be scored as periodic when the intermovement interval is between 5 and 90 s and there are at least four movements in succession. Muscle groups involved are the extensor hallucis as well as extensor digitorum, anterior tibialis, hamstrings, and less often iliopsoas. Arm muscles are still less often involved.
2. With each individual limb movement, there is an increase in heart rate on the order of 10 beats per minute and blood pressure on the order of 20/10 mmHg. These accelerations are slightly greater when PLMS are associated with arousal.
3. PLMS are measured with a periodic limb movement index or PLMI and a periodic limb movement arousal index or PLMAI. There are no studies to direct what numbers are clinically significant; however, PLMI>5 for younger adults and PLMI>10 for elderly are loosely taken as clinically significant while PLMAI>1 is potentially clinically significant. The lack of studies to determine what is of clinical significance should be stressed.
4. PLMS is seen in about 80–90 % of RLS sufferers but is also seen in a large percentage of the normal population without RLS, especially in the elderly. PLMS may also be seen with stroke, multiple sclerosis, myelopathy, peripheral neuropathy, or congestive heart failure.

EM is a 53-year-old female who presents to her physician with complaints of jumpiness in her legs. She has had borderline diabetes for the past 2 years which has been treated with diet and hypertension which is treated with lisinopril. The patient states that in the evening her legs begin to “jump” involuntarily. The jumpiness continues into the night and can prevent her from falling asleep.

Part I

Questions

1. What are the appropriate next questions to establish the most likely diagnosis?
2. Do you ever have an urge to move the legs with an uncomfortable feeling?
3. Do these symptoms occur more during the day or more at night?
4. Do these symptoms occur more if you are sitting still or walking?
5. Are these symptoms alleviated at least in part by movement?

Answers

1. The most likely diagnosis here is restless legs syndrome. Questions to determine this diagnosis aim to establish if the four essential criteria of RLS are present. Additional questions are also required to rule out common mimics of RLS.
2. Answer should be yes.
3. Answer should be at night.
4. Answer should be sitting.
5. Answer should be yes.

After it has been confirmed that the four essential criteria are present, it is often helpful to ask the patient describe the symptoms in his/her own words. The patient will often have difficulty describing the symptoms but may offer answers like numbness or tingling, creepy-crawly feelings, an inner restless feeling of the legs. Atypical answers such as pain or burning should prompt additional questioning to rule out entities such as nocturnal leg cramps and neuropathy.

Question

6. How does one determine how severe the RLS is?

Answer

6. It is important to ask questions to gauge the severity of the RLS. Like any other complaint to do this, one must first determine the duration and frequency. How often does this occur, specifically how many times out of the week and for how long has it occurred? Do the symptoms also occur during the day if you are inactive?

Since RLS is circadian it is also important to ask at what time do the symptoms begin as this can range anywhere from late afternoon, to late at night to on rare occasion occurring all day. Once the onset and frequency are established, it is important to determine to what extent does moving alleviate the discomfort. Again this can range broadly as certain individuals may get complete relief with minimal movement (a couple shakes of the legs) and others must move continuously (pacing back and forth) for hours. Once this information has been assessed, the clinician already often has a good idea of how severe the RLS is. Other important questions include the following: Does the RLS prevent you from falling asleep? How severe on a scale of 1–10 is the RLS? And does the RLS affect your well-being to a great degree and if so how?

Questions

7. What additional pieces of information are important regarding the sleep history and social history?
8. What aspects of the lower extremity exam are most important in patients with RLS or suspected RLS?

Answers

7. RLS is often accompanied by other sleep disorders such as excessive sleepiness and sleep apnea. History should be sought to assess for sleep apnea and to determine if the patient is excessively sleepy. The sleeping schedule also needs to be determined as a poor sleeping schedule, and sleep deprivation can exacerbate RLS and RLS can cause a prolonged sleep latency. The social history is also quite important in RLS as common ingestants such as coffee/caffeine and alcohol can exacerbate RLS. On the other hand, exercise can alleviate symptoms of RLS.
8. As vascular claudication can masquerade as RLS, it is important to assess for peripheral pulses. Peripheral edema may also cause an uncomfortable feeling in the legs, so assessing for edema is important. In terms of the neurologic exam, both peripheral neuropathy and central myelopathy can result in symptoms similar to RLS but also patients with these entities may also have comorbid RLS. The exam can be focused to exclude these entities. The motor exam is important to assess for peripheral or central patterns of weakness. Increased tone with increased reflexes is often seen in myelopathy, while normal tone with decreased reflexes occurs in peripheral neuropathy. The sensory exam should focus on pinprick, vibration, and joint-position sense. It is important to look for a gradient loss of these modalities in the feet but one should also determine if there is more proximal sensory dysfunction in the leg and even arms/hands. Finally, Babinski reflex should be sought with plantar stimulation of both feet.

This patient describes a creepy-crawly sensation which fulfills all four RLS criteria. The symptoms occur nightly and begin about 7 p.m. She has had these symptoms for about 25 years but they are getting more frequent. She gets only momentary relief by moving and must walk for 1–2 h in order for the symptoms to become tolerable. About 5 out of 7 nights per week, it takes her in excess of 2 h to fall asleep, usually because of the legs. She has a fairly regular sleep schedule going to bed at 11 p.m. and waking up at 7 a.m., but it often takes her 2 h to fall asleep. Her husband has complained that she snores loudly but has not observed her to stop breathing. She denies sleepiness. She does not drink alcohol but because of the tired feeling has been drinking coffee throughout the day, about 4–5 cups per day.

On exam, she is an obese female with a BMI of 31.3, blood pressure of 135/87, and pulse of 86. Her general medical exam is notable for a large tongue and a Mallampati of IV. She has no peripheral edema and good pulses. Her neurologic exam demonstrates normal strength with normal tone and reflexes. The sensory exam is intact to vibratory and joint-position sense, but there is very subtle decrease to pinprick in the feet. The plantar response is flexor.

Questions

9. What is the diagnosis and what is the severity?
10. What are some appropriate tests to perform?
11. What is the appropriate treatment here?

Answers

9. This is severe RLS.
10. The patient is obese and has been noted to snore loudly. Getting polysomnography is important here to assess for sleep apnea. On her exam, there is also some subtle loss of pinprick; also, she has been noted to be borderline diabetic. To start a hemoglobin A1c can be ordered to determine if diabetes is present. If this measurement is normal, a 4-h glucose tolerance test may be helpful, even though there may be some neuropathy present. Although there is some abnormality on the neurologic exam indicating small fiber neuropathy, the fact that the RLS has been present for 25 years suggests that this is primary RLS. A serum ferritin level is important to check here.
11. The patient should first be counseled on decreasing her caffeine intake. While ordering a ferritin and assessing for sleep apnea are important measures, it is unlikely that abnormalities in these measures could account for the leg symptoms. Given that there is a peripheral neuropathy here, the most appropriate medication here is gabapentin. First, mood should be assessed. If depression is present, one may want to consider a dopamine agonist or monitor the depression while starting on gabapentin. The gabapentin could be started once in the evening and once at bedtime for this patient as her symptoms begin early and before bedtime. One can start 100 mg twice per evening or 300 mg twice per evening depending on the individual. The medication can then be titrated up to 600 mg, 900 mg, and 1,200 mg twice nightly. The smallest effective dose should be used and side effects of depression, somnolence, and ataxia should be assessed. If low ferritin is found (<50 ng/mL), then treatment with oral ferrous sulfate 325 mg three times daily along with 500 mg of Vitamin C should be started. The use of ferrous sulfate may be limited by constipation.

IQ Case

IQ Case for Student

Goal: To explore the presentation, risk factors, evaluation, and short- and long-term treatment of a complaint of movement disorder during sleep.

Case Vignette

Pegs Driver is a 56-year-old Caucasian female who presents with discomfort in her legs and a complaint of poor sleep. She has had these problems "for years" but things seem to have really worsened in the past year. She now dreads going to sleep because of almost nightly symptoms. She remembers feeling "these creepy-crawly" feelings intermittently for over 20 years. After further questioning, you find that the sensations come on as early as 6 p.m. but are worse as she lies down to go to sleep. The symptoms go away if she stands up and walks around or exercises on the treadmill in her bedroom before sleep. They sometimes bother her when she wakes up in the middle of the night but are not noticed in the morning. In the past 6 months, two to three times per week, she might have a beer to help her sleep. Sometimes her feet feel cold. She denies claudication, back pain, or nerve problems.

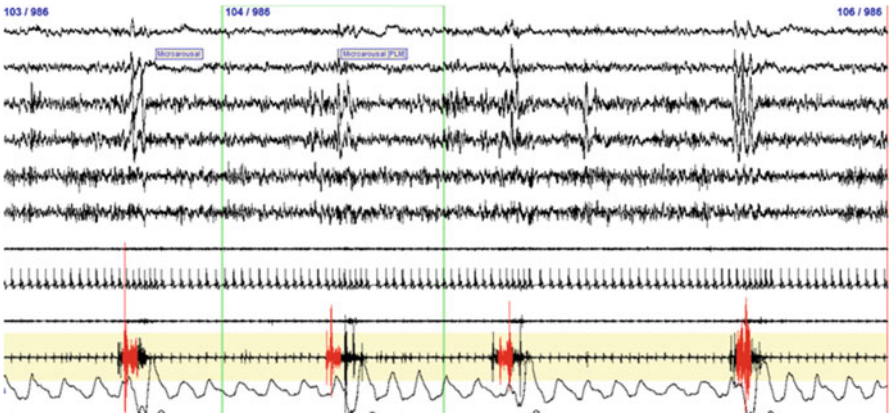
She is treated for hypertension and "migraine" by her PCP, and has been told that she is prediabetic. She takes metoprolol for blood pressure and topiramate for migraine.

Astutely you notice that her affect is somewhat flat. She admits to feeling sad some of the time, and an occasional "cry". She denies a sense of helplessness, hopelessness, or feeling that life is not worth living. She states that more times she feels tired and sleepy, rather than fatigued.

She goes to bed at midnight and it may take her 1½h to fall asleep, most often because of the leg sensations. She wakes up between two to four times per night and wakes up at 7:00 a.m. on the weekdays for work and 9:00 a.m. on weekends. She is known to snore but not to have witnessed apneas, and she wakes up with a dry mouth 1–2 times a week. The Epworth Sleepiness Scale score is 12/24 and states that about two times per week she will fall asleep at her desk at work as hospital librarian. She denies drowsy driving or near misses from sleepiness in recent years.

She has red hair. Head and neck, lung, and cardiac examinations are normal. On the physical exam of the legs, peripheral pulses are present; the temperature of the feet and legs seems normal and equal. Hair and skin appear normal. Touch and pinprick sensations are normal. Reflexes are normal.

The TSH level was normal 6 months ago. A ferritin blood level was drawn. Because of the symptoms of snoring, you decide to order sleep testing to rule out sleep apnea. There is no sleep apnea but on the sleep study you see many of these events.



The ferritin level was 66 mg% (normal 20–200 mg%). You decide to treat and choose ropinirole (REQUIP@). She asks you about the side effects and will this help her sleep; she asks about alternatives. After this discussion, she agrees to begin ropinirole 0.25 mg once in the early evening and once at bedtime going up to 0.5 mg in the early evening and at bedtime and finally 0.5 mg in the evening and 1.0 mg near bedtime going up 0.5 mg in 5-day increments. In addition, you recommend that she go to bed regularly at 11 p.m. and that she refrain from drinking beer at night.

The patient returns 6 weeks later stating she is significantly better on 0.5 mg in the evening and 1.5 mg at bedtime. She no longer has leg symptoms; she is feeling less tired, getting more sleep, and her migraines are occurring less frequently. You tell her that the diagnosis is restless legs syndrome and she asks if it puts her at risk for any other diseases.

One year later, she presents with symptoms again. They started about 4 months ago by starting earlier in the day. Her PCP took your previous plan and increased the ropinirole dose. Every 2 weeks the dose was increased, especially when the symptoms increased in severity and earlier in the day. She is now on 2 mg at 6 p.m. and 6 mg near bedtime, a regimen that had worked for a week but seems to not be wearing off. “What do you do now?” she asks.

IQ Case for Facilitator

Goal: To explore the presentation, risk factors, evaluation, and short- and long-term treatment of a complaint of movement disorder during sleep.

Objectives

A. Identify the chronobiology of restless legs syndrome.
B. Create a differential diagnosis for symptoms and signs in the evaluation of RLS.
C. Describe the therapeutic options relevant to the patient and the physician.
D. Describe the outcome points for therapy.
E. Discuss the mechanisms of augmentation.

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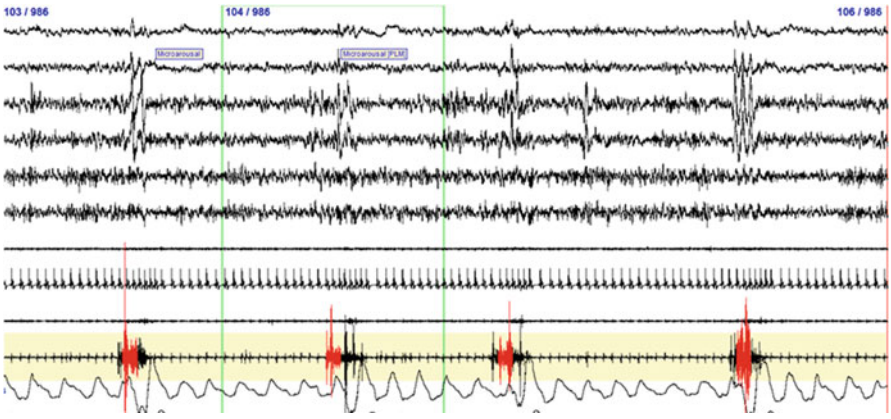

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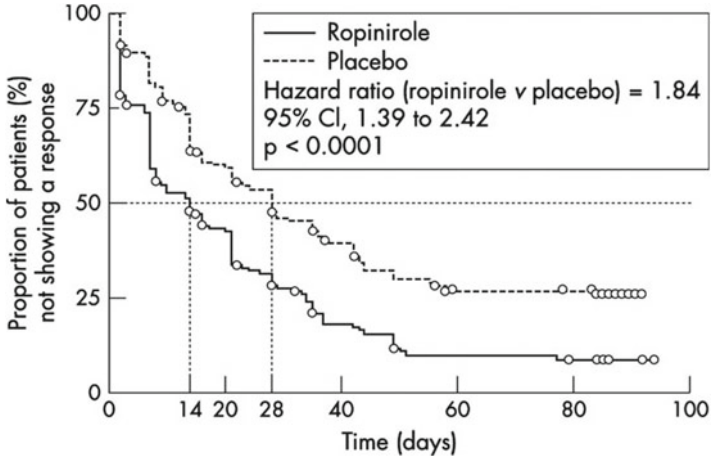

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She has had these problems “for years” but things seem to have really worsened in the past year to the point where she dreads going to sleep because of almost nightly symptoms. She remembers feeling “these creepy-crawly” feelings intermittently for over 20 years. After questioning the patient further, you find that the sensations come on as when she lies down to go to sleep, and go away if she stands up and walks around. She sometimes exercises before sleep. Two to three times per week, she might have a beer to help her sleep. Astutely you notice that her affect is somewhat flat and ask her about her mood.

Probing Questions

1. What is the most likely diagnosis and what needs to done to confirm this?
2. What is the significance of the medical history? Take each part of the medical history and discuss pertinence to RLS.
3. Is there an association between RLS and depression?
4. In terms of the use of antidepressants, what is the relationship between treatment and RLS symptoms? Is this true for all antidepressants?
5. What is the effect of alcohol on RLS symptoms?

Ideal Answers

1. The most likely diagnosis here is RLS. It is essential to verify that she fulfills are four of the essential RLS diagnostic criteria while she does not have a common mimic of RLS, like leg cramps or neuropathy.
2. RLS has a controversial association with hypertension. In some large epidemiologic cross-sectional studies, there seemed to be an increased prevalence of hypertension in RLS. In additional community studies, when controlling for such factors as age, sex, race, and BMI, there was no association between RLS and hypertension history. Increased prevalence of RLS has been shown in migraine. RLS is often comorbid with peripheral neuropathy, of which the most common type is diabetic peripheral neuropathy. It is important to remember that symptoms of peripheral neuropathy can mimic RLS. Studies are conflicting concerning if there is increased prevalence of diabetes in RLS.
3. Depression is increased twofold to fourfold in RLS. Quality of life of the RLS sufferer has been shown to be sufficiently low and comparable to persons affected with other chronic disorders such as diabetes and osteoarthritis. The sleep disturbance common in RLS is a factor which may underlie some of this comorbidity with depression. Treatment with dopamine agonists has not only been shown to improve symptoms of RLS but also depressive symptoms.
4. The treatment of depression in the setting of RLS is tricky. Many antidepressants have been associated with worsening of RLS symptoms, especially mirtazapine. Buproprion, perhaps because of its action on the dopaminergic system, has been considered to be neutral or even beneficial in regard to RLS.
5. Alcohol is associated with worsening of RLS symptoms.

She states that she feels sad some of the time but that she is not depressed. She denies a sense of helplessness, hopelessness, and feeling that life is not worth living. She states that more than sad, she feels tired and sometimes frankly sleepy. Her sleep schedule is such that she goes to bed at midnight and it may take her 1½ h to fall asleep often because of the legs. She states that she wakes up between two to four times per night and wakes up at 7:00 a.m. on the weekdays for work and 9:00 a.m. on weekends. She does endorse snoring and waking up with a dry mouth but no witnessed apneas. She has an Epworth Sleepiness Scale score of 12/24 and states that about two times per week she will fall asleep at her desk at work; she is a hospital librarian. She denies drowsy driving.

Probing Question

What are potential causes of excessive sleepiness in this case?

Ideal Answer

Potential causes of sleepiness include insufficient sleep, sleep apnea, and sleep disruption from periodic limb movements during sleep.

On examination, her blood pressure is 137/93 with a heart rate of 84. Her BMI is 32.3. She is pleasant and in no distress.

HEENT: Mallampati III, large tongue, no tonsils

Lung: clear

Heart: S1, S2, no murmurs or gallops

Extr: no edema and good peripheral pulses

Neuro: intact mental status, motor strength intact with normal reflexes, sensation intact to pinprick

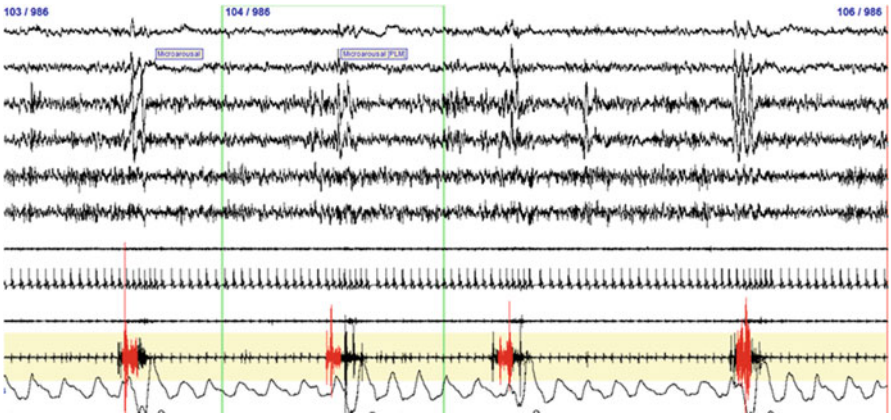
Probing Question

What is the importance of the physical examination in RLS?

Ideal Answer

On the physical exam of the legs, peripheral pulses should be palpated to ensure sufficient circulation. The temperature of the feet and legs should be noted. RLS sufferers often complain of cold feet. Hair and skin pattern should be noted as changes could suggest neuropathy or peripheral arterial disease. The neurologic exam for RLS is most important to rule out both peripheral neuropathy and central myelopathy. For this reason, the motor and sensory exams as well as the reflex exam should be focused on.

Because of the symptoms of snoring, you decide to order sleep testing to rule out sleep apnea. There is no sleep apnea but on the sleep study you see many of these events.



Probing Questions

1. What is the association between RLS and sleep apnea?
2. What is the significance of the scored signals in red?
3. Notice the cardiac accelerations associated with the signals? What is the significance of this and what other element increases with heart rate?

Ideal Answers

1. There does not seem to be an increased prevalence of sleep apnea in persons with RLS; however, since both sleep disorders are common, co-occurrence is not uncommon. There is also an interesting phenomenon in which the treatment of sleep apnea with positive pressure therapy decreases the symptoms of RLS. The mechanism underlying this effect is not known.
2. These are periodic limb movements during sleep.
3. Periodic limb movements are associated with increases in heart rate especially when accompanied by arousal. These cardiac accelerations are associated with increases in both systolic and diastolic blood pressure on the order of 20/10 mmHg. These changes reflect sympathetic hyperactivity and may have cardiovascular consequences, although this has never been proven.

You decide to treat and choose ropinirole. She does not know what this medication is and wants to know. She asks you about the side effects and will this help her sleep better. What do you answer?

Ropinirole is a dopaminergic agonist which is often used to treat Parkinson's disease. It acts on D2, D3, and D4 receptors but has highest affinity for D2 receptors. Action on the D3 receptor may exert most activity against symptoms of RLS. Ropinirole is effective at reducing symptoms of RLS with nearly two-thirds of patients describing significant improvement at 1.5 mg ropinirole. Treatment with ropinirole is also effective at decreasing periodic limb movements during sleep, decreasing the frequency of these events by approximately 75 %. Sleep latency is significantly reduced with ropinirole and stage N2 sleep significantly increases.

Common adverse effects include nausea, orthostatic hypotension, dyspepsia, somnolence, and sweating. Sudden sleep episodes, syncope, and compulsive behavior can also occur. Patients should be specifically counseled about the possibility of compulsive behavior such as pathological gambling or shopping.

Probing Question

In a starting dose and regimen, what are some of the important characteristics of the RLS that direct your decision making?

Ideal Answer

It is of course important to determine how severe the RLS is. Determining the frequency of RLS symptoms is imperative in making a decision on whether to treat or not. A simple question of "Do the symptoms bother you enough to take a medicine?" is often helpful. The time of onset is quite important to determine if medication needs to be taken only once at night, twice, or even three times daily. Severe

symptoms which begin in the early evening often require an evening and a bedtime dose, while symptoms that only occur in bed only require a nighttime dose.

The patient states that her symptoms begin at about 6 p.m. and continue until she falls asleep. They sometimes bother her when she wakes up in the middle of the night but less so that in the evening and before bed.

You begin ropinirole 0.25 mg once in the evening and once at night going up to 0.5 mg in the evening and at night and finally 0.5 mg in the evening and 1.0 mg at night going up in 5-day increments only if necessary. In addition, you recommend that she go to bed at 11 p.m. and that she refrain from drinking beer at night.

The patient returns 6 weeks later stating that her symptoms are significantly better. She no longer has the RLS symptoms, she is feeling less tired, and as a bonus her migraines are occurring less frequently. She asks you if the RLS puts her at risk for any other diseases, mostly cardiovascular.

Probing Questions

1. What is your answer?
2. Why did symptoms increase?

Ideal Answers

1. There may be an association between RLS and hypertension, although studies which controlled for age, obesity, and race did not show a relationship. Given the uncertainty, it is important to include this in the discussion, especially since PLMS is associated with discrete increases in blood pressure. There seems to be an increase in the prevalence of myocardial infarction, coronary artery disease, and stroke with odds of about twofold. To date, there are no studies that look at whether RLS is associated with incident cardiovascular disease.
2. Augmentation is the main complication of long-term dopaminergic treatment of RLS and is characterized by an overall increase in severity of RLS symptoms (earlier onset of symptoms during the day, faster onset of symptoms when at rest, spreading of symptoms to the upper limbs and trunk, and shorter duration of the treatment effect). Augmentation should be differentiated from early morning rebound, natural progression of the disease, tolerance, and neuroleptic-induced akathisia. The most effective preventive measure is to keep the dose of the dopaminergic medication as low as possible. Mild cases should be followed closely, however. In severe cases, a change of treatment (sometimes even within the same class of drugs) can be effective, although it should be verified that all factors that may affect augmentation (changes in lifestyle, iron deficiency, serotonin reuptake inhibitors) have been excluded.

IQ Case: Handout/Objectives

Goal: To explore the presentation, risk factors, evaluation, and short- and long-term treatment of a complaint of movement disorder during sleep.

Objectives

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Chapter 13
Sleep-Disordered Breathing

Kingman P. Strohl and George P. Fahed

Introduction

Obstructive sleep apnea-hypopnea is:

- The most commonly encountered condition in the practice of sleep medicine
- The most common finding and reported result in polysomnography
- The most common medical disorder causing sleepiness in the community

Of course, there are other respiratory disorders of sleep, central apneas, hypoventilation, and disorders of respiratory control secondary to medications, neurologic illness, or trauma. All entail the application of knowledge of neurophysiology, anatomy, pulmonary function, and pattern recognition skills to identify and manage abnormalities in respiratory rate, rhythm, and pattern during wakefulness as well as during sleep.

Knowledge and skills for Sleep Medicine Fellowship ACGME programs (http://www.acgme.org/acWebsite/downloads/RRC_progReq/520_sleep_medicine_06012004_1-YR_u_04122008.pdf: last accessed 9/17/2011) list apnea and its related disorders in all areas of expected general training competencies, for example, listing portable monitoring under system-based learning. Each program is required to have an "adequate number of patients" coming from other practice of sleep medicine for each trainee to gain an understanding of clinical presentations and management in adults and in children.

K.P. Strohl, M.D. (✉)
Case Western Reserve University, 11100 Euclid Avenue,
Cleveland, OH 44106-1716, USA
e-mail: kpstrohl@aol.com

G.P. Fahed, M.D.
Sleep and Pulmonary Medicine, 917 Ave Tito Castro, Ponce, Puerto Rico 00716
e-mail: gfahed@somnospr.com

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For this chapter, content domains were developed through examination of the ACGME requirements, discussions with sleep medicine faculty and prior fellows about current and/or best practice, and collection of existing material on the topic of training topics. Regarding the latter, there are articulations of general competencies in sleep for medical students and for pulmonary fellows, organized by faculty in the Sleep Academic Award program 1977–2003 and by a consensus group of the American Thoracic Society.

The topics were organized to construct a (non-comprehensive) list of suggested content domains relevant to a sleep medicine fellowship. These illustrate the landscape of clinically used material along with corresponding ACGME areas for general competencies are illustrated in Table 13.1. While not as comprehensive as one would find in a textbook, these areas touch upon all aspects of practice as well as the basic issues found in the sleep apnea and related syndromes. Some of the areas like epidemiology are solely knowledge-based in that through reading various relevant chapters and attending didactic presentations the program could test factual proficiency through standardized testing, exercises in matching, or structured essay answers, but also this content can be demonstrably applied in an IQ case discussion or clinical presentation. Other topics like Patient Assessments, while having theoretical underpinnings and a literature, are taught more commonly (without any organized effort to address effectiveness), by example, and assessed better by observation and immediate feedback. This is an art to the clinical assessments in practice, and individual styles may vary; however, here one should attempt to define trainee comprehension concerning relevant features of an assessment including the ordering of ancillary tests.

In regard to learning opportunities, the delivery of this content would be delivered through a variety of venues including apprenticeship underpinned by instructional objectives. In this approach the outcome is to be explicit and stated in such a manner as to capture what specific knowledge, skills, and attitudes a fellow should be able to exhibit following instruction. An objective directly links content and assessment. In this regard, some examples of objectives for each content area are presented in Table 13.2. Note that this list tries to avoid terms that are open to variable interpretation and focuses on work-related, measurable, or verifiable outcomes. Other instructional delivery can list the objectives either up front or at the middle or end of the instruction, but the goals of the instruction should be explicit. Approaches can be creative in when and how objectives are verified.

This list can be augmented or re-created by an individual training program and modified so as to address of strength or weakness in overall instructional plan or expertise. One can use these questions as a basis for Essay Questions to amplify a topic presented in another fashion by faculty, visiting faculty, or fellow. The faculty or fellow can use the list and choose to construct lectures based on one or more objectives. Working on this list can be a useful exercise to review prior presentations of topics or used as a springboard for written reviews or research. The IQ case is one that has some twists and turns and is a companion to the Chapter on Upper Airway Physiology.

An illustrative powerpoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/sleep-disordered-breathing.html). It may be reviewed by the student and the program or discussed in a group format before or after the Essay Questions or IQ case.

Table 13.1 Cognitive Map of the Content Domains Relevant to Sleep Apnea and Related Disorders

		Knowledge	Skills	ACGME competency
I.	*Epidemiology*	Yes	No	B, F
	Age			
	Risk factors			
	Special populations			
II.	*Mechanisms*	Yes	No	A, B
	Neurophysiology			
	Respiratory control			
	Upper airway physiology			
III.	*Risk factors*	Yes	No	A, B
	Environmental			
	Genetic			
	Developmental			
IV.	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatrics			
	Special populations			
V.	*Diagnostic measures and interpretation*	Yes	Yes	A, C, F
	Polysomnography			A, C
	Patient-based testing			A, B, F
VI.	*Disease management*	Yes	Yes	
	Presentation of therapeutic options			A, E, D, F
	Decisions on therapy			A, F
	Follow-up			A, F
VII.	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Pediatric sleep apnea			
	Bariatric surgery			
	Commercial driver assessment			
	Perioperative management			
	Neuromuscular diseases			
	Code for ACGME competencies			
	A. Patient care	D. Interpersonal skills		
	B. Medical knowledge	E. Professionalism		
	C. Practice-based learning and improvement	F. System-based practice		

Table 13.2 Examples of Topics

Item I. Epidemiology
- Contrast prevalence community studies of adult sleep apnea with those from selected groups (presenting to primary care practices, sleep clinics, to bariatric centers, to geriatric clinics, to neurologic clinics for neuromuscular disease, etc.)
- Describe a program to detect sleep apnea in commercial trucking industry
- Compare presentation profiles of obstructive sleep apnea with that of central apneas

Item II. Mechanisms of health and disease
- Draw the spatial relationships between pontine and medullary respiratory control centers
- Describe the critical closing pressure and loop gain as core physiologic features
- Genetic and epigenetic factors in the development of apnea
- List the manner how obesity predisposes to sleep-disordered breathing

Item III. Patient assessments
- List elements of the history and physical that are evidence based
- Contrast pretest probability in primary care patients to those presenting to a sleep clinic

Item IV. Diagnostic strategies
- Compare testing technology
- Level I, II, III, and IV monitoring
- Describe pretest probability and posttest uncertainty for diagnostic testing for sleep apnea
- Explain sensitivity and specificity for clinical outcomes

Item IV. Practice-based management
- Compare and contrast the principles of therapy
  - Behavioral
  - Mechanical
  - Surgical
  - Medical
  - Pharmacologic therapy
- Imagine novel approaches

Item V. Health and disease management pathways
- Describe the principles in the initiation of therapy
- Now that a patient has responded to therapy, list the factors for management of apnea as a chronic disease
- List patient expectations vs. physician objectives in terms of outcomes

Item VI. Practice-based learning and improvement
- Devise a quality improvement program for reporting PSG results to referring physicians
- Formulate a checklist for adherence for different therapy

Item VII. Interpersonal and communication skills
- Demonstrate and apply motivational interviewing techniques for treatment initiation and adherence
- Evaluate each other's notes and dictations for content and outcome

Item VIII. Professionalism
- Fabricate a fair and unbiased presentation of therapeutic alternatives
- Identify ethical conflicts in the conduct of sleep medicine

Item IX. System-based practice
- Disease management pathways
  - Concept map a plan to manage bariatric patients
  - Develop a reimbursement-based perioperative management plan for sleep apnea
- Evaluate inpatient consultations for indications and cost-effectiveness

Matching Test

Questions

A graph that depicts alveolar ventilation to arterial carbon dioxide levels. ☐
Absent in cases of congenital central hypoventilation syndrome. ☐
Brainstem terminus for vagal stretch receptors. ☐
Central apnea occurs when respiratory drive decreases below this threshold. ☐
Central congenital hyperventilation syndrome is caused by this gene. ☐
Drug that has been shown to reduce central apneas in the setting of heart failure.
Gene causing RETT syndrome. ☐
Measure of global properties of an upper airway during sleep, as measured by raising and lowering upstream pressure. ☐
Motor nerve for the genioglossal muscle. ☐
Proposed as a treatment for complex sleep apnea. ☐
Region of the respiratory system that excludes the lungs and chest wall. ☐
Responsible for the Hering-Breuer reflex. ☐
Rib cage and abdominal motion is measured by…. ☐
Sensory nerve for the carotid body. ☐
The pulmonary function test measurement used to detect respiratory muscle weakness.
The volume left in the lungs after a full expiration. ☐
This brainstem center drives the activation profile for the phrenic nerve. ☐
This brainstem region contains neurons which determine the inspiratory off-switch.
This term is the measure of metabolic rate. ☐
When this value falls below 40 % in neuromuscular disease, there is a need to consider bi-level ventilation. ☐

Answers

1. Acetazolamide
2. Aortic body
3. APAP or automatic CPAP
4. Apneustic center
5. Arousal threshold
6. ASV (assist controlled ventilation)
7. Bi-level ventilation
8. Breathholding time
9. Buspirone
10. Carbon dioxide production
11. Carbon dioxide threshold
12. Carotid body
13. Central apnea
14. Chemoreceptors
15. Cheyne-Stokes respiration
16. Complex sleep apnea
17. Controller gain
18. Cortex (cerebrocortex)
19. CPAP
20. Critical closing pressure
21. Dorsal respiratory group (DRG)
22. Downstream pressure
23. End-tidal carbon dioxide measurement
24. Esophageal pressure
25. Expiratory pressure (maximal)
26. Feedback control
27. Genioglossus
28. Genotype
29. Glossopharyngeal nerve
30. Hering-Breuer reflex
31. Hypercapnic drive
32. Hyperventilation
33. Hypoglossal nerve
34. Hypothalamus
35. Hypoventilation
36. Hypoxic drive
37. Inductance plethysmography (RIP)
38. Inspiratory pressure (maximal)
39. Leptin
40. Load compensation
41. Lung volume receptors
42. Mechanoreceptors
43. Mecp2 gene
44. Medulla
45. Metabolic curve
46. Mitochondria
47. Mixed apnea
48. Muscle spindles
49. Muscle strength testing
50. Negative pressure reflexes
51. Neuromuscular weakness
52. NREM sleep
53. Nucleus tractus solitarius (NTS)
54. Obstructive apnea
55. Orexin
56. Oxygen consumption
57. Phenotype
58. PHOX2B gene
59. Plant gain
60. Pneumotaxic center
61. Pons
62. Progesterone
63. REM sleep
64. Residual volume
65. Rib cage and abdominal motion
66. Shy-Drager syndrome
67. Starling resistor
68. Sum of rib cage and abdominal measurements
69. Upper airway
70. Upstream pressure
71. Vagal stretch receptors
72. Ventilatory response to carbon dioxide
73. Hypoxia
74. Ventral respiratory group (VRG)
75. Vital capacity

Questions with Answers

A graph that depicts alveolar ventilation to arterial carbon dioxide levels. 45
Absent in cases of congenital central hypoventilation syndrome. 72
Brainstem terminus for vagal stretch receptors. 53
Central apnea occurs when respiratory drive decreases below this threshold. 10
Central congenital hyperventilation syndrome is caused by this gene. 58
Drug that has been shown to reduce central apneas in the setting of heart failure. 1
Gene causing RETT syndrome. 43
Measure of global properties of an upper airway during sleep, as measured by raising and lowering upstream pressure. 20
Motor nerve for the genioglossal muscle. 33
Proposed as a treatment for complex sleep apnea. 6
Region of the respiratory system that excludes the lungs and chest wall. 69
Responsible for the Hering-Breuer reflex. 71
Rib cage and abdominal motion is measured by…. 37
Sensory nerve for the carotid body. 29
The pulmonary function test measurement used to detect respiratory muscle weakness. 38
The volume left in the lungs after a full expiration. 64
This brainstem center drives the activation profile for the phrenic nerve. 21
This brainstem region contains neurons which determine the inspiratory off-switch. 61
This term is the measure of metabolic rate. 9
When this value falls below 40 % in neuromuscular disease, there is a need to consider bi-level ventilation. 75

Essay Questions 1 and 2

Single essay questions cover content delivered by any format and can be given before or after the presentation or at intervals in the program. The use is to have the learner synthetize the material and reform it into their own words. You can assess not only the objectives but the written communication skills. In this instance, two essay questions are provided. It would be the expectation that only one would be completed by a fellow. "Ideal" answers are posted after the fellow submits their answers and discussion ensues.

Question #1

Instructions

Where you find multiple questions within the same question subpart, label your answer using the letter that corresponds to the letter in the question. Example: Question: (A) what is … (B) explain.... (C) describe… Answer: (A) definition is…, (B) the explanation is, (C) description.

Any control system has elements that control function (controller), a controlled system, and a sensor for the critical variable.

Questions

1. For the respiratory control system, what parts of the body represent the controller, the controlled system, and the sensors? (3–4 short sentences)
2. What can be the controlled variables regulated by this respiratory control system? (2–3 sentences)
3. Define and then describe the components of loop gain. (2–3 sentences)
4. Give an example of a disorder of respiratory drive in which controller function for carbon dioxide is absent and describes its effect in NREM sleep and with exercise. (Hint: the disease often presents in infancy.)

Ideal Answers

1. The controller is conventionally the brainstem and the medulla and pons having the most influence on respiratory rate and depth. The controlled system is represented by the upper airway, lungs, and chest wall as well as the nerves and muscles in these structures. The sensors for chemoresponsivity are the carotid body and the central brainstem receptors.
2. Arterial and tissue carbon dioxide through its action on intracellular pH. Arterial oxygenation rather than partial pressure of oxygen is another controlled variable.
3. Loop gain is comprised of the responsiveness in controller gain and in plant gain. Plant gain is the responsiveness of the controlled system.

4. Congenital central hypoventilation syndrome (CCHS) is a condition produced by an abnormal gene, PHOX2b. The number of tandem repeats in this gene determines the severity of hypoventilation. Hypoventilation and corresponding hypoxemia is greatest in NREM sleep. In wakefulness and with exercise, there is manifested increased respiratory drive, suggesting that responses to changes in metabolic rate might be key to this PHOX2b abnormality.

Question #2

Instructions

Where you find multiple questions within the same question subpart, label your answer using the letter that corresponds to the letter in the question. Example: Question: (A) what is … (B) explain.... (C) describe… Answer: (A) definition is…, (B) the explanation is, (C) description.

A mixed apnea is the result of a combination of absent breaths and obstructed breaths. Mixed apneas are often treated clinically in the same manner as obstructive apneas. Yet patients with mixed apneas appear to have unstable breathing during wakefulness and respond to CPAP treatment with the appearance of central apnea, and lead to the recognition of "complex sleep apnea." There is a therapy – Adaptive Support Ventilation (ASV) – used to treat this condition. ASV is a closed-loop ventilation mode that can act both as pressure support ventilation (PSV) and pressure-controlled ventilation.

Questions

1. Identify the factors that contribute to the generation of a mixed apnea. (2–3 short sentences)
2. Describe the feature of mixed sleep apnea that is treated with CPAP. (2–3 sentences)
3. Describe the features of complex sleep apnea that make it difficult to manage. (2–3 sentences)
4. What are the elements needed for a prescription of ASV?

Ideal Answers

1. There is the mechanical property of critical closing pressure that results in closure of the upper airway when atmospheric pressure exceeds the dilating force. Then there is the reduction in respiratory drive at the onset of apnea that is manifested by a "central" component, absence of airflow with absence of effort.
2. CPAP addresses the abnormality in Pcrit by providing a dilating force from the inside of the upper airway by positive nasal pressure.
3. This combination of drive and abnormal mechanical properties requires one to know that addressing the patient's correctable anatomic problem may not prevent sleep-disordered breathing and consider medical conditions and therapy related to high loop gain conditions.

4. There is a value for the expiratory pressure needed to keep the airway open, a minimal driving pressure to support an inspiratory breath (usually 4 cmH_2O), a maximal pressure (usually 20 cmH_2O) for the support, and a maximal pressure (often set at 25 cmH_2O). There may also be a backup rate and an average minute ventilation. [n.b. Different manufacturers have different settings for home machines.]

Sleep-Disordered Breathing

Instructions

Where you find multiple questions within the same question subpart, label your answer using the letter that corresponds to the letter in the question. Example: Question: (A) what is … (B) explain.... (C) describe… Answer: (A) definition is…, (B) the explanation is, (C) description.

Mr. Joe Smith, a 55-year-old man, presented to his physician with peripheral edema. He had a prior myocardial infarction at age 52. A coronary artery stent was placed in the right main and he was placed on atorvastatin 40 mg, aspirin 81 mg, and metoprolol 25 mg twice daily. He exercised once a week and had shortness of breath on walking up two flights of stairs. A history of loud snoring heard in the next room, observed pauses in breathing during sleep, difficulty in getting and maintaining an erection, and chest pain awakening him from sleep was elicited. He denies indigestion, reflux, or loss of weight. He has some fatigue during the day but does not fall asleep unexpectedly. The ESS is 10/24. He had a fall-asleep car crash when he was 22 years of age, ascribed to a long drive back home over Christmas, but no others in the past 20 years.

Examination: BP 153/92 mmHg, pulse 53 and regular, respirations 12/min. He was not in acute distress. The Mallampati score is 3, and there is no tonsillar hypertrophy or nasal obstruction. The tongue appears normal. JVP was elevated 2 cm above the sternal angle. Wheezing and rhonchi were absent and bibasilar rales were present at both bases. The cardiac impulse could not be seen. S1 was normal, S2 single, and no other extra sounds were appreciated. The abdominal and musculoskeletal examination was normal. Edema was present in both legs to just above the ankle.

A study was ordered.

Summary of Polysomnographic Findings

The patient was studied from 10:51 p.m. to 6:54 a.m. with a total time in bed of 483.0 min and 195.0 min total sleep time. Sleep maintenance efficiency was 55.4 %. Sleep architecture revealed sleep latency 130.0 min and REM latency 265.0 min. Sleep stage distribution, as a percent of total sleep time, was 5.1 %, stage-1; 34.9 %, stage-2; 29.2 %, SWS; and 30.8 %, stage REM sleep. There were 16 awakenings.

71 arousals were associated with respiratory events, 2 with periodic leg movements, as well as 42 spontaneous for a total arousal index of 35.4 per hour.

Respiratory recording revealed 43 obstructive apneas, 12 central apneas, 23 mixed apneas, 78 hypopneas, and 10 respiratory effort-related arousal events (RERA's). The REM-related AHI was 88.0. 161.5 min of sleep was recorded while the patient was in the supine position for an AHI of 51. REM/supine AHI is 88.0. Snoring was recorded 6.6 % of the study. Baseline oxygen saturation was 92 % with 32 % time less than 90 % saturation. The lowest saturation was 75.0 %. Average heart rate was 63.3 beats per minute. Periodic limb movement index was 8.3 per hour.

A therapeutic trial was instituted.

Sleep-Disordered Breathing

Part 1 (Total Points: 5)

Questions

1. Based on the given history and physical, create a differential diagnosis for the presentation of this patient.
2. What are the risk factors for sleep apnea in this patient?
3. Describe the putative effects of aspirin and metoprolol on the pathophysiology of obstructive sleep apnea. Limit response to 2–3 sentences.
4. In 2–3 sentences, describe the likely change in Mr. Smith's pretest probability of his BMI being 33 vs. 24.

Ideal Answers

1. Obstructive sleep apnea, central sleep apnea, Cheyne-Stokes respiration or recurrent central apneas, sleep apnea in the setting of hypothyroidism, and coronary heart disease with or without sleep-disordered breathing.
2. The collection of symptoms – snoring heard in the next room, pauses during sleep, nocturnal angina, HTN, and history of cardiovascular disease – leads to a high pretest probability. Sleepiness that is out of the ordinary is not present here but would be another risk factor supporting a high pretest probability. While emphasized in the popular literature, a history of erectile dysfunction is not sensitive or specific; neither is snoring alone, hypertension alone, or obesity alone.
3. Obstructive sleep apnea and central sleep apnea are associated with factors that both increase sympathetic activation and thrombotic risk. Beta blockers will reduce neuro-excitatory, sympathetic outflow, and aspirin is an antithrombotic and anti-inflammatory agent.
4. Obesity, as defined by a BMI >30, confers a sevenfold higher risk of sleep apnea, with many other risk factors (age, gender, hypertension, etc.) held constant. In this case, however, obesity may not play as large a risk given the concern for congestive heart failure.

Part 2 (Total Points: 5)

Questions

1. What is the numerical value of the AHI? Show your calculations. What is the severity as judged by this value?
2. Define and provide the numerical value for RDI?
3. Describe the differences and similarities between obstructive sleep apnea and mixed sleep apnea? Limit your response to 4–6 sentences.
4. In 3–5 sentences, describe the mechanisms that lead to hypertension in the setting of sleep-disordered breathing.

Ideal Answers

1. 23 OA, 17 CA, 28 MA, 78 H = 156/(195/60) = 156/3.25 = 48 total apnea-hypopnea index (AHI).
2. The respiratory disturbance index (RDI) is the AHI plus respiratory effort-related arousals and in this case is 166/3.25 or 51.
3. In an obstructive apnea, there is cessation of airflow for at least 10 s, and there appear efforts to breathe as indicated by esophageal pressure or measures of thoracic and/or abdominal movement. In a mixed apnea, there is a portion of the apnea where there is an absence of respiratory effort. Usually this appears in the first half rather than the second of the apnea event.
4. Systemic vascular resistance will increase at night due to arousals from sleep, hypoxemia, and changes in respiratory efforts leading to changes in preload. During the day, blood pressure remains elevated in the absence of apnea and is associated with indices of increased sympathetic nerve activity and excretion of norepinephrine.

Part 3 (Total Points: 5)

Treatment is recommended for the patient based upon his PSG result, and anatomy, and his insurance status.

Questions

1. What therapy would you choose and why?
2. What is the definition of Pcrit? Use 3–5 sentences to explain the measure.
3. In respiratory physiology, loop gain is the tendency to return to resting ventilation. What are the components of loop gain? Use 3–5 sentences to explain the measure.

Ideal Answers

1. Of the three major therapeutic options (surgery, CPAP, or oral appliance), the best evidence-based approach for this patient with a predominance of obstructive apneas and hypopneas is CPAP. The number of events is too high for immediate

consideration of an oral appliance, and this therapy may not be covered by insurance. Surgery could be considered if CPAP fails, as the predictability of CPAP effectiveness is generally lower than CPAP or oral appliance.
2. Pcrit stands for critical closing pressure of the airway and can be measured during sleep. In the context of sleep apnea, it represents the pressure when the airway nearly closes or is closed. People without snoring have a Pcrit that is negative, that is, the airway is in an open position and will require a negative pressure to close it. It may vary among individuals even if they are grouped into snorers or mild, moderate, or severe sleep apnea. The latter is associated with Pcrit values >4 cmH_2O. This critical closing pressure can be reduced (making the airway harder to close) by muscle activation, weight loss, electrical stimulation of the hypoglossal nerve, and position.
3. Loop gain is comprised of plant gain and controller gain. Plant gain is the stiffness or elasticity of the physical components of the respiratory system (upper airway, lungs, chest wall, and neuromuscular activation). Controller gain is the properties of the sensors for oxygen and carbon dioxide and the central control system. Both contribute to overall loop gain. A high loop gain is present in recurrent central apneas and plays a role in recurrent obstructive apneas. In this instance, the high number of central and mixed apneas represents a high loop gain.

Part 4 (Total Points: 5)

The type of sleep apnea represented by Mr. Smith, when adequately treated, should have some predictable outcomes.

Questions

1. In 2–4 sentences, list the health outcomes that are known to improve in randomized controlled trials of CPAP.
2. In 2–3 sentences, what predicts long-term adherence to CPAP?
3. In 2–3 sentences, what are potential long-term economic benefits to the individual and the health system?

Ideal Answers

1. It is the quality of life measures and sleepiness in particular that is the most consistent improvement in outcome trials. There is some evidence that blood pressure is reduced. In groups with high cardiovascular risk profiles, there may be a reduction in all cause mortality and stroke.
2. Short-term compliance to CPAP may be determined in the first week of therapy and is improved by education about the manner and purpose of therapy and by reacting to concerns and problems with CPAP use. The presence of sleepiness at the time of diagnosis is one well-recognized factor. Recent work has focused on individual features of self-efficacy as a predictor, possibly improved by motivational counseling.

3. Studies in managed care systems show that while prior to diagnosis the health-care utilization for those diagnosed with sleep apnea is higher than those presumably without sleep apnea, with diagnosis and intent to treat, there is a reduction in health-care utilization and prolongation of life expectancy, the latter equally true of older as well as younger individuals.

Part 5 (Total Points: 5)

Six months later, Mr. Smith feels better and more relaxed; others notice that he is more alert. The ESS is 8/24. Blood pressure is controlled well (120–125/75–80) on the same medications. He has no chest pain at night, and no lower extremity edema. However, Mr. Smith is a long-distance truck driver, and he has an excellent driving record. He is up for renewal of his commercial driver's license. The medical examiner asks him to see a sleep specialist to give an opinion as to his ability to operate a truck.

Questions

1. In 2–3 sentences, what features of the presentation and the testing put Mr. Smith at risk for a fall-asleep car crash secondary to sleep apnea?
2. In 2–3 sentences, what factor does the National Transportation and Safety Administration say is the most objective risk for sleep apnea?
3. In 2–3 sentences, what is your assessment of risk after CPAP therapy for OSA in Mr. Smith?

IQ Case

In the IQ case, the goal of this exercise is explicit and presented to the student group, but the learning objectives disclosed only after the fact, leaving the learner in the position of seeking and evaluating information toward the goal. The case here is designed as longer than an hour in the development of learning objectives and an hour in follow-up of the group on the objectives.

IQ Case #1 Ms. Ton Sil for Student

Goal: Understand the presentation associated with and mechanisms of normal breathing during sleep, abnormal breathing during sleep, its impact on behavior and mood, and how such properties are changed for the better or worse by surgical therapy.

Case Vignette

65 y/o AA F (BMI 41) was sent to sleep clinic for snoring. Patient's snoring very loud (heard from adjacent rooms). ESS 3/24, no drowsy driving. No narcolepsy/cataplexy, RLS, parasomnia, sleep paralysis.

- PMH: GERD, COPD, CHF, DJD, HTN, DM
- Never used alcohol. No caffeinated beverage
- MEDS: glyburide, metformin, Nexium, verapamil, lisinopril, HCTZ, Pro-Air, Advair, aspirin

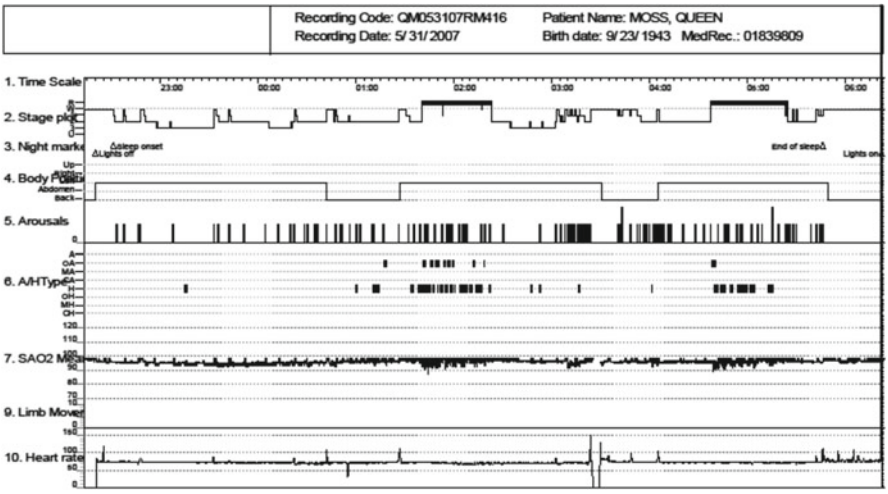
At bedtime, the patient turns out the light at 11 p.m. but otherwise has no routine for going to bed. Sleep onset is described as taking 15 min to get to sleep. Only occasionally does she have a "good night's sleep." Occasionally awakens from a dream with a choking sensation, sometimes in a sweat, and takes ~30 min to fall back asleep. She awakens and gets up in the morning feeling unrefreshed at 7 a.m. to get the grandchildren off to school. She feels tired all day long and loses her concentration and has lapses ("zoning out") more quickly than before. Her ESS is 4/24.

She states that when she was younger, her sleep was shorter. She does not smoke cigarette now but did when she was young. She has always drunk coffee and tea and now has increased her intake to "get going in the morning." She was diagnosed with hypertension 30 years ago. She was thin until the age of 44 year. Her snoring has increased gradually over the past 15 years. She no longer has hot flashes. Snoring was better on hormone replacement, but she was taken off because of breast cancer concerns.

A physical exam was performed.

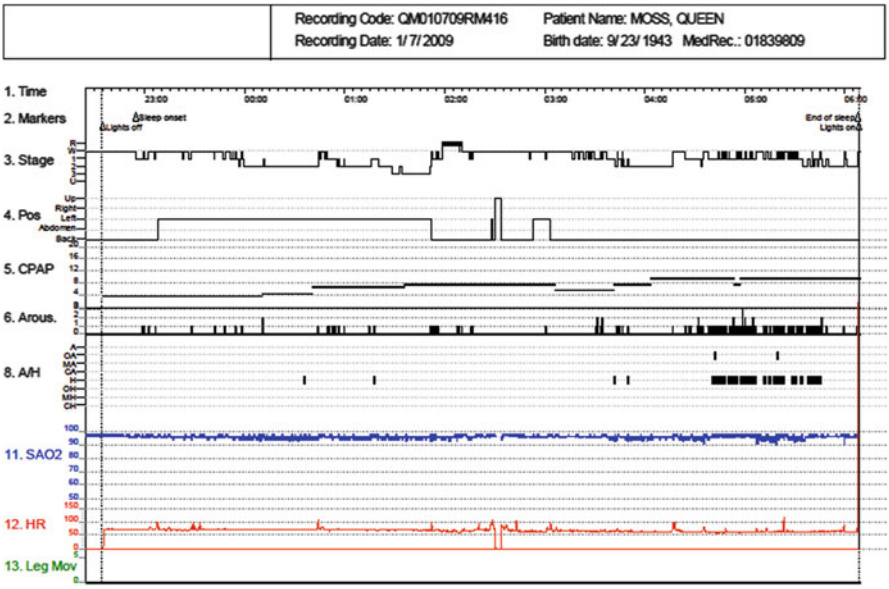
GA: Obese AA in NAD
VS: BP 132/67, HR 79, 97 % on RA
HEENT: neck circumference: 50 cm, nasal septal deviation to the right. Mallampati IV, 3+ tonsils, large uvula and tongue. No retrognathia
Lungs: clear B/L
Heart: S1, S2, RRR
Neuro: intact

On the basis of this history and physical, you decide order testing.
Below is a hyponogram of the study.

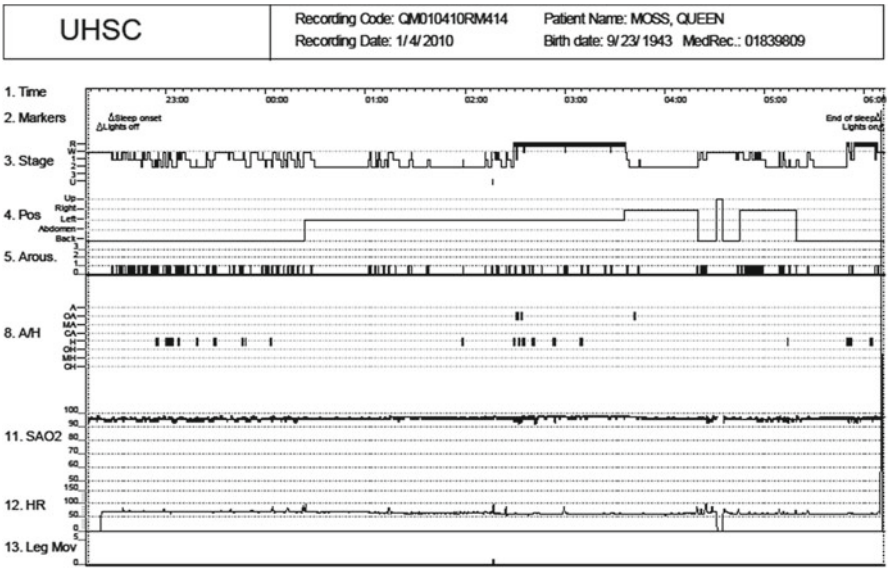


Sleep efficiency 79 % (380/491 min)
Sleep latency 11 min, REM latency 189
REM sleep 20 %, NREM 78 %
Supine 0 % of REM, 12 % of NREM
Overall AHI 11, REM AHI 38.9, NREM AHI 2.8
Baseline O_2 sat 97 %, lowest recorded 88 %

The patient was scheduled for a CPAP titration. Below is a hyponogram of this study.



The patient stated that this was the worst time of her life with sleep.



The procedure was a septoplasty, UPPP, and tongue reduction by somnoplasty. The patient at 1 year has no snoring and daytime energy levels are improved.

IQ Case # 1 Ms. Ton Sil for Facilitator

Goal: Understand the presentation associated with and mechanisms of normal breathing during sleep, abnormal breathing during sleep, its impact on behavior and mood, and how such properties are changed for the better or worse by surgical therapy.

Learning Objectives

A. Create a differential diagnosis for sleep-disordered breathing.
B. Name precipitating, perpetuating, and maintaining features for sleep apnea.
C. Relate the personal and societal cost of sleep apnea.
D. Correlate the neurophysiology of sleep and its different stages with that of respiratory control.
E. Apply the concepts of Pcrit and loop gain to the treatment of obstructive sleep apnea
F. Describe the mechanisms of actions, benefits, and side effects of surgical treatment of sleep apnea.

Case Vignette

65 y/o AA F (BMI 41) was sent to sleep clinic for snoring. Patient's snoring very loud (heard from adjacent rooms). ESS 3/24, no drowsy driving. No narcolepsy/cataplexy, RLS, parasomnia, sleep paralysis.

- PMH: GERD, COPD, CHF, DLD, HTN, DM
- Never used alcohol. No caffeinated beverage
- MEDS: glyburide, metformin, Nexium, verapamil, lisinopril, HCTZ, Pro-Air, Advair, aspirin

Probing Questions

1. What are the risk factors for sleep apnea in this patient?
2. Can clinical severity of sleep apnea be classified? Does this mean something in regard to pretest probability?
3. What is the significance of the past medical history?

At bedtime, the patient turns out the light at 11 p.m. but otherwise has no routine for going to bed. Sleep onset is described as taking 15 min to get to sleep. Only occasionally does she have a "good night's sleep." Occasionally awakens from a dream with a choking sensation, sometimes in a sweat, and takes ~30 min to fall back asleep. She awakens and gets up in the morning feeling unrefreshed at 7 a.m. to get the grandchildren off to school. She feels tired all day long and loses her concentration more quickly than before. Her ESS is 3/24.

Probing Questions

4. What things make going to sleep better or worse in this case?
5. Why does she wake up choking, sometimes in a sweat?

She states that when she was younger her sleep was shorter. She does not smoke cigarettes now but did when she was young. She has always drunk coffee and tea and now has her intake to "get going in the morning." Her snoring has increased over the past 15 years. She was diagnosed with hypertension 30 years ago. She was thin until the age of 44 years. She no longer has hot flashes. Snoring was better on hormone replacement.

Probing Questions

6. What is sleep hygiene?
7. Why ask about sleep habits and quality at a younger age?
8. What are the diagnostic features and differential diagnosis for snoring?
9. Can COPD, HF, or HTN cause sleep apnea?
10. What is the effect of hormone replacement on snoring?

A physical exam was performed.

GA: Obese AA in NAD
VS: BP 132/67, HR 79, 97 % on RA
HEENT: neck circumference: 50 cm, nasal septal deviation to the right. Mallampati IV, 3+ tonsils, large uvula and tongue. No retrognathia
Lungs: clear B/L
Heart: S1, S2, RRR
Neuro: intact

Probing Question

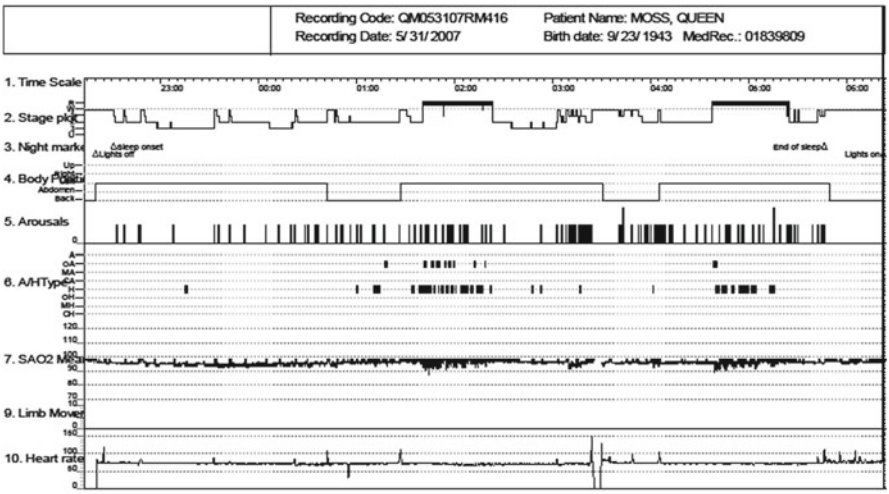
7. Does a physical examination have value in snoring?

On the basis of this history and physical, you decide order testing.

Probing Question

8. What are the indications?

Below is a hyponogram of the study.

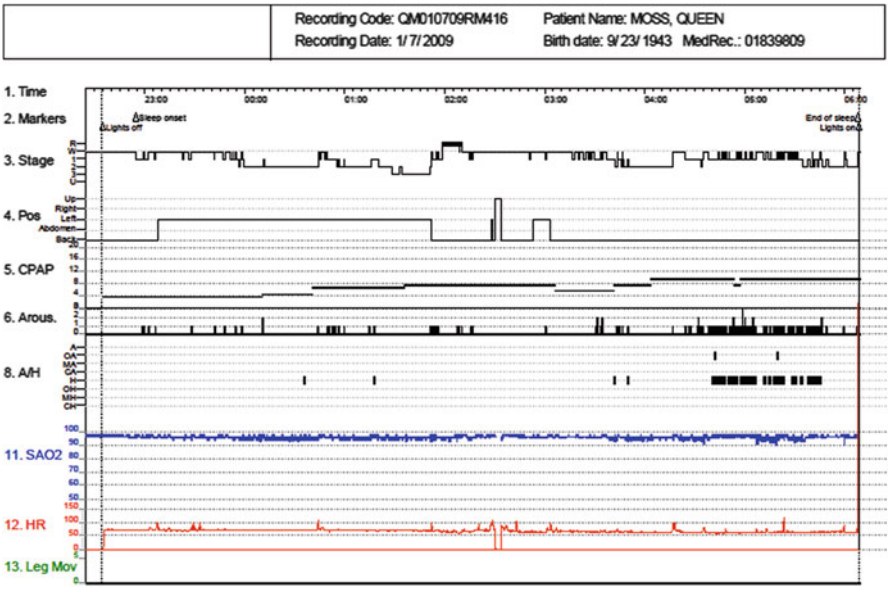


Sleep efficiency 79 % (380/491 min)
Sleep latency 11 min, REM latency 189
REM sleep 20 %, NREM 78 %
Supine 0 % of REM, 12 % of NREM
Overall AHI 11, REM AHI 38.9, NREM AHI 2.8
Baseline O_2 sat 97 %, lowest recorded 88 %

Probing Questions

9. What do you tell the patient?
10. What do you want to do now and why?

The patient was scheduled for a CPAP titration. Below is a hyponogram of this study.

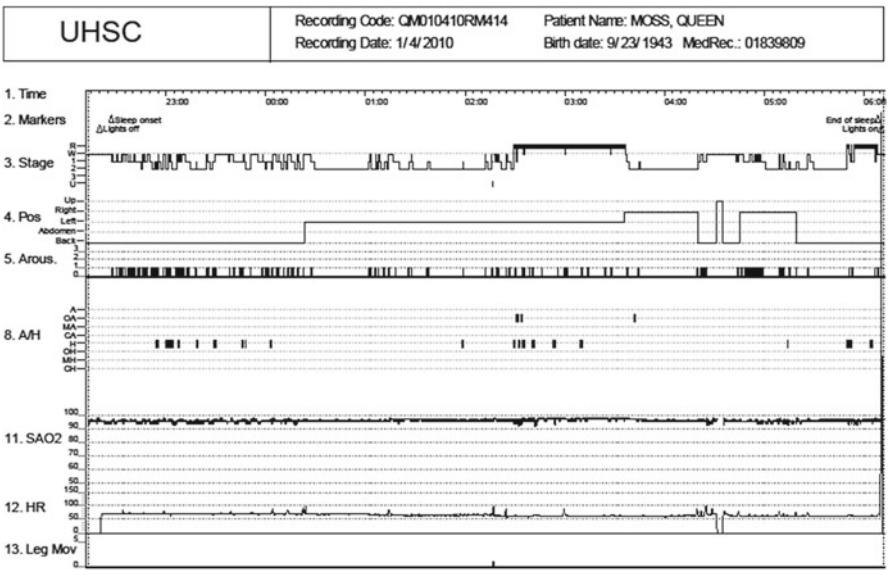


The patient stated that this was the worst time of her life with sleep.

Probing Questions

11. What do you tell the patient? What do you do now?

The patient had a consultation with an ENT surgeon, and 6 months later this was the hyponogram.



The patient has been symptom free for 1 year.

Probing Questions

12. What was performed or done?
13. Why did it work?
14. How likely is this to work?

Resources

Highly Recommended

Practice Parameters and Guidelines from the AASM

IQ Student Guide

Executive Summary: This case is designed to introduce the fellow to the general topic of sleep-disordered breathing. It has features in it which relate to epidemiology and societal impact, pathophysiology, personal impact on health and family, and management decisions. It is a model work-up with clinical issues that often occur.

At the end of this session the group should be able to recognize the generality of this presentation and utilize the approach described in the case vignette in a practice setting. There are two "twists." One is that this patient has a low apnea-hypopnea index (event rate or AHI) overall but a high REM-related event rate and hated CPAP. The other is the finding that her sleep problems are cured by surgery.

Probing Questions

1. *Probing questions*

   What the risk factors for sleep apnea in this patient?
   Can clinical severity of sleep apnea be classified? Does this mean something in regard to pretest probability?
   What is the significance of the past medical history?

2. *Probing questions*

   What things make going to sleep better or worse in this case?
   Why does she wake up choking, sometimes in a sweat?

3. *Probing questions*

   What is sleep hygiene?
   Why ask about sleep habits and quality at a younger age?
   What are the diagnostic features and differential diagnosis for snoring?
   Can COPD, HF, or HTN cause sleep apnea?
   What is the effect of hormone replacement on snoring?

4. *Probing questions*

   Does a physical examination have value in snoring?

5. *Probing questions*

   What do you tell the patient? What do you want to do now and why?

6. *Probing questions*

   What do you tell the patient? What do you do now?

7. *Probing questions*

   What was performed or done? Why did it work? How likely is this to work?

IQ Case #1 Sleep-Disordered Breathing: Handout/Objectives

Goal: Understand the presentation associated with and mechanisms of normal breathing during sleep, abnormal breathing during sleep, its impact on behavior and mood, and how they are changed for the better or worse by surgical therapy.

Learning Objectives

A. Create a differential diagnosis for sleep-disordered breathing.
B. Name precipitating, perpetuating, and maintaining features for sleep apnea.
C. Relate the personal and societal cost of sleep apnea.
D. Correlate the neurophysiology of sleep and its different stages with that of respiratory control.
E. Apply the concepts of Pcrit and loop gain to the treatment of obstructive sleep apnea
F. Describe the mechanisms of actions, benefits, and side effects of surgical treatment of sleep apnea.

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Chapter 14
Sleep and Neurologic Disorders

Jessica Vensel Rundo, Tina Waters, Charles Bae, Carlos Rodriguez, and Nancy Foldvary-Schaefer

Introduction

Sleep disturbances in neurologic disorders are common patient complaints, negatively impact patients by causing unrefreshing sleep, hypersomnia and/or insomnia, and may be the first sign of neurologic disease.

Knowledge and skills for sleep medicine fellowship ACGME programs (http://www.acgme.org/acWebsite/downloads/RRC_progReq/520_sleep_medicine_07012012.pdf) list neurologic disorders and its related disorders in all areas of expected general training competencies. For example, sleep fellows should have experience with and develop competence in sleep disorders associated with common medical, neurologic, and psychiatric conditions. Each program is required to have patients in the major categories of sleep disorders including idiopathic hypersomnia, narcolepsy, and sleep problems related to other factors and diseases, including medications, and psychiatric and other medical disorders. Additionally, sleep fellows should have formal instruction in polysomnograms with full EEG montages for seizure detection. Other chapters focus on primary disorders of sleep with a neurologic pathogenesis; this chapter addresses the presentation of sleep complaints and disorders in the context of primary neurologic disorders.

J. Vensel Rundo, M.D., M.S. • T. Waters, M.D. • C. Bae, M.D. • C. Rodriguez, M.D.
N. Foldvary-Schaefer, D.O., M.S. (✉)
Sleep Disorders Center, Cleveland Clinic Main Campus, 9500 Euclid Avenue,
Cleveland, OH 44195, USA
e-mail: foldvan@ccf.org

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For this chapter, content domains were developed through discussions with sleep medicine faculty and prior fellows about current and/or best practice and collection of existing material on the topic of training topics. The articulations of general competencies in sleep medicine for sleep medicine fellows in neurology are organized by the AAN (American Academy of Neurology) (Table 14.1). Additionally, core competencies and curriculum guidelines for neurologic disorders were reviewed for residencies in otolaryngology (American Board of Otolaryngology), pediatrics (American Board of Pediatrics, American Academy of Pediatrics, Council of Pediatric Subspecialties), family practice (American Academy of Family Practice, American Board of Family Practice), internal medicine (American Board of Internal Medicine, American College of Physicians: Internal Medicine, Alliance for Academic Internal Medicine), and psychiatry (American Psychiatry Association, American Board of Psychiatry and Neurology). When compared to the AAN sleep medicine competencies, there is significant variability in the depth of coverage of sleep disturbances and neurologic disorders listed in the other subspecialty guidelines and general competencies.

The chapter topics will focus on the most commonly encountered neurologic disorders in the sleep patient. This will include peripheral neuropathy in the setting of restless legs syndrome, stroke and sleep-disordered breathing, the differentiation of nocturnal seizures and parasomnias, and hypersomnia with secondary neurologic causes. Other neurologic problems to be addressed in this chapter include neurodegenerative diseases, headaches, head trauma, brain tumors, and neuromuscular disease.

Table 14.1 lists topics for content domains relevant to a sleep medicine fellowship. These illustrate the field of neurologic disorders in sleep along with corresponding ACGME competencies and are illustrated in Table 14.1. These areas touch upon all aspects of practice and basic issues. Some of the knowledge areas like epidemiology can be reading various relevant chapters and attending didactic presentations which the program could subsequently test for factual proficiency through standardized testing, exercises in matching, structured essay answers, etc. Topics like patient assessments are taught more commonly by example and assessed better by observation and immediate feedback. The art of the clinical assessments in practice will vary; however, here one should attempt to define a standard trainee expectation for relevant features of an assessment including the appropriate ordering of tests.

Some examples of objectives for a given content area are presented in Table 14.2. The delivery would be delivered through a variety of venues but with appropriate goals and learning objectives. Any presentation would address specific knowledge, skills, and attitudes a fellow should be able to exhibit following instruction. Note that this list tries to define work-related, measureable, or verifiable outcomes. One can list either the objectives up front or at the middle or end of the instruction. Approaches can be creative in when and how objectives are verified.

The individual training program should modify the list so as to address or strength or weakness in overall instructional plan or expertise. One can use Essay Questions to amplify a topic. A faculty or fellow can use the list and choose to construct lectures based on one or more objectives. Working on this list is a useful exercise to review prior presentations of topics or for year-end reviews.

Illustrations of Content Delivery and Formative Assessments

Also included in this chapter are Recall Matching Answer sets where the student is asked to match the "right" answer to any one or more of presented questions. Some of the questions may be straightforward definitions, while others may be presented in case-based or descriptive formats.

Essay Questions can be given before or after a presentation on the topic of neurologic disorders or at intervals during the fellowship to review a topic. The purpose is to have the learner synthesize the material and reform it and to assess not only the objectives but written communication skills. Essay Questions are provided for the material along with "ideal" answers for reference and discussion.

The IQ case has an explicit goal, but the learning objectives are disclosed only after the fact. The case here is designed as longer than an hour in the development of learning objectives and an hour in follow-up of the group on the objectives.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/sleep-in-neurologic-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the Essay Questions or IQ case.

Table 14.1. Content Covered and Competencies Assessed Examples

		Knowledge	Skills	ACGME competency
I	*Basic science*	Yes	No	
	Sleep and chronobiology			B
	Phylogeny of sleep			B
	Neurophysiology of sleep, basic brain mechanisms underlying REM and NREM sleep			B
	Neuropharmacological and neurochemical substrate			B
	Ontogeny of sleep – basic mechanism			B
	Circadian rhythmicity			
	Characteristics of the circadian clock			B
	Neural basis of circadian rhythmicity			B
	Interaction between activity, sleep, and circadian rhythm			B
	Metabolism – endocrine investigation and sleep			B
	Behavior and sleep: learning and memory, neurobiology of dreaming			B
II	*Pathophysiology/epidemiology*	Yes	No	
	The impact of sleep and chronobiology on the controls of all vital functions			B
	Genetics of sleep states and circadian rhythms			B
	Epidemiology of sleep disorders and sleep habits			A, B, F
	Central sleep apnea syndrome, from the central command to impairment of the muscular effector mechanism			B, F

(continued)

(continued)

		Knowledge	Skills	ACGME competency
III	*Clinical features*	Yes	Yes	
	Hygiene and sleep			A, B, D
	Disorders of initiating and maintaining sleep			A, B
	Disorders of excessive sleepiness			A, B
	Narcolepsy and the hypersomnias			A, B
	Sleep-disordered breathing			A, B
	Periodic limb movement and restless legs syndrome			A, B
	Other movement disorders and sleep (particularly Parkinson's and dystonia)			A, B
	Parasomnias			A, B
	Confusional arousals and terrors			A, B
	Somnambulism and REM behavior disorders			A, B
	Sundown syndromes			A, B
	The epilepsies and sleep			A, B
	The disorders of sleep/wake schedule			A, B
	Pediatric sleep disorders			A, B
IV	*Patient assessments*	Yes	Yes	
	Essentials of the patient interview in sleep medicine			A, B, D, E
V	*Diagnostic measurements and interpretation*	Yes	Yes	
	The diagnostic classification of sleep/wake disorders (ICSD-2)			B
	Physiological parameters and generation of electrical signals which are measured during the sleep studies			B
	Basic electronics and electrical safety			B
	Signal processing			B
	The essentials of sleep laboratory recordings			B
VI	*Disease management*	Yes	Yes	
	Treatment of disorders of initiating and maintaining sleep			A, B, C, F
	Sleep apnea treatment with nasal, bi-level, and auto continuous positive airway pressure (CPAP, BiPAP, autoCPAP)			A, B, C, F
	The role of nocturnal oxygen for sleep-disordered breathing			A, B, C, F
VII	*Health and disease clinical pathways*	Yes	Yes	
	The behavioral modifications and health benefits in regard to alertness and productivity			A, C, F
	The impact of pathophysiology and treatment of common diseases			A, C, F
	Major complications of sleep apnea: from stroke to cardiovascular disease			A, C, F
	The medicolegal aspects of sleep disorders			A, C, F
	Excessive sleepiness: industrial and driving accidents			A, C, F
	Effects on sleep and wakefulness of neurologic and psychiatric disorders			A, C, F

Code for ACGME competencies

A. Patient care	D. Interpersonal skills
B. Medical knowledge	E. Professionalism
C. Practice-based learning and improvement	F. System-based practice

Table 14.2 Examples of Topics with Education Objectives from AAN Competencies

Item I. Neurophysiology
- Define the stages of sleep and their electrodiagnostic and behavioral characteristics
- List the neurotransmitters/hormones that are active during wake, REM, and NREM sleep
- Describe the main pathways for controlling the circadian rhythm for sleep
- Explain the homeostatic and circadian regulation of sleep and include melatonin's effect
- Compare changes in hormone levels (TSH, prolactin, cortisol levels, etc.) to the circadian rhythm and onset of sleep

Item II. Epidemiology
- List the genes that have been linked to delayed sleep-phase syndrome and advanced sleep-phase syndrome
- Describe the age of onset, gender, and comorbid conditions frequently seen in patients with REM sleep behavior disorder
- Assess risk of stroke in patients with untreated obstructive sleep apnea
- Give the prevalence of narcolepsy in patients with multiple sclerosis
- Relate sleep quality and quantity to successful seizure control in epileptic patients

Item III. Mechanisms of health and disease
- List good sleep hygiene habits
- Review the impact of sleep deprivation on memory and cognitive function
- Explain how sleep habits can affect disorders of wakefulness, excessive daytime sleepiness, and sleep-disordered breathing
- Describe the mechanisms leading to central sleep apnea syndrome, including the central respiratory centers and muscular impairment
- Discuss primary and secondary types of disorders of initiating and maintaining sleep
- Explain the correlation between neurodegenerative diseases, such as Parkinson's disease, and REM sleep behavior disorder
- Give comorbid causes of restless legs syndrome
- Propose the mechanism for why nocturnal seizures occur more frequently during sleep/wake transitions

Item IV. Patient assessments
- Determine essential features of the clinical history in a patient complaining of hypersomnia
- Review the portion of the neurologic exam that is important to perform in any patient with RLS
- Discuss the importance of sleep logs and actigraphy in patients suspected of having a circadian rhythm disorder
- Review how to approach a patient with dementia, also complaining of difficulties with sleeping

Item V. Diagnostic measures and interpretation
- List the physiological parameters required for in-lab attended polysomnograms versus home sleep testing
- Give the pertinent lab tests that should be performed in patients with RLS and peripheral neuropathy
- Determine when neuroradiographic imaging should be considered in patients with narcolepsy

Item VI. Disease management
- Explain strategies that could be used to help a patient with neurologic dysfunction (weakness from a stroke, rigidity from Parkinson's disease, etc.) to tolerate a CPAP mask for treatment of OSA
- Determine parameters for monitoring of stimulants in patients with narcolepsy

Give a treatment plan for patients with poorly controlled RLS symptoms, suffering with augmentation from dopamine agonists

Matching Test

Questions

Obstructive sleep apnea is genetically associated with which neurodegenerative disorder? ☐
The pathophysiology of fatal familial insomnia includes destruction of which brain structure? ☐
Sundowning is more commonly seen in which neurodegenerative disorder? ☐
Based on AAN Practice Parameters, noninvasive ventilation is typically started on ALS patients when the FVC reaches less than which percentage? ☐
Which headache type only occurs with sleep? ☐
Which condition is characterized by visual loss which is associated with nocturnal sleep-related visual hallucinations? ☐
Which fatigable autoimmune neuromuscular junction disease is associated with sleep apnea? ☐
Interictal epileptiform discharges in focal epilepsies tend to be the lowest during which stage of sleep? ☐
Which genetic disorder associated with an abnormality on chromosome 19 has a high prevalence of narcolepsy and sleep-related breathing disorders? ☐
What is the average period of the human circadian pacemaker? ☐
Which hormone is sleep dependent? ☐
In the setting of a traumatic coma, which of the following is associated with a better prognosis? ☐
What nerve conduction study waveform is inhibited during cataplexy? ☐
Researchers have speculated that demyelinating lesions in this brainstem pathway which regulates the motor control of the upper respiratory tract may be responsible for sleep-related breathing disorders in multiple sclerosis patients. ☐
Which parasomnia is characterized by a sudden loud noise or sense of explosion in the head either at the sleep–wake transition or upon waking during the night? ☐
Which tremor continues during sleep? ☐
Sleeping sickness is caused by an infection from which parasite? ☐
Which is the most common form of focal epilepsy in adults and adolescents? ☐
What is a preferred treatment for patients with RBD who have balance problems? ☐

Answers

1. Charles Bonnet syndrome
2. Lambert–Eaton myasthenic syndrome
3. Early appearance of sleep–wake cycling
4. Eszopiclone
5. Clonazepam
6. 24.2 h
7. Lennox–Gastaut syndrome
8. Nocturnal frontal lobe epilepsy
9. Trypanosoma evansi
10. Melatonin
11. 50 %
12. Trypanosoma cruzi
13. Growth hormone
14. Essential tremor
15. Confusional arousal
16. Thunderclap headache
17. Tectospinal tract
18. Spinal trigeminal tract
19. F-wave
20. REM
21. Trypanosoma brucei
22. M wave
23. Early appearance of hypersomnia during recovery
24. Early appearance of diffuse monophasic alpha waves
25. Cortisol
26. TSH
27. 24.4 h
28. 24.0 h
29. Reticulospinal tract
30. Down syndrome
31. Angelman syndrome
32. N3
33. Dorsomedial thalamic nucleus
34. Cervical myelopathy
35. Absence seizures
36. Migraine headache
37. H-reflex
38. Exploding head syndrome
39. 60 %
40. 40 %
41. Parkinson's disease
42. Multiple-system atrophy
43. Ventrolateral preoptic nucleus of the hypothalamus
44. Tuberomammillary nucleus
45. Alzheimer's disease
46. Lewy body dementia
47. Creutzfeldt–Jakob disease
48. Myasthenia gravis
49. N1
50. Botulism
51. Palatal tremor
52. Resting tremor
53. Progressive supranuclear palsy
54. Temporal lobe epilepsy
55. Shy–Drager syndrome
56. Hypnic headache
57. Myotonic dystrophy

Questions with Answers

Obstructive sleep apnea is genetically associated with which neurodegenerative disorder? 45

The pathophysiology of fatal familial insomnia includes destruction of which brain structure? 33

Sundowning is more commonly seen in which neurodegenerative disorder? 53

Based on AAN Practice Parameters, noninvasive ventilation is typically started on ALS patients when the FVC reaches less than which percentage? 11

Which headache type only occurs with sleep? 56

Which condition is characterized by visual loss which is associated with nocturnal sleep-related visual hallucinations? 1

Which fatigable autoimmune neuromuscular junction disease is associated with sleep apnea? 48

Interictal epileptiform discharges in focal epilepsies tend to be the lowest during which stage of sleep? 20

Which genetic disorder associated with an abnormality on chromosome 19 has a high prevalence of narcolepsy and sleep-related breathing disorders? 57

What is the average period of the human circadian pacemaker? 6

Which hormone is sleep dependent? 13

In the setting of a traumatic coma, which of the following is associated with a better prognosis? 3

What nerve conduction study waveform is inhibited during cataplexy? 37

Researchers have speculated that demyelinating lesions in this brainstem pathway which regulates the motor control of the upper respiratory tract may be responsible for sleep-related breathing disorders in multiple sclerosis patients. 29

Which parasomnia is characterized by a sudden loud noise or sense of explosion in the head either at the sleep–wake transition or upon waking during the night? 38

Which tremor continues during sleep? 51

Sleeping sickness is caused by an infection from which parasite? 21

Which is the most common form of focal epilepsy in adults and adolescents? 54

What is a preferred treatment for patients with RBD who have balance problems? 10 [1–4]

Essay Questions

Case Study 1

A 69-year-old male presents with difficulty falling asleep and recurrent awakenings from sleep. On further questioning, he complains of an urge to move his legs associated with an uncomfortable sensation which has a burning quality. This urge to move the legs is worse with rest and at night when he goes to sleep. The sensation is transiently alleviated by movement. On review of systems, he relates having some unsteadiness and has recently begun experiencing falls.

Questions

1. What is the likely diagnosis and what is in the differential diagnosis of this patient?
2. Explain what specific findings you should look for on examination of this patient.
3. Describe the initial workup for this patient. Would you obtain a polysomnogram?
4. How would you treat this patient? Are there medications you might want to avoid?

Ideal Answers

1. This patient meets the diagnostic criteria for restless legs syndrome (RLS). The differential diagnosis includes a variety of other conditions characterized by abnormal sensorimotor disturbances of the lower extremities. Akathisia is characterized by a generalized need to move the body in association with the use of dopamine receptor antagonists. Sleep-related leg cramps involve muscle hardening or pain that requires forceful stretching of the muscle rather than simple movement for relief. There is often residual pain or soreness at the site. Sleep starts or hypnic jerks are involuntary movements which occur at sleep onset without an associated urge to move the legs. Positional discomfort resolves by changing body position and is not associated with an urge to move the legs. Given the complaint of unsteadiness and falls, this patient may have a neurologic disorder consisting of peripheral neuropathy with or without central nervous system involvement.
2. Every patient with suspected RLS should have a neurologic examination including motor, sensory, and reflex testing to evaluate for peripheral neuropathy and myelopathy whether or not they have sensory or motor complaints as RLS has been associated with these conditions. Findings on neurologic examination in patients with peripheral neuropathy include atrophy and fasciculations of the lower extremity muscles; weakness of the lower extremity muscles; loss of light touch, pinprick, temperature, vibratory sensation, and proprioception of the lower extremities; and areflexia or hyporeflexia at the Achilles and patellae. Myelopathic findings include weakness of the lower extremities; increased tone of the lower extremities; loss of pinprick, temperature, vibratory sensation, and

proprioception of the lower extremities; sensory level involving the chest or abdomen; hyperreflexia at the Achilles and patellae; and a positive plantar (Babinski) response. Of note, crossed motor and sensory findings also can be seen with myelopathy.

On examination, the patient has normal motor strength, bulk, and tone. He has decreased temperature and pinprick sensation distal to the midshin bilaterally and decreased proprioception at the great toe bilaterally. Deep tendon reflexes are normal (2+) except at the patellae where reflexes are reduced (1+) and at the Achilles bilaterally where they are absent (0).

3. In addition to the standard lab testing for RLS that includes ferritin, iron, and total iron-binding capacity, a workup for peripheral neuropathy should be conducted as the patient has findings consistent with a distal symmetric peripheral neuropathy. Nerve conduction studies and electromyography (EMG) should be considered in the patient presenting with RLS and peripheral neuropathy. In patients with distal symmetric polyneuropathy, the highest yield lab screening tests are blood glucose, serum B12 with metabolites (methylmalonic acid with or without homocysteine), and serum protein immunofixation electrophoresis (AAN Practice Parameter by England et al.). Given the characteristic clinical features of RLS, a thorough history is usually all that is needed to diagnose RLS, and thus polysomnography is not indicated.
4. Although dopaminergic agonists have been considered the first-line treatment for RLS, the use of anticonvulsants like gabapentin and pregabalin should be considered in patients with both RLS and painful peripheral neuropathy. These agents reduce RLS symptoms and pain associated with peripheral neuropathy. Antidepressants agents which are commonly used for pain control in peripheral neuropathy like duloxetine, venlafaxine, and amitriptyline can precipitate or aggravate RLS and thus are best avoided. If a secondary source of RLS is identified, treatment of the underlying source should be initiated. If the serum ferritin is <50 ng/mL, treatment with ferrous sulfate and vitamin C should be initiated and a source of blood loss should be sought.

Case Study 2

A 56-year-old right-handed male with a past medical history of hypertension and hyperlipidemia presented with acute onset of aphasia and a right hemiplegia. He was diagnosed with a left middle cerebral artery (MCA) occlusion that was partially recanalized with intravenous tissue plasminogen activator (tPA). His deficits improved, but he was left with dysfluent speech and a moderate right hemiparesis rendering him disabled. While hospitalized he had a portable, four-channel polysomnogram (PSG) that showed an apnea–hypopnea index (AHI) of 8 with oxygen desaturations to 84 %. Over a decade earlier, his primary care physician referred him for a PSG due to snoring and witnessed apnea reported by his wife. He had a body mass index (BMI) of 40 kg/m^2 and a neck circumference of 18 in.

He cancelled the PSG since he felt that he had no sleep problems. Over the years, he refused several other sleep evaluations.

Questions

1. Describe the prevalence of stroke in the setting of untreated sleep-disordered breathing? What types of sleep-disordered breathing are common in patients with stroke?
2. What is the risk of stroke in the setting of untreated sleep apnea?
3. How would you have evaluated this patient for sleep apnea?
4. What are some barriers to PAP adherence after a stroke?

Ideal Answers

1. Sleep-disordered breathing affects the majority of patients with stroke. While central sleep apnea and Cheyne–Stokes respirations are observed, the majority of cases are of the obstructive type. A 2010 meta-analysis showed that up to 72 % of stroke patients have obstructive sleep apnea. Only 7 % of patients have primarily central apneas.
2. The Sleep Heart Health Study found that patients with sleep apnea have a risk of stroke roughly three times that of the general population (hazard ratio 2.86) after adjusting for cerebrovascular risk factors.
3. Laboratory PSG is the preferred study in patients with suspected sleep-disordered breathing and comorbid conditions including stroke. Laboratory PSG will provide a more accurate estimation of the AHI and event type, as well as the extent of hypercapnia and hypoxia in sleep, and the identification of periodic limb movements that are common in neurologic patients. A limited channel portable study in the acute setting can underestimate the degree of sleep-disordered breathing and/or mischaracterize the type of respiratory events. This patient had a laboratory PSG 2 months after discharge and was found to have an AHI of 64 with oxygen desaturations to 74 % and intermittent periodic breathing.
4. Cognitive impairment and neurologic deficits including aphasia and hemiparesis can significantly impair one's ability to understand the importance of PAP use and operate the device appropriately. Patients with motor deficits have difficulty with interface placement and adjustments, especially if the dominant hand is affected. Facial weakness can interfere with a good interface fit, producing excessive leaking. Most stroke patients require caregiver support to optimize PAP adherence.

IQ Cases

Nocturnal Seizures Versus Parasomnia for Student

Case Vignette

Mrs. Mary Jones, a 49-year-old female, presented with a complaint of abnormal behaviors in sleep. Nocturnal episodes were first recognized during her elementary school years, but were infrequent, occurring no more than once or twice per year. She had a normal electroencephalogram (EEG) and head computerized topography. Phenytoin was prescribed for suspected seizures but episodes continued. When she reached her early 20s, the frequency of nighttime episodes increased, becoming more disruptive to her sleep and daytime functioning. Episodes occurred within a couple hours of bedtime and were characterized by a sudden arousal from sleep associated with a feeling of anxiety and palpitations. She would roll over and grab the headboard involuntarily but with partial preservation of awareness. She would laugh softly or sigh afterwards and then return to sleep. Typical duration was 20–40 s and episodes occurred at least 2–3 nights per week, sometimes repeatedly during the night. She snored lightly but denied witnessed apnea and symptoms of restless legs. She had had numerous EEGs over the years that were normal. She had been treated with numerous antiepileptic drugs (AEDs), antidepressant medications, and benzodiazepines all without benefit. She was taking carbamazepine at the time of presentation. She had a vagus nerve stimulator (VNS) that was turned off weeks prior to presentation due to neck discomfort. Her brother and a niece had somnambulism in childhood that remitted before adulthood. On examination, vital signs were normal and the body mass index was 22.8 kg/m^2. General and neurologic examinations were normal. The Friedman tongue position was 1 and there was no nasal obstruction or retrognathia.

A polysomnogram (PSG) with video EEG study was ordered:

Summary of Findings

The patient was studied from 10:51 p.m. to 9:36 a.m. with a total sleep time of 511 min resulting in a sleep efficiency of 82 %. Sleep architecture revealed a sleep latency of 63 min and a REM latency of 94 min. Sleep stage distribution, as a percent of total sleep time was 10.5 %, stage 1; 69.7 %, stage 2; 5.8 %, stage 3; and 14.1 %, stage REM sleep. There were 8 awakenings and 78 arousals resulting in an arousal index of 9.1 per hour.

Light snoring was noted. Respiratory recording revealed 1 obstructive apnea, 3 central apneas, and 3 hypopneas. The apnea–hypopnea index (AHI) was 0.8 (REM AHI of 5; supine AHI of 3). Baseline oxygen saturation was 95 % with 7 % of sleep time spent below 90 %. The lowest saturation was 88 %. Average heart rate was 67, with a range of 55–90 bpm.

There were no periodic limb movements. EMG tone in REM sleep was not augmented.

The EEG recording showed a normal awake background rhythm of 9 Hz. No epileptiform discharges or localized slowing was observed. No abnormal behaviors or ictal patterns were noted.

Given the PSG result and clinical history further evaluation is required to differentiate nocturnal seizures from parasomnia.

The type of epilepsy represented by Mrs. Jones is commonly confused with disorders of arousal.

It has been hypothesized that NFLE and disorders of arousal from NREM sleep have a shared pathophysiology resulting in their overlapping clinical manifestations.

Nocturnal Seizures Versus Parasomnia for Facilitator

Case Vignette

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Part 1 **Total Points: 5**

Questions

1. Based on the given history and physical, create a differential diagnosis for the presentation of this patient.
2. What are the most common risk factors for seizures that should be elicited in this patient? Limit response to 2–3 sentences.
3. Describe the putative effects of VNS on PSG parameters. Limit response to 2–3 sentences.
4. In 2–3 sentences, describe the likelihood that Mrs. Jones' sleep-related behaviors are due to VNS-induced sleep-related breathing disorder (SRBD).

Ideal Answers

1. Nocturnal seizures, specifically nocturnal frontal lobe epilepsy (NFLE), disorder of arousal from NREM sleep (confusional arousal variant), nocturnal panic attacks, and automatic behavior due to obstructive sleep apnea.
2. The most common risk factors seen in patients presenting with focal epilepsy include a history of febrile seizures, central nervous system infection (meningoencephalitis), closed head injury, and a positive family history of epilepsy. Other types of insults involving the cerebral cortex, including tumors, stroke, and malformations of cortical development, can cause seizures. The most common etiology of medically resistant focal epilepsy in patients treated with epilepsy surgery is malformations of cortical development (cortical dysplasia).
3. The emergence or worsening of apneas and hypopneas with VNS therapy has been reported in adults and children. Both peripheral and central mechanisms of

vagus nerve activation have been proposed. Correlation of stimulation artifact using a left lateral neck EMG electrode with airflow and effort sensors is required to fairly attribute respiratory events to VNS therapy.

4. While the PSG as performed with VNS deactivated cannot rule out VNS-induced SRBD, this is unlikely given the clinical history and examination features. The patient is a relatively thin female without upper airway crowding or obstruction. The history of light snoring and absence of symptoms of choking, gasping, or witnessed apnea make it unlikely she has a clinically significant SRBD. Important to ascertain by history is that events and clinical symptoms were unchanged with VNS deactivation.

Part 2 **Total Points: 5**

Questions

1. What is your interpretation of the video PSG–EEG study?
2. Describe how the results of this study confirm or refute a diagnosis of nocturnal seizures or parasomnia. What would have increased the yield of the recording? Limit your response to 3–4 sentences.
3. In 3–4 sentences, describe the provoking factors of nocturnal seizures and disorders of arousal from NREM sleep. Considering these factors, what could have been done in this case to increase the likelihood of recording a typical episode?
4. What polysomnographic findings would be expected in patients with disorders of arousal from NREM sleep? Limit your response to 1–2 sentences.

Ideal Answers

1. There is no evidence of SDB, periodic limb movements, or abnormal behaviors. The awake EEG background is in the normal range (8–13 Hz) for an adult. The study shows only mild aberrations in sleep architecture.
2. The study neither confirms nor refutes a diagnosis of nocturnal seizures or a parasomnia. The EEG can be normal in patients with focal epilepsy arising from deep or midline structures. Patients with NFLE often have normal interictal and ictal EEGs despite repeated and prolonged recordings. Recording typical episodes is required to accurately characterize the nature of complex behavioral episodes in sleep that have failed to respond to standard therapies.
3. Sleep deprivation and stress are typical provoking factors for patients with seizures and disorders of arousal. In addition, alcohol ingestion, menses, flashing lights, and physical exhaustion increase seizures in some patients with epilepsy. The use of sleep deprivation is commonly used to provoke seizures and interictal discharges in the outpatient EEG laboratory and the inpatient epilepsy monitoring unit. A recommendation for sleep deprivation during the 24-hour period prior to PSG may have increased the likelihood of recording a typical episode.
4. Since disorders of arousal most often arise from stage N3 sleep, affected patients may have spontaneous arousals from N3 or runs of hypersynchronous delta activity preceding arousal.

Part 3 **Total Points: 5**

Given the PSG result and clinical history, further evaluation is required to differentiate nocturnal seizures from parasomnia.

Questions

1. What further testing would you recommend? Limit your response to 2–3 sentences.
2. How can the timing of episodes in relation to the sleep–wake cycle be used to differentiate nocturnal seizures and parasomnias. Limit response to 2–3 sentences?
3. How can episode duration and semiological features be used to differentiate nocturnal seizures and disorders of arousal from NREM sleep. Limit response to 3–4 sentences?

Ideal Answers

1. Further EEG recording either in the sleep laboratory, or preferably, in an inpatient video EEG monitoring unit should be considered to record typical episodes. Depending on the clinical history and index of suspicion for nocturnal seizures, neuroimaging with a high-resolution brain magnetic resonance imaging (MRI) may be warranted.
2. Seizures can occur from any stage of sleep across the night, although they are common during sleep–wake transitions and occur in NREM sleep preferentially. Disorders of arousal typically arise from stage N3 in the first one-third of the sleep period. REM sleep behavior disorder presents from REM sleep typically in the last one-third of the sleep period.
3. Nocturnal seizures in patients with focal epilepsy are characterized by complex motor behaviors typically lasting less than one minute, sometimes on the order of a few seconds. Patients with arousal disorders from NREM sleep typically last for several minutes. Seizures are characterized by stereotyped behaviors, often having tonic, dystonic, or hypermotor features, typically not observed in arousal disorders. Patients with nocturnal frontal lobe seizures often have preserved awareness, while consciousness is usually impaired in parasomnia episodes.

Part 4 **Total Points: 5**

The type of epilepsy represented by Mrs. Jones is commonly confused with disorders of arousal.

Questions

1. In 3–5 sentences, describe the epilepsy syndrome and its etiology.
2. A 3T MRI revealed a hyperintensity in the right superior frontal sulcus suggestive of a malformation of cortical development. Noninvasive EEG was entirely normal with the exception of marked tachycardia during episodes. Invasive EEG

evaluation localized seizure onset to the depth of the sulcus within the MRI lesion. A lesionectomy was performed, and Mrs. Jones has been seizure-free for nearly 5 years. In 2–3 sentences, predict the natural course of Mrs. Jones' seizure control assuming no change in therapy was made.
3. In 2–3 sentences, what are the long-term risks of poorly controlled epilepsy?

Ideal Answers

1. Nocturnal frontal lobe epilepsy (NFLE) is a heterogeneous disorder characterized by seizures having asymmetric tonic posturing, dystonic, dyskinetic, and hypermotor activity as well as agitated wandering. Most episodes are brief and repetitive, with sudden onset and offset and accompanied by marked autonomic activation. Due to the bizarre motor manifestations in sleep and normal EEG, NFLE may be misdiagnosed as a parasomnia. The familial form, known as autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), constitutes as many as 25 % of cases. Linkage studies localized genes for ADNFLE to chromosomes 20q13 and 15q24 with mutations in the transmembrane region of the neuronal nicotinic acetylcholine receptor (nAChR) alpha4-subunit (CHRNA4), beta2-subunit (CHRNB2), and alpha2-subunit (CHRNA2).
2. Among patients with focal epilepsy, the response to initial AED trials predicts future response to therapy. When two appropriately chosen AEDs fail to achieve complete seizure control, patients should be referred for presurgical evaluation.
3. Patients with drug-resistant epilepsy are at risk for seizure-related injuries, medical comorbidities including mood disorders, and sudden unexplained death in epilepsy (SUDEP). SUDEP affects 1 in 200 patients with drug-resistant epilepsy per year.

Part 5 **Points: 5**

It has been hypothesized that NFLE and disorders of arousal from NREM sleep have a shared pathophysiology resulting in their overlapping clinical manifestations.

Questions

1. What are common pattern generators and what role do they play in the pathophysiology of seizures and parasomnias? Limit your response to 1–2 sentences.
2. In 2–3 sentences, describe the neurotransmitter system involved in activation of common pattern generators that produce both seizures and parasomnias.
3. In 2–3 sentences, what is nocturnal (or hypnogenic) paroxysmal dystonia (NPD)?

Ideal Answers

1. Common pattern generators are genetically determined neuronal aggregates in the mesencephalon, pons, and spinal cord subserving innate motor behaviors essential for survival. Activation of common pattern generators by an ictal discharge as in the case of NFLE or an abnormal arousal response from sleep

as in the case of disorders of arousal from NREM sleep can produce similar sleep-related behaviors, including alimentary, emotional, locomotory, and defensive or predatory behaviors.
2. The shared pathophysiology of NFLE and disorders of arousal involves the cholinergic pathway in the ascending arousal system. Neuronal nicotinic acetylcholine receptors are ion channels distributed widely on neuronal and glial membranes in cortical and subcortical regions of the brain that regulate the release of acetylcholine, gamma-hydroxybutyric acid, and glutamate and have a modulatory effect on arousals at the cortical and thalamic levels. Receptor mutations are thought to cause changes in neuronal excitability preferentially affecting the mesial prefrontal area in NFLE and regulate microarousals thereby destabilizing sleep in disorders of arousal from NREM sleep.
3. The term "NPD" was coined in 1981 by Lugaresi and colleagues to describe recurrent, brief motor attacks with dystonic–dyskinetic features arising from NREM sleep. Over a decade later, invasive EEG studies confirmed the epileptic nature of these events. Now, NPD is accepted to represent NFLE.

IQ Case Ms. Smith for Student

Goal: Describe the presentation, evaluation, and pathogenesis of hypersomnia presenting in a patient with multiple sclerosis, the indication and interpretation of the multiple sleep latency test (MSLT), and comorbidity of REM sleep behavior disorder (RBD).

Case Vignette

Ms. Smith is a 23-year-old female who presents to the sleep clinic with a complaint of daytime sleepiness. It dates back to her high school years when she would fall asleep in classes and her teachers would send communications to her mother suggesting she was lazy. She was scolded by her mother for not getting sufficient sleep at night. In college she avoided early morning classes, although she fell asleep in afternoon classes. Over the past couple of months, she has noticed acute worsening of daytime sleepiness. She now has episodes of drowsy driving with many near misses. She recently enrolled in graduate school and currently works in a coffee shop. She is attending classes in the evenings and is working in the coffee shop during the day. Her employer has observed her falling asleep on the job. She has been reprimanded for mood swings and poor customer service (spilling drinks, getting orders wrong, etc.) and for drinking too much coffee. Her Epworth Sleepiness Scale is 18/24.

During workdays, Ms. Smith goes to bed at 10–10:30 p.m. and wakes up at 7 a.m. She works from 7:30 a.m. to 5 p.m. and attends classes 3 days a week from 7 p.m. to 9 p.m. She has no trouble falling asleep but never wakes up feeling

refreshed. On days without classes, she typically takes a 1 h nap after work, which is not always refreshing. On her days off, she will often stay up until 1 a.m. and sleep until 11 a.m. She wakes up feeling slightly more refreshed on these days. While working, she endorses drinking 3–5 espressos daily with limited improvement in her daytime sleepiness. At night she denies an urge to move her legs, nocturnal leg kicking, sleep paralysis, sleep-related hallucinations, and cataplexy. She has been told recently by her sleep partner that she has episodic snoring. She admits to vivid dreams; in the last month, her significant other has awakened her three times when she appeared to act out a dream with punching and kicking and hitting him. She felt remorseful about this.

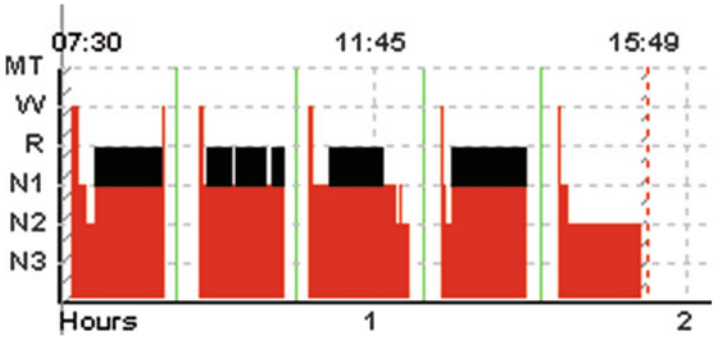
At age 22, she had a diagnosis of multiple sclerosis and is taking glatiramer, a multivitamin, and vitamin D. She denies alcohol, tobacco, and recreational drug use. On review of symptoms, Ms. Smith admits to often feeling cold, intermittent tremor in her hands, fatigue, numbness in her left leg, and apathy. She denies any head injuries, loss of consciousness, or infections.

On physical examination, she appears tired but has a normal mental status. Her body mass index (BMI) is 28 kg/m^2. The upper airway exam is notable for a Grade II Friedman tongue position. The neurologic exam is remarkable for a mild postural tremor, slight dysarthria, and brisk deep tendon reflexes bilaterally.

All blood work was unremarkable. The pregnancy test was negative. A recent brain MRI with and without contrast was notable for scattered periventricular T2-weighted high intensity lesions in the white matter of both cerebral hemispheres along with an enhancing nodule in the pons.

A polysomnogram (PSG) revealed a sleep efficiency of 83 %, TST of 388 min, SL of 8 min, and REM latency of 32 min. The apnea–hypopnea index (AHI) was 4/h (8 in REM), the periodic limb movement (PLM) index was 23, and movements causing arousal <5. Leg electromyography recording revealed an augmentation of tone occurring in 40 % of REM sleep and fragmented REM in the three episodes of REM recorded that night.

The MSLT was performed the next day.



Analysis revealed a mean SL of 0.9 min with four sleep onset REM periods. You are asked to recommend a treatment plan [5].

The PCP is also concerned about the implications of the excessive sleepiness in regard to driving risk and asks whether you or he will report this patient to the state department of motor vehicles.

The patient asks about the impact of the diagnosis on her career choice.

You use this case as preparation for a presentation on the neurotransmitter mechanisms of her sleep disorders.

IQ Case Ms. Smith for Facilitator

Goal: Describe the presentation, evaluation, and pathogenesis of hypersomnia presenting in a patient with multiple sclerosis, the indication and interpretation of the multiple sleep latency test (MSLT), and comorbidity of REM sleep behavior disorder (RBD).

Learning Objectives

A. Create a differential diagnosis for hypersomnia and RBD.
B. Describe the historical elements of the sleep history in the evaluation of hypersomnia.
C. Discuss sleep disorders commonly seen in multiple sclerosis patients and specifically the relevance of DR2 DQB1*0602 and of demyelination.
D. Apply concepts of MSLT interpretation to differentiate narcolepsy from other disorders, e.g., delayed sleep-phase syndrome.
E. Discuss the pathophysiology of RBD in patients with multiple sclerosis and the significance of pontine lesions.
F. Describe treatment options for patients with multiple sclerosis and comorbid narcolepsy and RBD, including the use of steroids.

Case Vignette

Ms. Smith is a 23-year-old female who presents to the sleep clinic with a complaint of daytime sleepiness. It dates back to her high school years when she would fall asleep in classes and her teachers would send communications to her mother suggesting she was lazy. She was scolded by her mother for not getting sufficient sleep at night. In college she avoided early morning classes, although she fell asleep in afternoon classes. Over the past couple of months, she has noticed acute worsening of daytime sleepiness. She now has episodes of drowsy driving with many near misses. She recently enrolled in graduate school and currently works in a coffee shop. She is attending classes in the evenings and is working in the coffee shop during the day. Her employer has observed her falling asleep on the job. She has been reprimanded for mood swings and poor customer service (spilling drinks, getting orders wrong, etc.) and for drinking too much coffee. Her Epworth Sleepiness Scale is 18/24.

Probing Questions

1. What is a comprehensive differential diagnosis based on the ICSD-2 for this patient?

   - Narcolepsy with/without cataplexy
   - Idiopathic hypersomnia with/without long sleep time
   - Hypersomnia due to medical condition
   - Behaviorally induced insufficient sleep
   - Delayed sleep-phase syndrome
   - Obstructive sleep apnea syndrome

2. What further history would be necessary to differentiate these diagnoses?

   - Sleep history including bed/wake times during work and non-workdays
   - Screening questions for parasomnias
   - Screening questions for sleep-related movement disorders
   - Screening questions for sleep-disordered breathing
   - History of potential precipitants, such as drug use or head injury or central nervous system disorders

During workdays, Ms. Smith goes to bed at 10–10:30 p.m. and wakes up at 7 a.m. She works from 7:30 a.m. to 5 p.m. and attends classes 3 days a week from 7 p.m. to 9 p.m. She has no trouble falling asleep but never wakes up feeling refreshed. On days without classes, she typically takes a 1 h nap after work, which is not always refreshing. On her days off, she will often stay up until 1 a.m. and sleep until 11 a.m. She wakes up feeling slightly more refreshed on these days. While working, she endorses drinking 3–5 espressos daily with limited improvement in her daytime sleepiness. At night she denies an urge to move her legs, nocturnal leg kicking, sleep paralysis, sleep-related hallucinations, and cataplexy. She has been told recently by her sleep partner that she has episodic snoring. She admits to vivid dreams; in the last month, her significant other has awakened her three times when she appeared to act out a dream with punching and kicking, and hitting him. She felt remorseful about this.

Probing Questions

3. Given this additional information, what revisions would you make to the differential diagnosis?

   - Hypersomnia due to medical condition
   - Narcolepsy due to medical condition
   - REM sleep behavior disorder (RBD)
   - Obstructive sleep apnea syndrome

4. What are common sleep disturbances in multiple sclerosis?

   - Insomnia
   - Circadian rhythm disorders
   - Drug-induced sleep disturbances

- Nocturnal movement disorders
- Sleep-related breathing disorders of various types
- Narcolepsy
- RBD

5. What are pertinent physical examination findings in this case?
6. What diagnostic testing should be performed?
7. Is a multiple sleep latency test (MSLT) necessary in this case?
8. How should the MSLT be timed to help distinguish between delayed sleep-phase syndrome and narcolepsy?

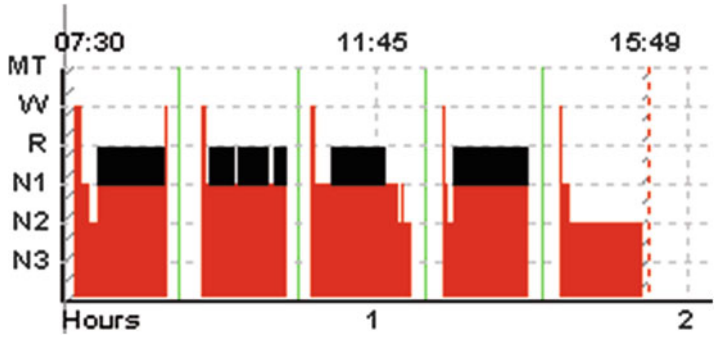
At age 22, she had a diagnosis of multiple sclerosis and is taking glatiramer, a multivitamin, and vitamin D. She denies alcohol, tobacco, and recreational drug use. On review of symptoms, Ms. Smith admits to often feeling cold, intermittent tremor in her hands, fatigue, numbness in her left leg, and apathy. She denies any head injuries, loss of consciousness, or infections.

On physical examination, she appears tired but has a normal mental status. Her body mass index (BMI) is 28 kg/m^2. The upper airway exam is notable for a Grade II Friedman tongue position. The neurologic exam is remarkable for a mild postural tremor, slight dysarthria, and brisk deep tendon reflexes bilaterally.

All blood work was unremarkable. The pregnancy test was negative. A recent brain MRI with and without contrast was notable for scattered periventricular T2-weighted high intensity lesions in the white matter of both cerebral hemispheres along with an enhancing nodule in the pons.

A polysomnogram (PSG) revealed a sleep efficiency of 83 %, TST of 388 min, SL of 8 min, and REM latency of 32 min. The apnea–hypopnea index (AHI) was 4/h (8 in REM), the periodic limb movement (PLM) index was 23, and movements causing arousal <5. Leg electromyography recording revealed an augmentation of tone occurring in 40 % of REM sleep and fragmented REM in the three episodes of REM recorded that night.

The MSLT was performed the next day.



Analysis revealed a mean SL of 0.9 min with four sleep onset REM periods. You are asked to recommend a treatment plan [5].

The PCP is also concerned about the implications of the excessive sleepiness in regard to driving risk and asks whether you or he will report this patient to the state department of motor vehicles.

The patient asks about the impact of the diagnosis on her career choice.

You use this case as preparation for a presentation on the neurotransmitter mechanisms of her sleep disorders.

Probing Questions

9. How do you interpret this MSLT?
10. How do the MRI findings impact the patient's complaints?

- The pontine lesion likely involves the pedunculopontine nucleus, which projects to the locus coeruleus and the reticular formation.
- The cholinergic projections from the pedunculopontine nucleus stimulate the reticularis magnocellularis nucleus of the medulla via the lateral tegmentoreticular tract. The reticularis magnocellularis nucleus hyperpolarizes spinal motoneurons through the ventrolateral reticulospinal tract producing paralysis. Lesions involving this pathway cause a loss of spinal motoneuron inhibition and normal atonia in REM sleep.

11. What counseling should be offered with regard to the development of sleep paralysis, cataplexy, and sleep-related hallucinations?

- The onset of narcolepsy with cataplexy occurs most typically between the ages of 15 and 25 years. Sleepiness is usually the first symptom to develop. Cataplexy often occurs within the first year of symptom onset, but may precede the onset of sleepiness or may develop up to 40 years later.
- Sleep-related hallucinations, sleep paralysis, and disturbed nocturnal sleep often manifest later in the course of the disease.

12. What other neurologic disorders have been associated with narcolepsy?

- Head trauma
- Myotonic dystrophy
- Prader–Willi syndrome
- Parkinson's disease
- Multiple-system atrophy

13. What other disorders are associated with secondary narcolepsy with cataplexy?

- Hypothalamic tumors
- Sarcoidosis involving the hypothalamus
- Paraneoplastic syndrome with anti-Ma2 antibodies (seen in germ cell tumors of testis, lung cancer, other solid tumors)
- Niemann–Pick type C disease (autosomal recessive disorder involving splenomegaly, variable neurologic deficits, and the storage of sphingomyelin caused by mutations of NPC1 and NPC2 genes that result in impaired cellular processing and transport of low-density lipoprotein cholesterol)
- Coffin–Lowry syndrome

14. What is Ms. Smith's final diagnosis?

- Narcolepsy due to medical condition (multiple sclerosis)
- Secondary RBD – parasomnia due to medical condition

15. What treatment options are available?

- If symptoms of RBD in a patient with multiple sclerosis are associated with an exacerbation of the underlying neurologic condition, a course of intravenous corticosteroids is warranted.
- The first-line treatment for RBD is clonazepam which has been shown to be effective in patients with idiopathic RBD and RBD due to multiple sclerosis and other neurologic disorders.
- Wake-promoting medications including modafinil, armodafinil, and traditional stimulants are indicated for the treatment of daytime sleepiness.
- If cataplexy develops, sodium oxybate or antidepressant agents should be considered. However, if RBD symptoms persist, take caution in prescribing selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors, and tricyclic antidepressants as they can exacerbate RBD.
- Lifestyle modifications in the form of scheduled daily naps, daily exercise, and strategic caffeine use are useful in alleviating hypersomnia.

IQ Case Ms. Smith Handout/Objectives

Goal: Describe the presentation, evaluation, and pathogenesis of hypersomnia presenting in a patient with multiple sclerosis, the indication and interpretation of the multiple sleep latency test (MSLT), and comorbidity of REM sleep behavior disorder (RBD).

Learning Objectives

A. Create a differential diagnosis for hypersomnia and RBD.
B. Describe the historical elements of the sleep history in the evaluation of hypersomnia.
C. Discuss sleep disorders commonly seen in multiple sclerosis patients and specifically the relevance of DR2 DQB1*0602 and of demyelination.
D. Apply concepts of MSLT interpretation to differentiate narcolepsy from other disorders, e.g., delayed sleep-phase syndrome.
E. Discuss the pathophysiology of RBD in patients with multiple sclerosis and the significance of pontine lesions.
F. Describe treatment options for patients with multiple sclerosis and comorbid narcolepsy and RBD, including the use of steroids.

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Chapter 15
Sleep in Psychiatric Disorders

Roobal Sekhon and Kingman P. Strohl

Introduction

Sleep disturbances in psychiatric disorders are common because:

- Sleep disturbances occur in a large number of patients with mental illness and are an essential feature of the diagnostic criteria for some psychiatric disorders.
- Sleep disorders such as insomnia and sleep-disordered breathing can lead to worsening of psychiatric disorders.
- Improvement in sleep can be indicative of improvement in psychiatric disorders and deterioration of sleep can be an indicator of worsening psychiatric illness.
- Medications associated with the treatment of psychiatric disorders can exacerbate sleep disorders.

Program requirements for Graduate Medical Education in Sleep Medicine by the ACGME list sleep disorders and its related disorders in all areas of expected general training competencies (http://www.acgme.org/acgmeweb/Portals/0/PFAssets/ProgramRequirements/520_sleep_medicine_07012012.pdf). Sleep fellows should have experience with and develop competence in sleep disorders associated with common psychiatric conditions. Each program is required to have patients in the major categories of sleep disorders, sleep problems related to other factors and diseases, including psychiatric and psychologic disorders.

If there is one area where the sleep medicine specialists should focus their attention, it would be depression. Depression is common, morbid, and potentially fatal if

R. Sekhon, D.O.
Sleep Medicine Specialist, Fairfield, 37 Quail Ct, Walnut Creek, CA 94596, USA
e-mail: roobal@gmail.com

K.P. Strohl, M.D. (✉)
Case Western Reserve University, 11100 Euclid Avenue, Cleveland,
OH 44106-1716, USA
e-mail: kpstrohl@aol.com

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not recognized in its severest form. Questions about depression or the prompt interpretation of scales such as the Beck Depression Scale must be incorporated into your practice, without regard to whether you have an "interest" in psychiatry. Knowing your resources for emergent, immediate, or prompt referrals will be important in your practice for many patients presenting for evaluation of sleep disorders.

For this chapter, content domains were developed through examination of the ACGME requirements as well as discussion with faculty and prior fellows about current and/or best practice. The topics covered in this chapter focus on the illustrative psychiatric disorders in the patient with sleep disorders and vice versa. Some categories include psychotic disorders, depressive/bipolar disorders, traumatic disorders, and anxiety disorders. Specific attention will be focused on schizophrenia, depression, bipolar disorder, and PTSD as prototypic examples. The corresponding ACGME areas for general competencies are listed in Table 15.1. While not as comprehensive as one would find in a textbook, these areas touch upon all aspects of practice as well as the basic issues found in sleep and psychiatric disorders. Some of the areas like epidemiology are solely knowledge based.

The topics in Table 15.2 are organized to construct a non-comprehensive list of content domains relevant to a sleep medicine fellowship. We do not intend for sleep medicine trainees to be expert in psychiatric illnesses but the examples should illustrate the landscape of clinically useful material for referrals and assessments. After requiring reading various relevant chapters and attending didactic presentations, the program could test factual proficiency through standardized testing, exercises in matching, or structured essay answers. This content can also be demonstrably applied in an IQ case discussion or clinical presentation. Other patient assessment tools, while having theoretical underpinnings and a literature, are taught more commonly (without any organized effort to address effectiveness) by example and assessed better by observation and immediate feedback. There is an art to the clinical assessments in practice, and individual styles may vary; however, here one should attempt to define trainee comprehension concerning relevant features of an assessment including the ordering of ancillary tests.

In regard to learning opportunities, the delivery of this content would be delivered through a variety of venues including apprenticeship underpinned by instructional objectives. In this approach, the outcome is to be explicit and stated in such a manner as to capture what specific knowledge, skills, and attitudes a fellow should be able to exhibit following instruction. An objective directly links content and assessment. In this regard, some examples of objectives for each content area are presented in Table 15.2. Note that this list tries to avoid terms that are open to variable interpretation and focuses on work-related, measureable, or verifiable outcomes. Other instructional delivery can either list the objectives up front or at the middle or end of the instruction, but the goals of the instruction should be explicit. Approaches can be creative in when and how objectives are verified.

This list can be augmented or recreated by an individual training program and modified so as to address strength or weakness in overall instructional plan or expertise. One can use these questions as a basis for essay questions to amplify a topic presented in another fashion by faculty, visiting faculty, or fellow. The faculty or fellow can use the list and choose to construct lectures based on one or more

objectives. Working on this list can be a useful exercise to review prior presentations of topics or used as a springboard for written reviews or research.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/sleep-in-psychiatric-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 15.1 Cognitive Map of the Content Domains Relevant to Psychiatric Disorders

		Knowledge	Skills	ACGME competency
I	*Epidemiology*	Yes	No	B, F
	Age			
	Risk factors			
	Special populations			
II	*Mechanisms*	Yes	No	A, B, D
	Neurophysiology			
	Behavioral modification			
	Psychopharmacology			
III	*Risk factors*	Yes	No	A, B
	Biological			
	Psychologic			
	Social			
IV	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatrics			
	Special populations			
V	*Diagnostic measures and interpretation*	Yes	Yes	A, B, C, F
	Mental status exam			
	Actigraphy			
	Sleep diaries			
VI	*Disease management*	Yes	Yes	A, E, D, F
	Presentation of therapeutic options			
	Coordination of care			
	Follow-up in various settings			
VII	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	PTSD/nightmares			
	Agitated psychosis			
	Benzodiazepine use in anxiety vs. sleep disorders			
	Sleep disorders in institutional settings			
	Depressive and bipolar disorders			
	Code for ACGME competencies			
	A. Patient care		D. Interpersonal skills	
	B. Medical knowledge		E. Professionalism	
	C. Practice-based learning and improvement		F. System-based practice	

Table 15.2 Examples of Topics

Item I. Epidemiology
- Consider the prevalence of sleep disorders in VA populations with PTSD
- Describe a program to detect sleep apnea in patients in a community mental health center
- Compare presentation profiles of ADHD vs. narcolepsy

Item II. Mechanisms of health and disease
- Describe the role of the raphe and locus coeruleus in sleep
- Consider the predictive ability of changes in sleep quality in bipolar disorder
- Discuss the role of various antidepressants on chronobiology
- Discuss the role of antipsychotics in sleep medicine and mental illness

Item III. Patient assessments
- Discuss the importance of the mental status exam to a thorough sleep evaluation
- Contrast pretest probability of sleep disorders in patients at a private psychiatric practice vs. a community mental health center

Item IV. Diagnostic strategies
- Discuss the importance of screening for depression vs. bipolar disorder in patients with poor sleep
- Discuss the use of actigraphy and sleep diaries
- Explain sensitivity and specificity for clinical outcomes

Item IV. Practice-based management
- Compare and contrast the principles of therapy
  - Behavioral
  - Environmental
  - Social
  - Medical
  - Pharmacologic
- Consider novel approaches to therapy

Item V. Health and disease management pathways
- Describe the principles in the initiation of therapy for sleep disorders in mental illness
- Consider the interplay between sleep disorders and mental illness as well as management in chronic illness
- List patient expectations vs. physician objectives in terms of outcomes

Item VI. Practice-based learning and improvement
- Devise methods to improve adherence to appointments as well as prescribed therapy in patients with severe mental illness
- Formulate a teaching program to educate patients as well as professionals regarding sleep disorders that are comorbid with various mental illnesses
- Discuss ways to overcome the effects of stigma in patients with mental illness and delivery of adequate care

Item VII. Interpersonal and communication skills
- Understand the role of families, case managers, psychiatrists, and the sleep physician in patients with severe mental illness and the use of an interdisciplinary treatment team
- Assess communication using evaluation of charts as well as patient feedback

(continued)

(continued)

Item VIII. Professionalism

- Obtain input from faculty, peers, and patients on the trainee's performance in treatment of patients with psychiatric disorders with respect to honesty, integrity, and ability to meet responsibilities
- Identify areas in psychiatry and sleep medicine where the trainee can improve

Item IX. Systems-based practice

- Evaluate an inpatient psychiatric facility or a community mental health center and work with staff to find ways to improve patient outcomes by using the trainee's sleep medicine expertise
- Work with a colleague or behavioral health professional in a group therapy setting

Matching Test

Questions

The mood-elevating effects of sleep deprivation can be detrimental in patients with this Axis I diagnosis. ☐

This sleep disorder can be exacerbated by SSRIs or alcohol withdrawal and is often seen in older males with Parkinsonian symptoms. ☐

This is not a common sign of schizophrenia but can be associated with certain sleep disorders. ☐

Decreased REM latency can be seen shortly after stopping medications in this class which work in the locus coeruleus. ☐

Serotonin, a neurotransmitter, is released in this part of the brain which has been implicated in major depression and sudden infant death syndrome. ☐

Hypervigilance, avoidance of specific stimuli, and reexperiencing of specific events such as recurrent nightmares are consistent with this diagnosis. ☐

This second-generation antipsychotic is one of the most commonly prescribed off-label sleep aids. ☐

Insomnia, in addition to low energy, and poor concentration are often seen with sleep-disordered breathing but are also cardinal symptoms of this common psychiatric disorder. ☐

In addition to treatment of the underlying mood disorder, this treatment been shown to be the best long-term treatment of insomnia in depressed patients. ☐

This antidepressant may have some efficacy in the treatment of sleep apnea/hypopnea; however, long-term use can lead to weight gain. ☐

Answers

1. Actigraphy
2. Acute stress disorder
3. Agoraphobia
4. Anhedonia
5. Asthenia (low energy)
6. Atypical antipsychotics
7. Auditory hallucinations
8. Autism
9. Autonomic hyperarousal
10. Benzodiazepines
11. Biopsychosocial
12. Bipolar I disorder
13. Bupropion
14. Buspirone
15. Claustrophobia
16. Cognitive-behavioral therapy
17. Delirium
18. Dementia
19. Depression
20. Dorsal raphe
21. Generalized anxiety disorder
22. Hypothalamic-pituitary-adrenal axis
23. Lithium
24. Locus coeruleus
25. Mania
26. Monoamine oxidase inhibitors
27. Mirtazapine
28. Nightmares
29. Obsessive-compulsive disorder
30. Panic disorder
31. Post-traumatic stress disorder
32. Quetiapine
33. REM behavior disorder
34. Schizophrenia
35. Short REM latency
36. Sleep diary
37. Sleep hygiene
38. Serotonin-norepinephrine reuptake inhibitor
39. Selective serotonin reuptake inhibitor
40. Suicidal ideation
41. Tricyclic antidepressants
42. Trazodone
43. Typical antipsychotics
44. Visual hallucinations

Questions with Answers

The mood-elevating effects of sleep deprivation can be detrimental in patients with this Axis I diagnosis. 12

This sleep disorder can be exacerbated by SSRIs or alcohol withdrawal and is often seen in older males with Parkinsonian symptoms. 33

This is not a common sign of schizophrenia but can be associated with certain sleep disorders. 44

Decreased REM latency can be seen shortly after stopping medications in this class which work in the locus coeruleus. 38

Serotonin, a neurotransmitter, is released in this part of the brain which has been implicated in major depression and sudden infant death syndrome. 20

Hypervigilance, avoidance of specific stimuli, negative alterations in cognition/mood, and reexperiencing of specific events such as recurrent nightmares are consistent with this diagnosis. 31

This second-generation antipsychotic is one of the most commonly prescribed off-label sleep aids. 32

Insomnia, in addition to low energy, and poor concentration are often seen with sleep-disordered breathing but are also cardinal symptoms of this common psychiatric disorder. 19

In addition to treatment of the underlying mood disorder, this treatment been shown to be the best long-term treatment of insomnia in depressed patients. 16

This antidepressant may have some efficacy in the treatment of sleep apnea/hypopnea; however, long-term use can lead to weight gain. 27

Essay Questions

Study Case 1

A 36-year-old female presents to the sleep clinic after being treated by her primary care doctor for difficulty sleeping over the past 6 months. She doesn't think she has slept at all in over 1 month although she stays in bed most of the time trying "really hard" to sleep. She indicates that she has no desire to do anything, feels miserable because "I can't eat and I can't sleep" and she states she is feeling guilty because now she is missing her social obligations. She says she is always tired because of the poor sleep and her life feels "unbearable." She is taking alprazolam 1 mg 5–6 times per day to help her sleep and feel better but has found that it no longer works.

Questions

1. What is the most likely diagnosis in this patient? What is the differential diagnosis?
2. Describe the workup of this patient.
3. What therapeutic modalities would you consider for the most likely diagnosis?
4. Consider the use of various common sleeping medications in this patient.

Ideal Answers

1. The most likely diagnosis in this patient is major depressive disorder even though she doesn't explicitly endorse depressed mood. She endorses anhedonia, poor appetite, insomnia, guilt, lack of energy, and possible suicidal ideation. A differential could include a variety of other psychiatric disorders such as bipolar disorder or an anxiety disorder. The patient's use of alprazolam should be further evaluated to see if there is a substance use disorder. Sleep-disordered breathing should also be considered.
2. The patient should have a thorough psychiatric examination in addition to a routine history and physical. Evaluation for mood, anxiety, and psychotic disorders should be done along with a suicide risk assessment. An evaluation for substance abuse and sleep disorders should also be done. A thorough sleep history should be obtained and the patient should be asked to do a sleep diary along with actigraphy. Based on evaluation, further sleep testing may be considered.
3. Moderate to severe depression responds well to antidepressants. Cognitive-behavioral therapy should also be strongly considered focused on the patient's depression and insomnia. In the case of mild to moderate depression, cognitive-behavioral therapy may be used as a first-line intervention.
4. FDA-approved treatments for insomnia such as zolpidem may be used as an adjunct but primary treatment should focus on treatment of the underlying disorder. Antidepressants such as mirtazapine or amitriptyline, used off-label to treat insomnia, are appropriate and FDA approved for patients with depression after considering risks and benefits. Atypical antipsychotics such as quetiapine are

generally not indicated in this patient unless one finds psychotic features or bipolar illness in follow-up. Benzodiazepines are CNS depressants that can cause cognitive impairment, and long-term use is generally not recommended.

Case Study 2

A 31-year-old male with a BMI of 35 presents to your office stating that he is having difficulty sleeping. He is referred by the mental health clinic where he is treated for schizophrenia, chronic paranoid type. He states that he initially had a lot of difficulty with treatment but has been doing very well over the past 3 years since starting on a long-acting injection of risperidone. However, he has gained a lot of weight and has started having trouble sleeping. He is noted to be irritable and have trouble sitting in his chair, tapping his feet, and slowly rocking back and forth.

Questions

1. What is akathisia? Discuss the importance of akathisia in the context of schizophrenia and RLS.
2. Describe the disturbances in REM sleep, SWS, and total sleep time in a patient with schizophrenia.
3. Describe the effect of antipsychotics on sleep disorders.

Ideal Answers

1. Akathisia is a syndrome characterized by an inner restlessness and an urge to move, sometimes associated with irritability, aggression, and rarely suicidal ideation. It can be precipitated by medications used to treat schizophrenia such as typical or atypical antipsychotics. There are significant similarities to RLS; however, a diurnal variation is usually seen primarily in RLS while stereotyped movements such as body rocking are more often seen in akathisia.
2. A decrease of total sleep time in patients with schizophrenia has been linked with agitated psychosis. There are data indicating that disturbances in REM are related to positive symptoms and disturbances in SWS that are related to negative symptoms and cognitive functioning. Although data is limited, long-term sleep disturbances in schizophrenia have been generally associated with worse clinical outcomes.
3. Antipsychotics act by acting on various dopaminergic, cholinergic, histaminergic, alpha-adrenergic, and serotonergic mechanisms, usually by a blockade mechanism or partial agonism. These medications may exacerbate underlying RLS or periodic leg movements. Weight gain is a common side effect of many antipsychotics, both first-generation (typical) and second-generation (atypical) antipsychotics, and may lead to worsening of sleep-disordered breathing. Sedation with antipsychotics is also common and may be involved in improving clinical outcomes in patients, however may be problematic for patients with excessive daytime sleepiness due to various sleep disorders.

Case Study 3

Post-traumatic Stress Disorder

Mr. Jones is a 25-year-old male who presents to the sleep clinic at the VA after discharging his firearm at night while sleeping in his bed with his wife at home. His wife and two young children are present with him. He is a veteran who saw active duty for 4 years in Afghanistan and has been home for approximately 6 months. He has had significant difficulty sleeping according to his wife but has been unwilling to seek help until this latest incident. The patient is very reluctant to speak and states he "really can't remember much" other than he was dreaming about his military service. He also states that he had several "close calls" when he was on active duty and had started getting "bad dreams" prior to his honorable discharge.

His sleep has progressively gotten worse. Initially he had trouble going to sleep and staying asleep but was taking OTC sleeping aids which helped somewhat. He also would drink on occasion to help him "wind down." He began having severe "episodes" where he wakes up screaming. He would initially tell his wife about the nightmares but he is now reluctant to share. His wife indicates that the nightmares were always about his military service. As the nightmares became worse, so did his intake of sleeping pills and alcohol. His wife indicates that the patient appears paranoid as he is always looking outside the windows and only sleeps with a loaded gun under his pillow. He appears to "jump" at every sudden sound. She recalls a visit to see a baseball game where "they had couple of fireworks and he nearly had a heart attack" and "we had to leave immediately." He now rarely shows any emotion until he has severe outbursts of extreme anger. He is recluse, often not leaving his house for days at a time. The patient also indicates that his nightmares, which occur almost every night, have gotten to the point where he is afraid to go to sleep.

PE: blood pressure, 146/91; respiratory rate, 16; Pulse, 98; Pox 99 %; BMI 21; Neck 15 in. Mallampati I, no retrognathia, and 1+ tonsils with a midline uvula.

ESS was 3/24.

MSE: AAOx3. Pleasant and cooperative with appropriate grooming and hygiene. Mood "okay" with an anxious affect that is restricted in range. Mild psychomotor agitation and patient is looking around the room and sits after moving his chair to back against the wall and face the door. Thought is linear, coherent, and organized without loose associations or flight of ideas. There is no evidence of internal stimulation, hallucinations, or frank delusion although the patient appears guarded. He denies suicidal, violent, or homicidal ideation. His speech is normal in volume and prosody but there is limited spontaneity.

The rest of the physical exam was unremarkable.

A polysomnogram was ordered.

PSG results: The patient was studied from 11:05 to 06:23 with a total sleep time (TST) of 299 min resulting in a sleep efficiency of 68 %. Sleep architecture revealed

a sleep latency of 47 min and a REM latency of 55 min. Sleep stage distribution, as a percent of total sleep time, was 29.0 %, stage 1; 38.7 %, stage 2; 11.5 %, stage3; and 21.4 %, stage REM sleep. REM density was 5.1. There were 27 awakenings and 73 arousals resulting in an arousal index of 14.6 per hour.

Very light, occasional snoring was noted. Respiratory recording revealed 0 obstructive apnea, 0 central apneas, and 2 hypopneas. The apnea-hypopnea index (AHI) was 0.4 (REM AHI of 1.9; supine AHI of 0.3). Baseline oxygen saturation was 97 % with 0 % of sleep time spent below 90 %. The lowest saturation was 92 %. Average heart rate was 78, with a range of 64–106 bpm.

Periodic limb movements were not seen. There was no augmentation in EMG tone during REM sleep.

Questions

Part 1: Total Points: 5

Questions

1. Based on the history, create a differential diagnosis for this patient.
2. What are some of the symptoms of PTSD in this patient?
3. Consider the increasing alcohol use in this patient in the context of PTSD.

Ideal Answers

1. Various sleep disorders such as insomnia, nightmares, sleep-disordered breathing as well as night terrors, REM behavior disorder, and somnambulism should be considered. PTSD or another traumatic disorder, depressive disorder, and anxiety disorders should also be considered. Nightmares in the context of PTSD are most likely given the presentation.
2. The patient has had exposure to a traumatic event. Subsequently he has reexperiencing of the event through nightmares and by triggers such as fireworks. He has had changes in cognition, saying he can't remember and attempts to avoid talking about the events. He also shows hypervigilance, anger, and irritability.
3. Patients with PTSD often have comorbid substance use, particularly alcohol. Alcohol contributes to worsened sleep and perpetuates the symptoms of PTSD, particularly those associated with avoidance. Treatment of comorbid depression or anxiety symptoms can also be complicated by the use of alcohol.

Part 2: Total Points: 5

Questions

1. What is your interpretation of the patient's mental status exam?
2. How do the findings of the PSG contribute to the patient's diagnosis?
3. Discuss the benefits vs. shortcomings of in-lab PSG in this patient.

Ideal Answers

1. The patient appears to be showing signs of increased overall arousal with some guarded/paranoid behavior such as sitting to face the door. His restricted affect and limited speech may indicate numbing. There are no signs of psychosis or mania.
2. The patient had fragmented sleep with a delayed sleep onset and increased REM density. There was no evidence of clinically significant sleep-disordered breathing or increased EMG tone. While this is not diagnostic of PTSD or nightmares, it does support the diagnosis. It is important to note that similar outcomes may be seen with depression/insomnia.
3. An in-lab PSG will give the most complete data based on that night's sleep. However, it is important to assess the role of the environment in the patient's symptoms including the patient's sense of safety, the effect of the family, and the patient's use of alcohol.

Part 3: Total Points: 5

Questions

1. Discuss the role of the sleep physician in coordination of care for the treatment of the patient's nightmares.
2. What are the effects of PTSD on levels of cortisol, epinephrine, and norepinephrine?
3. Consider some of the ethical implications of this patient's presentation.

Ideal Answers

1. The sleep physician's main role is to treat the nightmares but to also understand that the nightmares are part of a larger disease process. Working with psychiatrists, primary care physicians, and substance abuse specialists are important.
2. Hyperarousal of the sympathetic system is a hallmark of PTSD. Reexperiencing in the form of nightmares or flashbacks is generally associated with a hypernoradrenergic activity and also with elevated levels of cortisol as well as epinephrine.
3. The patient may be at risk to himself or others and a thorough risk assessment should be performed.

Part 4: Total Points: 5

Questions

1. What are the commonly used medications used to treat nightmares associated with PTSD?
2. What are the effects of SSRIs and SNRIs on nightmares vs. PTSD?
3. What are non-pharmacologic measures that can be used to treat this patient?

Ideal Answers

1. The most commonly used medication used to treat nightmares is prazosin. Clonidine, another sympatholytic medication like prazosin, may be considered for therapy. The AED/mood stabilizers such as gabapentin or topiramate and atypical antipsychotics such as quetiapine have been used with some success. Occasionally, tricyclic antidepressants or trazodone are used but limited data is available.
2. SSRIs, particularly sertraline and paroxetine, are the only FDA-approved medications for the treatment of PTSD. SNRIs such as venlafaxine are also commonly used for the treatment of PTSD symptoms. However, SSRIs and particularly SNRIs have an inconsistent effect on nightmares and can exacerbate them at times.
3. Behavioral therapy is often very successful in PTSD and nightmares. Cognitive-behavioral therapy, primarily Imagery Rehearsal Therapy or IRT, is the most commonly used therapy in nightmares associated with PTSD. Various other forms of behavioral therapy such as systematic desensitization or progressive muscle relaxation have been used in nightmares not associated with PTSD.

Part 5: Total Points: 5

After a combination of individual therapy, group therapy, and medication management, Mr. Jones is feeling better and sleeping better. He is regularly going to AA meetings and no longer having nightmares. His PTSD symptoms are under control with treatment from psychiatry.

Questions

1. In 2–3 sentences, discuss ways that symptom recurrence can be prevented or minimized.
2. How would this patient's prognosis be different if he were 30 years older and 30 lbs heavier?
3. Consider how the patient's family may have had their sleep altered by his symptoms.

Ideal Answers

1. PTSD and nightmares do not have to be a chronic condition, particularly if treated early. Full treatment followed by patient getting education regarding PTSD, teaching the value of a support system, and knowing what to do in case of symptom exacerbation are keys to prevention/minimizing relapse. This is done best via an interdisciplinary model.
2. Patients with chronic PTSD can often be much more difficult to treat with medications alone and often require more intensive intervention. They can also be at risk for more other comorbid disorders such as sleep-disordered breathing,

substance dependence, and mood/anxiety disorders as well as other medical disorders.

3. Consideration of the patient's family should be taken into account in a case like this. Family members often feel high levels of stress, guilt, and anxiety. Sleep problems associated with depression and anxiety or simply because of disrupted sleep can occur.

IQ Case

Mandy Pression for Student

Goal: Understand the presentation associated with insomnia and hypersomnia with different mood disorders, the impact of medications used to treat mood disorders, and how comorbid sleep disorders can impact mood disorders.

Case Vignette

A 38-year-old female (BMI 35) presents to the sleep clinic for evaluation of trouble sleeping. Patient states that she has been a poor sleeper since a young age and has tried multiple medications without consistent efficacy and "it's getting worse!" She snores loudly with occasional periods where her husband has noted that she makes gasping sounds and her snoring has gotten worse since she has gained some weight over the past 2–3 years. She states that she is very tired during the day and her Epworth Sleepiness Score is 13/24.

She has a childhood history of bipolar disorder. Her husband of 15 years indicates that sometimes she goes days without needing more than 3–4 h of sleep but most of the time she appears exhausted but cannot fall asleep "even though I try really hard!" She was fired from her job 3 years ago after a manic episode where she went to visit her sister in Florida without telling anyone. She has been seeing a psychiatrist for bipolar disorder and was doing well but recently has stopped taking her quetiapine because of weight gain. Her husband states that he has noticed that she is again not sleeping much and she is more moody than normal, particularly in the past week.

She states that she sleeps from 8 p.m. and usually gets out of bed anywhere from 3 to 10 a.m. or "you know, whenever I am ready to get up!" It usually takes her a long time to go to sleep and she often wakes up several times during the night. She also indicates that she takes "short catnaps" during the day on the couch while watching TV, etc. She watches TV in bed, uses the computer, and often reads in bed in an effort to "try to go to sleep." She complains of mild RLS and bruxism symptoms but denies narcolepsy/cataplexy and parasomnias and has never been a shift worker. She denies drowsy driving.

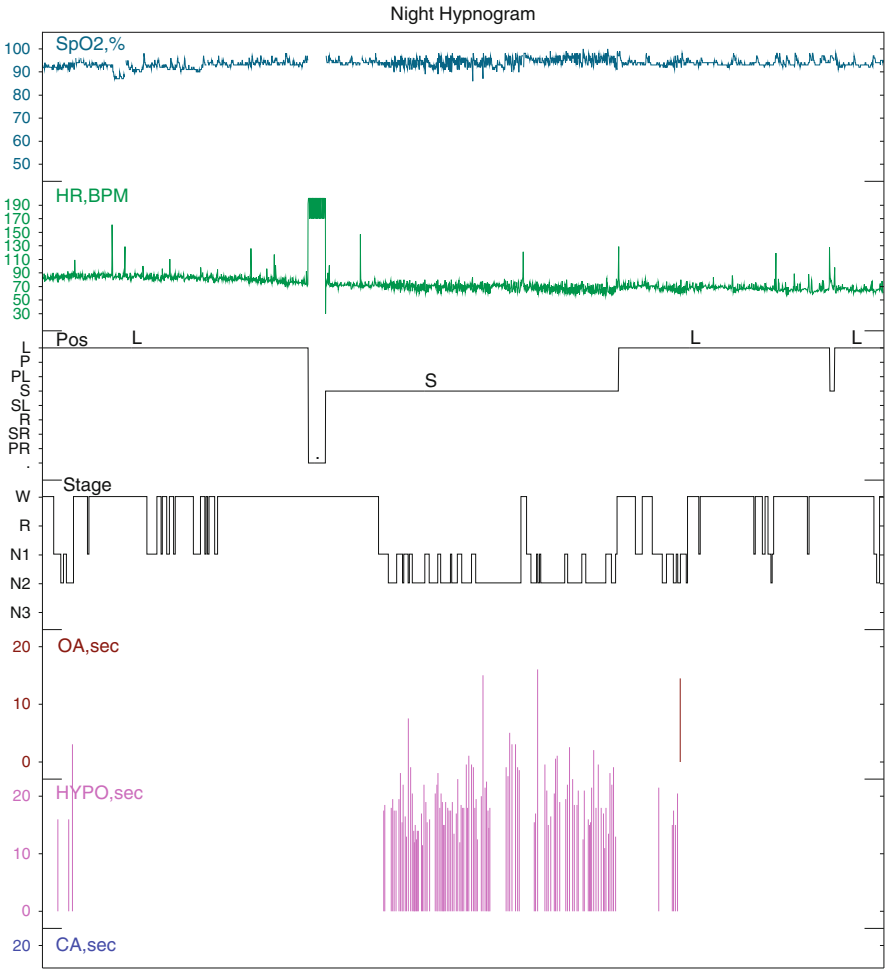
PMHX: Bipolar I, HTN
Meds: venlafaxine, quetiapine, metoprolol, OTC sleep aids
Denies alcohol or tobacco use except has gone on binges during her manic phases, last use more than 2 years ago. Drinks caffeine on occasion, 1–2 cups of coffee in the morning.

On physical exam:

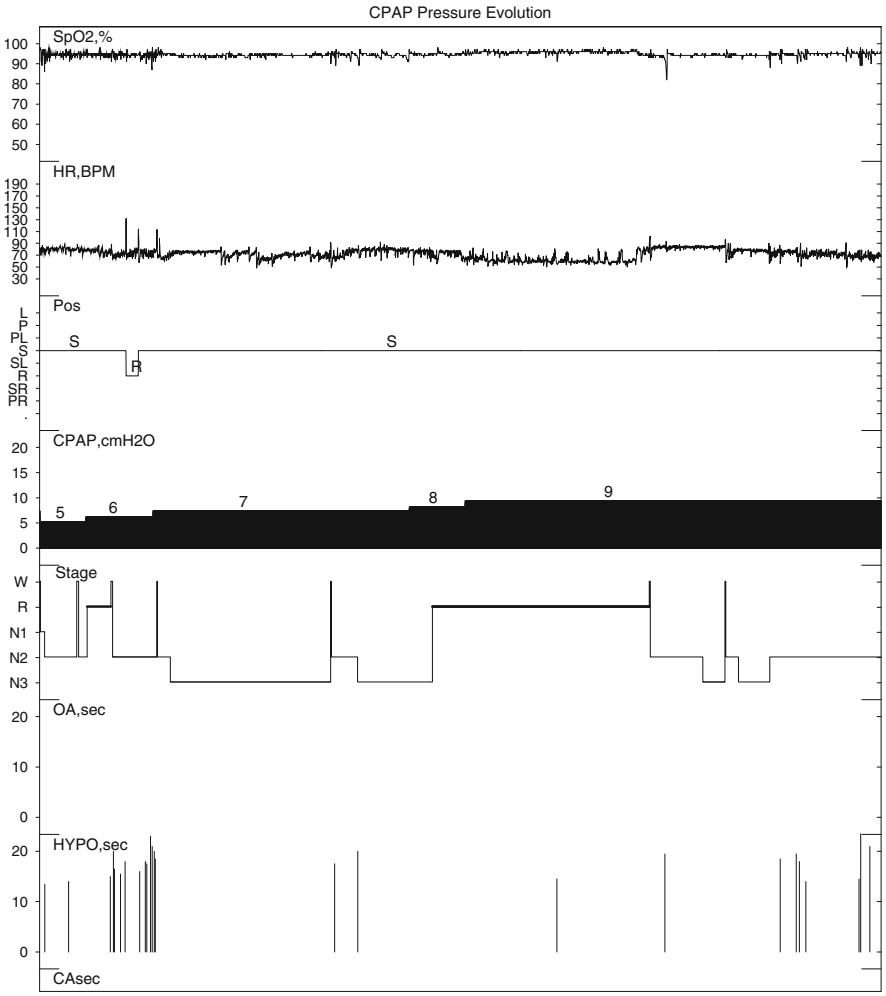
Mental status exam: Cooperative and engages appropriately. Mild psychomotor agitation; animated speech that is pressured but interruptible. Circumstantial without tangential thought or flight of ideas. No hallucinations, delusions, or loose associations, but mild grandiosity is present. Denies suicidal ideation. Mood is "pretty great" and affect is expansive and labile as the patient goes from being very happy to being irritated 2–3 times with me and her husband for brief periods of time.
VS: BP 115/78, HR 73, 99 % on RA, neck 14.5 in.
HEENT: MMM, Mallampati III, 1+ tonsils, midline uvula with scalloping of the tongue. No retrognathia
Lungs: CTAB
Heart: RRR
Neuro: No gross motor or sensory deficits

A sleep study is ordered and the results are as follows:

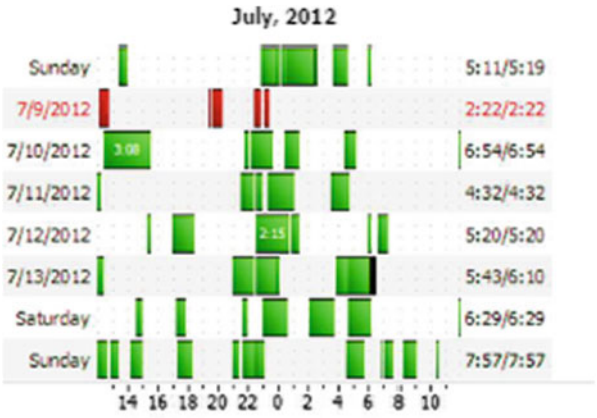
Sleep efficiency 41 % (121/298 min).
Sleep latency 4 min, REM latency no REM achieved.
REM sleep 0 %, NREM 100 %.
Overall AHI: 56.3.
Baseline O_2 sat 95 %, lowest recorded 84 %.
Below is the hypnogram of the PSG.



The patient was scheduled for a follow-up CPAP titration and the hypnogram is shown below.



She was prescribed a CPAP and followed up in 2 months with complaints of poor sleep. She had been changed from quetiapine to lamotrigine to decrease weight loss and now was taking the lamotrigine regularly. Her husband indicated that she appeared significantly improved from the previous few years with no manic symptoms but she still had problems with insomnia. The CPAP data from the last week is shown below:



Days used: 58/58
Hours used on average: 5:33 min
Time in large leak per day: 1 min and 13 s
Average residual AHI: 1.2
CPAP setting: 9 cm H_2O

Mandy Pression for Facilitator

Goal: Understand the presentation associated with affective illness and sleep complaints, the impact of medications used to treat mood disorders, and how comorbid sleep disorders can impact mood disorders.

Learning Objectives

A. Understand the diagnosis of bipolar disorder and major depressive disorder.
B. Create a differential diagnosis of insomnia in bipolar disorder.
C. Consider the role of sleep disturbance as a harbinger of affective illness.
D. Understand the challenges faced in treatment of sleep-disordered breathing in patients with bipolar disorder.
E. Discuss the common PSG findings seen in a patient with mood disorders.
F. Describe the treatment of mood disorders in patients with co-occurring sleep disorders.

Case Vignette

A 38-year-old female (BMI 35) presents to the sleep clinic for evaluation of trouble sleeping. Patient states that she has been a poor sleeper since a young age and has tried multiple medications without consistent efficacy and "it's getting worse!" She snores loudly with occasional periods where her husband has noted that she makes

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PMHX: Bipolar I, HTN

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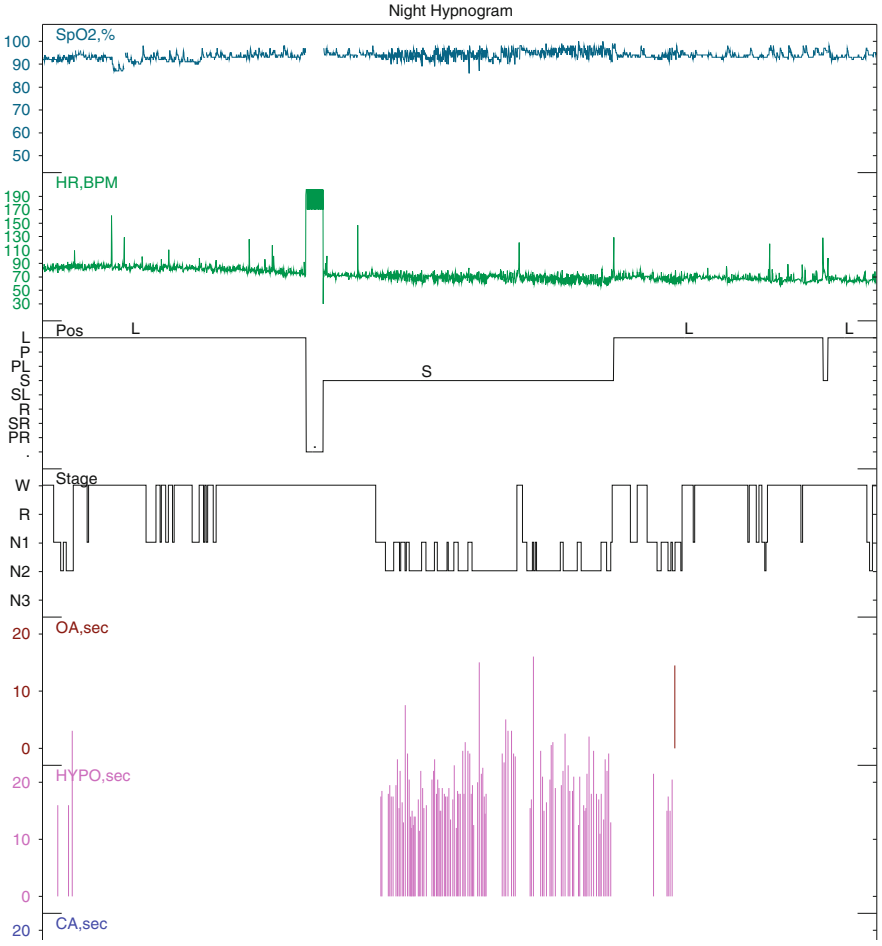

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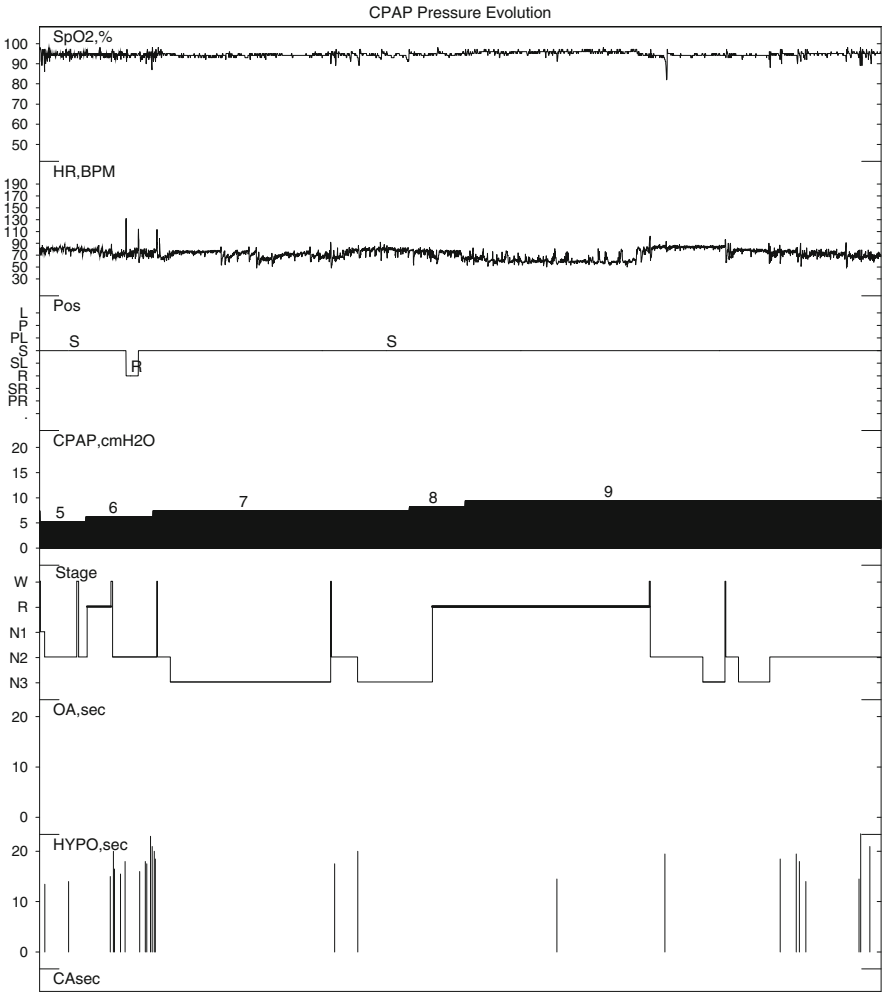
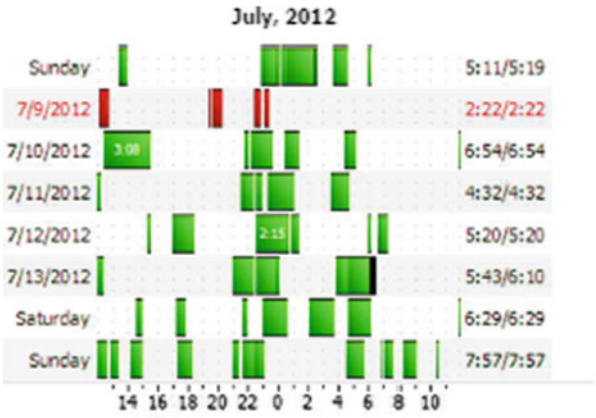


She was prescribed a CPAP and followed up in 2 months with complaints of poor sleep. She had been changed from quetiapine to lamotrigine to decrease weight loss and now was taking the lamotrigine regularly. Her husband indicated that she appeared significantly improved from the previous few years with no manic symptoms but she still had problems with insomnia. The CPAP data from the last week is shown below:



Days used: 58/58
Hours used on average: 5:33 min
Time in large leak per day: 1 min and 13 s
Average residual AHI: 1.2
CPAP setting: 9 cm H_2O

Probing Questions

1. What is the differential diagnosis for the patient's sleep complaints?
2. What are the risk factors for OSA in this patient?
3. What is the relevance of patient's report of being a poor sleeper since "a young age"?
4. What are the diagnostic criteria for bipolar disorder?
5. What is the relationship between OSA and bipolar disorder?
6. Consider the role of sleep as a predictor of mania and as a marker of response in mania.
7. Based on the additional information, how does this impact your previous answers regarding differential diagnosis as well as the report of sleep problems at a young age?
8. What is the relationship between sleep architecture and bipolar disorder?
9. What is the risk of sleep restriction therapy in the treatment of insomnia in bipolar disorder?
10. What is the value of the mental status exam in assessing sleep disorders?
11. What is the risk of sleep restriction therapy in the treatment of insomnia in bipolar disorder?
12. What is the relationship between OSA and bipolar disorder?
13. What do you tell the patient and what is your treatment plan?
14. What do you expect to see after OSA treatment?
15. What are the common PSG findings in a patient with bipolar disorder? Major depression?
16. How does this affect your differential diagnosis?

17. How do you think this will impact the patient's bipolar disorder and sleep complaints going forward?
18. Evaluate the CPAP download data and how the various diagnoses of bipolar, insomnia, and OSA interact.
19. What treatment modalities are recommended for this patient, if any?

IQ Case Handout/Objectives

Goal: Understand the presentation associated with insomnia and hypersomnia with different mood disorders, the impact of medications used to treat mood disorders, and how comorbid sleep disorders can impact mood disorders.

Learning Objectives

A. Describe the sleep disorders commonly seen in bipolar disorder.
B. Consider the role of serotonin and norepinephrine in sleep and affective illness.
C. Discuss the evaluation of insomnia in a patient with bipolar disorder.
D. Discuss the common PSG findings seen in a patient with depression.
E. Describe the treatment of bipolar disorder in the settings of RLS and narcolepsy.
F. Consider the treatment of mood disorders with sleep deprivation and light therapy.

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Chapter 16
Sleep in Medical Disorders

Coleen G. Lance, Lamia Ibrahim, and Dennis Kelley

Introduction

Sleep disorders are problems with sleeping, including trouble falling or staying asleep, falling asleep at the wrong times, too much sleep, or abnormal behaviors during sleep. The over 90 distinct sleeping and waking disorders present grouped into a few main categories: difficulty falling and staying asleep, excessive wake time sleepiness, sleep-wake rhythm problems, and sleep-disruptive behaviors. Some like insomnia are very common in a healthy population (see Chap. 4). Some sleep disorders appear or reappear during a change in life stages such as the perimenopausal period of life or transition to frailty. Hence it would not be unexpected that patients with medical disorders may express complaints about sleep quality and length. Nor would it be surprising that in medical illness and with medications for chronic disease, there might occur alterations in sleep architecture, sleep continuity, and sleep organization. One problem in developing a content area here is to define the causality or association and impact of the sleep disorder on any given medical disorder.

For instance, one can consider an interaction among sleep length and glycemic control and point to the prevalence of diabetes and the prediabetic state with sleep apnea; however, the results of interventions to unlock this association suggest that causality of sleep leading to poor glycemic control occurs in nonobese rather than obese subjects. The implications here are that seeking a connection to sleep apnea in the patient with diabetes probably is better directed at least at the present time on

C.G. Lance, M.D. (✉) • L. Ibrahim
Department of Pulmonary and Critical Care Medicine, University Hospitals Case Medical Center, 11100 Euclid Ave, Cleveland, OH 44106, USA
e-mail: colleen.lance@uhhospitals.org; delimafam@gmail.com

D. Kelley
Sleep Disorders Program, Louis Stokes DVA Medical Center, 10701 East Boulevard, Cleveland, OH 44106, USA
e-mail: Dennis.Kelley@va.gov

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behavioral issues rather than metabolic control. A similar argument can be made for hypertension. There are many studies of connections among sleep interruptions, sleep apnea, and blood pressure, but current practice guidelines for the management of hypertension are still focused on strong evidence for medical control, rather than treatment of sleep apnea. This overall impact is still missing. Nevertheless, there are important implications of the impact of sleep and circadian rhythm on the pathogenesis and presentations of common medical disorders – hypertension, heart disease, COPD, chronic fatigue syndrome, etc.

On the other hand, there are instances where the insight from sleep medicine affects disease management. With coexistence of hypothyroidism and sleep apnea, treatment of the sleep apnea should precede the institution of thyroid replacement, because increasing oxygen consumption without treatment of hypoxia can produce mismatching of optimal oxygen delivery to the heart and precipitate ischemic complications. Another instance is when restless legs syndrome is diagnosed *and* ferritin levels are found to be low enough for iron treatment, the sleep physician needs to coordinate with the primary care provider to search for a possible cause for iron loss.

The domains discussed in this chapter are echoed in Chaps. 9, 10, 11, 12, and 13. Content domains in this chapter were developed through the examination of ACGME requirements and review of existing material relevant to training in the intersections among general internal (adult) medicine and sleep. There are some guidelines in undergraduate medical education and in pulmonary/critical care medicine, but no specific guidelines in other postgraduate training programs. Since sleep medicine trainees can come from a variety of non-internal medicine programs, there cannot be a simple assumption that fundamental understanding of the recognition of comorbid medical disorders and need for comanagement when sleep problems or disorders are present. This includes indications for referral.

The chapter topics are meant as suggested content. Table 16.1 lists example domains and maps them to the ACGME competencies, with domains listed as knowledge and/or skill based. Some areas are easily accomplished in nonclinical venues, such as independent reading or didactic sessions. Demonstration by trainees of skill-based domains fits into the new ACGME framework of attaining training milestones. Some domains are assessed in clinical environments, using notes, conceptual maps for an individual patient, or follow-up plans. The listing of domains will assist program directors and trainees to track exposure to the necessary variety of patients.

Table 16.2 gives examples of educational objectives and assessments for the discussion of this content area. Additional tools for assessing competence and milestones included in this chapter are a recall matching test, essay questions, and an IQ case.

Unique to the adult section of training in sleep medicine is the need for the trainee to demonstrate the ability to interact with others in the management of chronic disease when addressing sleep disorders. This ability to identify the key features of current medical management and to integrate the sleep issues into that management plan should be assessed where relevant in the objectives and other assessment tools. Trainees whose primary background is not in internal medicine may require additional mentorship and direction to ensure competency in this regard.

Table 16.1 Cognitive Map of the Content Domains Relevant to Medical Disorders

		Knowledge	Skills	ACGME competencies
I	*Epidemiology*	Yes	No	B, F
	Prevalence in clinical practice			
	Caregiver Fatigue/sleepiness			
	Sleep health and mortality			
II	*Mechanisms*	Yes	No	A, B, D
	Biologic interactions			
	Sleep-wake habits			
	Metabolic syndromes			
III	*Risk factors*	Yes	No	A, B
	Co-risk factors			
	Impact of primary disease			
	Drug/OTC effects			
IV	*Patient assessments*	Yes	Yes	A, C, D, E
	Adult			
	Pediatric			
	Preoperative evaluation			
V	*Diagnostic measures and interpretation*	Yes	Yes	A, B, C, F
	Epworth Sleepiness Scale			
	Mental Status Exam			
	Fatigue Severity Scales			
	Sleep Diary			
VI	*Disease management*	Yes	Yes	A, E, D, F
	Presentation of therapeutic options			
	Explanation of PSG testing			
	Follow up with outcome Goals			
VII	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Heart failure			
	Hypertension			
	Diabetes			
	Adherence			
	Preoperative assessment			
	Driving risk			

Code for ACGME competencies

A. Patient care	D. Interpersonal skills
B. Medical knowledge	E. Professionalism
C. Practice-based learning and improvement	F. System-based practice

Table 16.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
- Compare the effects of short sleep and long sleep on mortality and morbidity
- Describe the risk factors for and prevalence of sleep disorders in heart failure
- Compare sleep abnormalities associated with menopause
- Identify the risks to sleep with aging and frailty

Item II. Mechanisms of health and disease
- What are proximate causes for sudden death in sleep and how to prevent it?
- Compare the presentation of sleep/fatigue complaints in chronic fatigue syndrome to that of fibromyalgia
- Describe the features of sleep impacted by thyroid disease

Item III. Risk factors
- Describe how environmental and behavioral factors may influence sleep onset and sleep
- Recount the patterns of presentation of sleep disorders in HIV/AIDS
- Describe how environment affects the sleep of a geriatric patient

Item IV. Patient assessments
- Compare and contrast the optimal office visit for a patient with COPD to that with heart failure
- How medications are assessed for an effect on sleep and circadian rhythm
- What features in the performance of the sleep history and physician relevant to chronic medical disease?

Item V. Diagnostic measures and interpretation
- Interpret the interpretations of pulmonary function testing and echocardiography
- List features in the metabolic and endocrine tests that are of relevance to the presentations of sleep disorders

Item VI. Disease management
- List the principal outcome measures for managing sleep in heart disease
- Compare the priorities for treatment of nocturnal angina and paroxysmal nocturnal dyspnea
- Delineate the proper noninvasive ventilation modality for the proper diagnostic category

Item VII. Health and disease clinical pathways
- Describe the indications for sleep evaluations in patients with hypertension compared to resistant hypertension
- List outcomes for sleep complaints and disorders in the treatment of hypothyroidism
- Describe how you would talk about the treatment effects for sleep disorders to a patient with fibromyalgia or chronic fatigue syndrome
- Describe how you would approach the sleep complaints of a perimenopausal patient

Matching Test

Questions with More Than One Answer

H. pylori is a causative agent. ☐

Has been reported as associated with new onset adult sleep walking and NREM parasomnias and when treated sleep complaints remit. ☐

Can produce apneas by both anatomic and respiratory control mechanisms. ☐
One criterion is exertional malaise that lasts >24 h. ☐
African sleeping sickness. ☐
One cause for ICU psychosis. ☐
Condition produced by chemotherapy for ovarian or breast cancer. ☐
High hypoxemic risk resulting from REM sleep. ☐
Symptom with ~17-fold increase in the pretest probability for obstructive sleep apnea. ☐
Marker for Cheyne-Stokes respiration. ☐
Placed in the same category as sudden unexpected nocturnal death syndrome (SUNDS). ☐
A scale for COPD severity based on spirometry. ☐
A scale for functional severity in heart failure and pulmonary arterial hypertension. ☐
The combination of COPD and sleep apnea. ☐
A marker for instability in chronic asthma. ☐
Gastric measure that does not increase in NREM or REM sleep in patients with duodenal ulcer. ☐
Associated with frequent awakenings with or without pain and nonrestorative sleep.
Causative agent for African sleeping sickness. ☐
Oral medicine causing sleep-onset insomnia in ~20 % of asthma patients. ☐
Associated with difficulty initiating and maintaining sleep and nightmares. ☐
Obsessive risk taking or gambling. ☐
Half-life 5–7 h; effects up to 15 h. ☐
May produce anticholinergic side effects and prolong drowsiness. ☐
Characterized by tenderness with 4 kg of digital force on at least 11 of 18 tender spots. ☐
Used in treatment of seizures, neuropathy, RLS; associated with weight gain. ☐
Worsens OSA. ☐
Produced by endozepines in the setting of hepatic disease. ☐
Cause of SUNDS. ☐
Decrease in N3 sleep and increase in REM latency. ☐
Lowered with sleep deprivation. ☐
Raised in sleep deprivation. ☐
Drug used in prostate cancer, associated with hot flashes. ☐
Anecdotal reports of subjective improvement in alpha-delta sleep. ☐
Night-shift nurses. ☐
Symptoms of OSA associated with increased ADH secretion. ☐
Agents used to help with nasal obstruction in CPAP compliance. ☐
Agents used to help with nasal obstruction in CPAP compliance. ☐
Agents used to help with nasal obstruction in CPAP compliance. ☐
Antidepressants known to worsen RLS. ☐
Antidepressants known to worsen RLS. ☐
Antidepressant neutral in RLS. ☐

Answers

1. Cardiac arrhythmias
2. Heart failure
3. Peptic ulcer disease
4. Reflux esophagitis
5. Hyperthyroidism
6. Hypothyroidism
7. Chronic renal failure
8. Chronic fatigue syndrome
9. Trypanosomiasis
10. Sleep deprivation
11. Menopause
12. COPD
13. Asthma
14. Diabetes type II
15. Diabetes type I
16. Nocturnal angina
17. Paroxysmal nocturnal dyspnea
18. Brugada syndrome
19. Hypertension
20. GOLD classification
21. AHA class
22. Overlap syndrome
23. Nocturnal cough
24. Interstitial lung disease
25. pH
26. Irritable bowel syndrome
27. Testosterone
28. Celiac disease
29. Alpha-delta sleep
30. Trypanosomiasis
31. Corticosteroids
32. Long-acting beta agonists
33. Beta-blockers
34. Dopaminergic agents
35. Caffeine
36. Diphenhydramine and doxylamine
37. Chronic alcoholism
38. Fibromyalgia
39. Pregabalin
40. Smoking
41. Recurrent stupor
42. Long-QT trait
43. Rheumatoid arthritis
44. Biological therapy
45. Leptin
46. Ghrelin
47. Lupron
48. Amitriptyline
49. Increased risk breast cancer
50. Nocturia
51. Nasal saline washes
52. Nasal steroids
53. Nasal ipratropium
54. Serotonin reuptake inhibitors
55. Selective norepinephrine and SSRIs
56. Bupropion

Questions with Answers

H. pylori is a causative agent. 3
Has been reported as associated with new onset adult sleep walking and NREM parasomnias and when treated sleep complaints remit. 5
Can produce apneas by both anatomic and respiratory control mechanisms. 6
One criterion is exertional malaise that lasts >24 h. 8
African sleeping sickness. 9
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Condition produced by chemotherapy for ovarian or breast cancer. 11
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Half-life 5–7 h; effects up to 15 h. 35
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Characterized by tenderness with 4 kg of digital force on at least 11 of 18 tender spots. 38
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Cause of SUNDS. 42
Decrease in N3 sleep and increase in REM latency. 44
Lowered with sleep deprivation. 45
Raised in sleep deprivation. 46
Drug used in prostate cancer, associated with hot flashes. 47
Anecdotal reports of subjective improvement in alpha-delta sleep. 48
Night-shift nurses. 49

Essay Questions

Case #1

This 67-year-old male is followed for "labile hypertension" but is on no medications. He was advised to go on a diet and lose weight. At a routine visit, the PCP reported snoring, choking, and observed apnea with an inability to do routine daywork without feeling tired and sleepy. The ESS was 14/24. Sleep was unrefreshing for the past 2 years, and in the last 6 months, there occurred fearful dreams as well as regular dreams. Bedtime was 11 p.m. and wake time was 6:30 a.m., with an alarm clock. The review of systems suggested generalized, non-localized weakness and weight gain over 4 months, puffiness in the face which increased during the daytime, and a lowering of his voice. He has had chest pain on exertion and has awakened once in the past month with epigastric pain. There is a family history of snoring, hypertension, and hyperlipidemia.

Temp	37.2C
Pulse	60/min
BP	160/90 mmHg
RR	19/min

Systematic Examination

Height 5″8″ Weight 340 pounds BMI 35	
Skin	Coarse skin with a doughy consistency
Upper airway	Crowded pharynx (Mallampati IV)
	Lateral grooving of a tongue which looks large
Resp	Normal vesicular breath sound, no added sound
C.V.S.	S1, S2 heard, 2/6 precordial systolic murmur without radiation
Abdomen	No tenderness
Throat	No swelling
Extremities	1+ pretibial edema
CNS	Decreased reflex in elbow, knee jerks

Polysomnography

Sleep time: 363 min. All stages of sleep were present, and no abnormal sleep behavior was noted except an AHI 24 (AI 12) with a REM AHI 31. Baseline saturation: 93 %, 20 % time below an oxygen saturation of 90 %

Questions

1. What medical conditions other than obstructive sleep apnea are suggested by this presentation? Briefly provide a rationale and differential diagnosis.
2. Please interpret the thyroid function tests and the standard therapy.

The thyroid function tests

Date: XX-XX-XXXX		(Normal values)
Serum T3:	0.15 ng/mL	(0.45–1.37 ng/mL)
Serum T4:	1.08 ug/dL	(4.5–12.0 ug/dL)
Serum TSH:	115 uIU/mL	(0.49–4067 UlU/mL)

3. Briefly explain your plan to follow up on the results and manage this patient.

Ideal Answers

1. Chest pain is highly suggestive of coronary artery disease. Risk factors are hypertension, obesity, male gender, and family history. The differential diagnosis could include GERD or musculoskeletal pain. Hypothyroidism is suggested by weakness, weight gain, change in the voice, large tongue, and edema. These are rather soft signs. The differential might include diabetes, heart failure, or acromegaly, but these are less likely. Hypertension could result from hypothyroidism but could also from the patient's genetic background and/or sleep apnea.
2. The low T4 and high TSH are consistent with hypothyroidism. The ideal therapy is thyroid replacement therapy.
3. You explain the results and the current therapeutic alternatives for OSA, and prepare the patient for a titration study to initiate therapy. You would refer the patient to a cardiologist for work-up of potential coronary artery disease and to either this PCP or an endocrinologist with two cautionary notes. First, in this age and with these risk factors, replacement therapy should be gradual and supervised by an experienced PCP or endocrinologist. Second, replacement therapy without addressing evident sleep apnea is risky as thyroid replacement will increase oxygen demand. As obstructive apneas decrease oxygen availability, the potential for creating a morbid mismatch during sleep with recurrent obstructive apnea. In short, treatment for hypothyroidism should not be instituted until treatment of OSA is commenced and shown successful.

Case #2

A 72-year-old male presents with fatigue and shortness of breath that is also accompanied by poor sleep and an observation by his wife that he seems to stop breathing during sleep. She sometimes has to touch him to get him to breathe again. He has a history of hypertension, hyperlipidemia, refractory atrial fibrillation, and treated by cardioversion 6 months ago. Medications include Lasix, Aldactone, metoprolol, niacin, and an ACE inhibition.

Questions

1. Compare and contrast the major risk factors for recurrent central vs. obstructive apneas.
2. Briefly define Cheyne-Stokes respiration and its root causes.
3. Compare the intrathoracic and cardiac effects of obstructive vs. central apneas.

Ideal Answers

1. The principal risk factors for recurrent central apneas are male sex, hypocapnia, atrial fibrillation, and increasing age, whereas the principal risk factors for obstructive apnea do include obesity but not atrial arrhythmia.
2. Cheyne-Stokes respiration is a form of central sleep apnea characterized by periodic breathing in which central apneas and hypopneas alternate with periods of hyperventilation with a waxing-waning pattern of tidal volume. Unlike OSA, CSA likely arises as a consequence of HF, and the presence of CSA may alert the physician to the necessity of intensifying HF therapy. The current debate is whether CSA is simply a reflection of severely compromised cardiac function with elevated left ventricular filling pressures, or whether, for the same degree of cardiac dysfunction, CSA exerts unique and independent pathological effects on the failing myocardium. The mechanisms include sympathetic excitation and the creation of a neuroexcitatory state.
3. Central apneas have a different pathophysiology than obstructive apneas and are not associated with the generation of exaggerated negative intrathoracic pressure; they both increase sympathetic nervous system activity (SNA). Increases in blood pressure and heart rate with recurrent apneas including subsequent daytime effects lead to an increased myocardial O_2 demand in the face of reduced supply. Such events contribute to a vicious cycle on myocardial performance.

Case #3

This 68-year-old woman has a 10-year history of nightly hot flashes. She went through menopause with cessation of menstrual cycles 12 years previously. Hot flashes were a predominant symptom for her which persisted despite cessation of menses. Over the ensuing decade, she would awaken multiple times nightly with symptoms. She was placed on Effexor by her primary care physician. The symptoms lessened, but she had worsening of her blood pressure control, so she stopped the medication.

Her bedtime is 11 p.m. nightly. 10 years ago she was able to fall asleep within 20 min; however this has increased to 60 min within the last 2 years. During the night she would have arousals approximately every 2 h. She describes her arousals where she would awaken covered in sweat with a rapid pulse and then fall back to sleep in 15 min. She would then awaken to start her day at 6:30 a.m. She did not have daytime complaint of sleepiness, but felt that her concentration and memory were worsening. In addition symptoms of anxiety were worsening, particularly

around bedtime. Thoughts of worry about her multiple nighttime wakings were predominant. Bedtime routine included reading in bed and doing Sudoku. She is a widow and does not have a bed partner. When she travels with friends, they have noted mild snoring and bruxism.

Family history significant for a daughter and sister with breast cancer:

Temp	37.4C
Pulse	80/min
BP	155/72 mmHg
RR	14/min

Systematic Examination

Height 5″6″ Weight 133 pounds BMI 21	
General	Nervous appearing
Upper airway	High arched palate
	Micrognathia
Resp	Normal
C.V.S.	Normal S1, S2; S4 present otherwise normal
Extremities	No edema
CNS	Normal reflexes
Skin	Normal

Questions

1. What would be your next step in evaluation? Give justification.
2. How would you manage her persistent hot flashes?
3. What other compounding factors are present that worsen her sleep initiation insomnia? Comment on management.

Ideal Answers

1. Normally in the postmenopausal period, there is a cessation of hot flashes over time. In a small percentage of women, hot flashes can persist for more than a decade. One could argue for management solely targeted at symptomatic relief of the hot flashes with pharmacological agents. However she has difficulty with memory, concentration, and mood. She has been noted to have snoring and bruxism, and the anatomy of her airway is suggestive of a risk for obstructive respiration at night. In this situation polysomnography is warranted. Thyroid function testing is indicated since it may mimic or drive hot flash symptoms. This patient had normal thyroid function.
   Polysomnography

Sleep time: 350 min. All stages of sleep were present, with a slight reduction in REM. Bruxism noted. AHI 6, all hypopneas. REM AHI 31. Baseline saturation: 97 %, no time below an oxygen saturation of 90 %

Titration to CPAP 7 cm H_2O eliminated all obstructive respirations and eliminated bruxism. The patient was initiated on CPAP but had difficulties tolerating. An oral mandibular advancing dental appliance was constructed and advanced. On repeat polysomnography, there was resolution of all obstructive events and bruxism. She was able to use the appliance nightly. Her hot flashes were reduced by half but still present. Mood memory and concentration were reported to be improved. Sleep latency was still 60 min.

Further history revealed that she consumes spicy foods and a large amount of caffeinated beverages, but no alcohol or tobacco. She does exercise regularly, golfing three times weekly.

2. The rationale behind treatment of the obstructive respirations and lessening of the hot flash symptoms comes from reduction in the increased sympathetic tone associated with obstructive respirations. Historically hormonal supplementation was the mainstay for management of perimenopausal symptoms. With concern for increased risk of breast cancer and poor cardiovascular outcomes in this form of therapy, it is used less frequently and in reduced dosages. For this patient, hormonal supplementation would not be indicated due to the fact that her sister and daughter have breast cancer. Alternative therapies include antidepressants. Options would include serotonin reuptake inhibitors or selective norepinephrine and serotonin reuptake inhibitors. The Effexor she had taken had a side effect of increasing her blood pressure. A serotonin reuptake inhibitor would be a better choice for her. Other pharmacologic agents could include clonidine or gabapentin.

   Lifestyle modifications can also be beneficial. Consumption of spicy foods, caffeine, tobacco, and alcohol can all worsen hot flash symptoms. Physical exercise also improves the symptoms. This patient corrected all lifestyle choices to reduce her symptoms and started a serotonin reuptake inhibitor. This in conjunction with keeping her room cool at night eliminated her nocturnal symptoms of hot flashes.
3. Over the previous decade, she had developed psychophysiologic insomnia and poor sleep hygiene. Targeted cognitive behavioral therapy and initiation of proper sleep hygiene would resolve the sleep initiation insomnia.

Case #4

This 67-year-old male is referred for snoring, choking, and observed apnea with an inability to do routine daywork without feeling tired and sleepy. The ESS was 14/24. Sleep was unrefreshing for 2 years, and in the last 6 months, there occurred fearful dreams as well as regular dreams. Bedtime was 11 p.m. and wake time was 6:30 a.m., with an alarm clock. The review of systems suggested generalized weakness and weight gain over 4 months, puffiness in the face which increased during the daytime, and a lowering of his voice. He has rarely had chest pain on exertion. He is followed for "labile hypertension" but is on no medications; instead he was advised

to go on a diet and lose weight by his physician at a routine visit. There is a family history of snoring, hypertension, and hyperlipidemia.

Temp	37.2C
Pulse	60/min
BP	160/90 mmHg
RR	19/min

Systematic Examination

Height 5″8″ Weight 340 pounds BMI 35	
Skin	Coarse skin with a doughy consistency
Upper airway	Crowded pharynx (Mallampati IV)
	Lateral grooving of a tongue which looks large
Resp	Normal vesicular breath sound, no added sound
C.V.S.	S1, S2 heard, 2/6 precordial systolic murmur without radiation
Abdomen	No tenderness
Throat	No swelling
Extremities	1+ pretibial edema
CNS	Decreased reflex in elbow, knee jerks

Polysomnography

Sleep time: 363 min. All stages of sleep were present, and no abnormal sleep behavior was noted except for sleep-disordered breathing. AHI 24 (AI 12). REM AHI 31. Baseline saturation: 93 %, 20 % time below an oxygen saturation of 90 %

Questions

1. What medical conditions other than obstructive sleep apnea are suggested by this presentation? Briefly provide a rationale and differential diagnosis.
2. Please interpret the thyroid function tests and the standard therapy.

The thyroid function tests

Date: XX-XX-XXXX		(Normal values)
Serum T3:	0.15 ng/mL	(0.45–1.37 ng/mL)
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Serum TSH:	115 uIU/mL	(0.49–4067 UlU/mL)

3. Briefly explain your plan to follow up on the results and manage this patient.

Ideal Answers

1. Chest pain on exertion are highly suggestive of coronary artery disease. Risk factors are hypertension, obesity, male gender, and family history. The differential diagnosis could include GERD or musculoskeletal pain. Hypothyroidism is suggested by weakness, weight gain, change in the voice, large tongue, and edema. These are rather soft signs. The differential might include diabetes, heart failure, or acromegaly, but these are less likely. Hypertension could result from hypothyroidism but could also from genetic background and/or sleep apnea.
2. The low T4 and high TSH are consistent with hypothyroidism. The ideal therapy is thyroid replacement therapy.
3. You explain the results and the current therapeutic alternatives for OSA, and prepare the patient for a titration study to initiate therapy. You would refer the patient to a cardiologist for work-up of potential coronary artery disease and to either this PCP or an endocrinologist with two cautionary notes. First, in this age and with these risk factors, replacement therapy should be gradual and supervised by an experienced PCP or endocrinologist. Second, replacement therapy without addressing evident sleep apnea is risky as thyroid replacement will increase oxygen demand. As obstructive apneas decrease oxygen availability, the potential for creating a morbid mismatch during sleep with recurrent obstructive apnea. In short, treatment for hypothyroidism should not be instituted until treatment of OSA is commenced and shown successful.

Case #5

A 72-year-old male presents with fatigue and shortness of breath that is also accompanied by poor sleep and an observation by his wife that he seems to stop breathing during sleep. She sometimes has to touch him to get him to breathe again. He has a history of hypertension, hyperlipidemia, and refractory atrial fibrillation.

Questions

1. Compare and contrast the major risk factors for recurrent central vs. obstructive apneas.
2. Briefly define Cheyne-Stokes respiration and its root cause.
3. Compare the intrathoracic and cardiac effects of obstructive vs. central apneas.

Ideal Answers

1. The principal risk factors for recurrent central apneas are male sex, hypocapnia, atrial fibrillation, and increasing age, whereas the principal risk factors for obstructive apnea do include obesity but not atrial arrhythmia.
2. Cheyne-Stokes respiration is a form of central sleep apnea characterized by periodic breathing in which central apneas and hypopneas alternate with periods of hyperventilation with a waxing-waning pattern of tidal volume. Unlike OSA, CSA likely arises as a consequence of HF, and the presence of CSA may alert the

physician to the necessity of intensifying HF therapy. The current debate is whether CSA is simply a reflection of severely compromised cardiac function with elevated left ventricular filling pressures, or whether, for the same degree of cardiac dysfunction, CSA exerts unique and independent pathological effects on the failing myocardium. The mechanisms include sympathetic excitation and the creation of a neuroexcitatory state.

3. Central apneas have a different pathophysiology than obstructive apneas and are not associated with the generation of exaggerated negative intrathoracic pressure; they both increase sympathetic nervous system activity (SNA). Increases in blood pressure and heart rate with recurrent apneas including subsequent daytime effects lead to an increased myocardial O_2 demand in the face of reduced supply. Such events contribute to a vicious cycle on myocardial performance.

IQ Case for Student

Goal: To assess patients for medical causes for insomnia and follow the work-up and management of a patient with restless legs syndrome

Case Vignette

A 30-year-old woman has a complaint of poor sleep, particularly a difficulty in initiation sleep at night. She reports a bedtime of 11 p.m., but unable to fall consistently asleep until 1–2 a.m. Her wake-up time is 6 a.m. during weekdays in order to get children ready for school and be on time for work. On the weekend or on vacation she sleeps in. Epworth Sleepiness Scale is 15/24. She has odd feelings in her legs at night which she describes as crawling and itchy, which is relieved by movement. The symptoms start as early as 7 p.m. every evening. Her husband does not report any leg kicks/movements at night, but does endorse some light snoring while on her back. When she awakens she does not have the leg sensations. She has bloating at night. She snores and awakens without a dry mouth.

She has a history of heavy menses and in the past has been on iron supplementation after her two pregnancies for jumpy legs. Children are now 9 and 6 years of age. She has been able to donate blood without being rejected on the basis of anemia.

She consumes 4–5 eight ounce caffeinated beverages throughout the day in order to compensate for daytime sleepiness. Her diet also consists of a large quantity of chocolate and refined sugar products. She does not smoke and does have 3–4 glasses of wine in the evenings weekly.

Medications: oral contraceptives, multivitamins, fish oil, rose hips.

Allergies: peanuts and lactose deficiency.

Family history of her mother who had restless legs and periodic limb movements at night, diagnosed at age 44.

On physical examination, blood pressure is 130/85, HR 72, and BMI 24. The Mallampati is 2/4 and there is a 1 + tonsillar hypertrophy. The heart, lung, GI, joint, and neurologic examination are normal.

Polysomnography is ordered because the PCP had just listened to an online CME on sleep apnea and the patient snored, had poor sleep, and was sleepy. She heard from the program that a PSG was “always” a good choice. Results were as follows: lights off, 12:05 a.m.; sleep onset, 39 min; REM latency, 135 min; and sleep time, 245 min but had to awaken to get back home. All stages of sleep were present, and no abnormal sleep behavior was noted except an AHI 6 (AI 2) with a REM AHI 12. Baseline saturation: 93 %, 2 % time below an oxygen saturation of 90 %. PLMs noted before sleep onset. PLMI 31/h. Arousal index: 24/h. PLM arousals 19/h. The interpretation indicated mild sleep apnea (AHI >5<15 and sleepiness) and PLMD (PLM arousals>AHI).

After the sleep study, you order the following iron studies:

- Ferritin: 30 ng/mL (normal: 12–250 ng/mL)
- Iron: 28 μg/dL (normal: 26–μg/dL)
- TIBC: 298 μg/dL (normal: 262–μg/dL)
- Transferrin saturation: 9 % (normal: 20–50 %)

Because all values are "within normal limits," you discuss the use of dopamine agonists and comment on the precautions. In addition you comment that perhaps her caffeine use is contributing to the symptoms and start a conversation about sleep hygiene.

Ropinirole was started at a low dose and increased incrementally for 3 weeks. She called in to ask for a refill because it was "working really well." 6 months later her husband says that you need a follow-up for what he calls "odd behaviors" and wonders about her mind.

At the next visit, the patient looks embarrassed and is accompanied by her husband. Her sleepiness and restless legs are gone. She then apologizes to her husband and blurts out that she has a "gambling problem." She went to a casino 2 months ago and now goes almost every day during the day to play the slots and blackjack. She is now a "high roller" at the casino and has spent ~$6,000 of her own money and has $500 on her husband's credit card. She also has rung up $600 on the Home Shopping Network for revealing pajamas. She picked up the children late twice in the past week because she was either in the casino or trying to get an HSN deal. She denies a change in neurologic symptoms, a change in medications, head injury, confusion, and memory problems.

You review her chart and medications. You are called in as the sleep specialist and suggest iron supplements rather than ropinirole.

Two weeks later the PCP calls back to thank you because the patient has her life back and is cured of the RLS. She says that her colleagues were equally perplexed about the case and want you to talk about sleep disorders in primary care and not only just about sleep apnea. She also questions whether a sleep study is always needed.

IQ Case for Facilitator

Goal: To assess patients for medical causes for insomnia and follow the work-up and management of a patient with restless legs syndrome

Learning Objectives

1. Identify risk factors for insomnia from a presentation from a PCP.
2. List the criteria for a syndromic diagnosis of restless legs syndrome and differentiate from periodic limb disorder.
3. Critically evaluate referrals for polysomnography for patients and identify those that are inappropriate.
4. Create a management plan for treatment of restless legs syndrome for a PCP provider.
5. Plan an educational intervention towards family and internal medicine physicians for sleep disorders and to reduce inappropriate polysomnography referrals for conditions of insomnia or restless legs or an obvious behavioral factor producing sleep problems or a sleep disorder.

Case Vignette

A 30-year-old woman has a complaint of poor sleep, particularly a difficulty in initiation sleep at night. She reports a bedtime of 11 p.m., but unable to fall consistently asleep until 1–2 a.m. Her wake-up time is 6 a.m. during weekdays in order to get children ready for school and be on time for work. On the weekend or on vacation she sleeps in. Epworth Sleepiness Scale is 15/24. She has odd feelings in her legs at night which she describes as crawling and itchy, which is relieved by movement. The symptoms start as early as 7 p.m. every evening. Her husband does not report any leg kicks/movements at night, but does endorse some light snoring while on her back. When she awakens she does not have the leg sensations. She has bloating at night. She snores and awakens without a dry mouth.

She has a history of heavy menses and in the past has been on iron supplementation after her two pregnancies for jumpy legs. Children are now 9 and 6 years of age. She has been able to donate blood without being rejected on the basis of anemia.

Probing Question: What are the leading candidates for the presentation?

She consumes 4–5 eight ounce caffeinated beverages throughout the day in order to compensate for daytime sleepiness. Her diet also consists of a large quantity of chocolate and refined sugar products. She does not smoke and does have 3–4 glasses of wine in the evenings weekly.

Probing Question: Why are these important here in this presentation?

Medications: Oral contraceptives, multivitamins, fish oil, rose hips.

Allergies: Peanuts and lactose deficiency.

Family history of her mother who had restless legs and periodic limb movements at night, diagnosed at age 44.

Probing Question

1. Does this tell you anything about patient risk or presentation?

On physical examination, blood pressure is 130/85, HR 72, and BMI 24. The Mallampati is 2/4 and there is a 1 + tonsillar hypertrophy. The heart, lung, GI, joint, and neurologic examination are normal.

Polysomnography is ordered because the PCP had just listened to an online CME on sleep apnea and the patient snored, had poor sleep, and was sleepy. She heard from the program that a PSG was "always" a good choice. Results were as follows: lights off, 12:05 a.m.; sleep onset, 39 min; REM latency, 135 min; and sleep time, 245 min but had to awaken to get back home. All stages of sleep were present, and no abnormal sleep behavior was noted except an AHI 6 (AI 2) with a REM AHI 12. Baseline saturation: 93 %, 2 % time below an oxygen saturation of 90 %. PLMs noted before sleep onset. PLMI 31/h. Arousal index: 24/h. PLM arousals 19/h. The assessment was "mild sleep apnea (AHI >5<15 and sleepiness) and PLMD (PLM arousals>AHI). Iron studies are indicated."

Probing Question

2. What was the result of this test? How informative is this?

After the sleep study, you order "iron studies":

- Ferritin: 30 ng/mL (normal: 12–250 ng/mL)
- Iron: 28 μg/dL (normal: 26–98 μg/dL)
- TIBC: 298 μg/dL (normal: 262–474 μg/dL)
- Transferrin saturation: 9 % (normal: 20–50 %)

Probing Question

3. How do you interpret this?

The iron and ferritin are within normal limits for laboratory testing. What is important to note is that laboratories report the normal ranges of iron for heme synthesis. What one is interested in with respect to restless legs syndrome is dopamine synthesis. With that in mind, the goal ferritin is >50 ng/mL. In the face of acute inflammation, the serum ferritin may be spuriously elevated, and the addition of serum transferrin may be helpful. This patient would benefit from iron supplementation in addition to pharmacotherapy.

Because all values are "within normal limits," you discuss the use of dopamine agonists and comment on the precautions.[1] In addition you comment that perhaps her caffeine use is contributing to the symptoms and start a conversation about sleep hygiene.

Ropinirole was started at a low dose and increased incrementally for 3 weeks. She called in to ask for a refill because it was "working really well." Six months later her husband says that you need a follow-up for what he calls "odd behaviors" and wonders about her mind.

At the next visit, the patient looks embarrassed and is accompanied by her husband. Her sleepiness and restless legs are gone. She then apologizes to her husband and blurts out that she has a "gambling problem." She went to a casino 2 months ago and now goes almost every day during the day to play the slots and blackjack. She is now a "high roller" at the casino and has spent ~$6,000 of her own money and has $500 on her husband's credit card. She also has rung up $600 on the Home Shopping Network for revealing pajamas. She picked up the children late twice in the past week because she was either in the casino or trying to get an HSN deal. She denies a change in neurologic symptoms, a change in medications, head injury, confusion, and memory problems.

Probing Question

4. What is this from? What could it be?

You review her chart and medications. You are called as the sleep specialist who interpreted the study and suggest iron supplements rather than ropinirole.

The cause of this patient's restless legs is multifactorial in nature. In addition to the low ferritin, there are agents that the patient is consuming that are contributing to the symptoms. The addition of caffeine was to counteract the daytime sleepiness; however it is actually making the situation worse. Caffeine has a 15 h half-life, and without cessation it will be difficult to control the RLS symptoms. Chocolate, refined sugar, alcohol, and tobacco can also contribute to symptoms. When obtaining a sleep-wake diary from the patient, information about these substances will also be of benefit.

Two weeks later the PCP calls back to thank you because the patient has her life back and is cured of the RLS. She says that her colleagues were equally perplexed about the case and want you to talk about sleep disorders in primary care and not only just about sleep apnea. She also questions whether a sleep study is always needed.

Probing Question

5. What would be the objectives for such a presentation?

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[1] *There are two dopamine agonists available. Pramipexole is dependent on renal excretion and ropinirole dependent on hepatic metabolism. They act on D2, D3, and D4 receptors. Since there is a circadian rhythm for the symptoms of RLS, it is important to know the timing of the patient's symptoms. The agent should be given 30–45 min prior to the patient's onset of symptoms and may require a second dose at bedtime. For those patients who have symptoms very early in the day, long-acting dopamine agonist may be required. The most common side effects include nausea, dyspepsia, sudden sleepiness, or even insomnia. Care must be taken in prescribing this class of agent in elderly patients due to the risk of orthostatic hypotension. A more rare complication, but one for which there must be counseling, is that of compulsive behavior such as pathological gambling, shopping, or hypersexuality.*

IQ Case Final Handout/Objectives

Goal: To assess patients for medical causes for insomnia and follow the work-up and management of a patient with restless legs syndrome

Learning Objectives

1. Identify risk factors for insomnia from a presentation from a PCP.
2. List the criteria for a syndromic diagnosis of restless legs syndrome and differentiate from periodic limb disorder.
3. Critically evaluate referrals for polysomnography for patients and identify those that are inappropriate.
4. Create a management plan for treatment of restless legs syndrome for a PCP provider.
5. Plan an educational intervention towards family and internal medicine physicians for sleep disorders and to reduce inappropriate polysomnography referrals for conditions of insomnia or restless legs or an obvious behavioral factor producing sleep problems or a sleep disorder.

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Chapter 17
Pediatric Sleep Medicine

Kristie R. Ross and Carol Rosen

Introduction

Sleep is crucial to the well-being of children in terms of their physical health, cognitive and emotional development, and social functioning. As children grow from infancy to adolescence, sleep requirements, architecture, and pathology go through considerable changes. The ACGME requirements for training in sleep fellowship include the availability of "infants, children, and adolescents" with problems in each of the major categories of sleep disorders (circadian rhythm disorders, idiopathic hypersomnia, narcolepsy, parasomnias, insomnia, sleep-related breathing disorders, sleep-related movement disorders, and sleep problems related to other factors and diseases). Fellows are required to demonstrate clinical competence in the diagnosis and management of childhood sleep disorders in these domains, irrespective of their training background.

Content domains in this chapter were developed through the examination of ACGME requirements, discussions with sleep medicine fellows and faculty, and review of existing material relevant to training in pediatric sleep medicine.

The chapter topics are meant to supply content for a pediatric sleep medicine curriculum. Table 17.1 lists example domains relevant to the ACGME competencies. The domains are also categorized as knowledge and/or skill based. Some areas are easily accomplished in nonclinical venues, such as independent reading or didactic sessions. Demonstration by trainees of skill-based domains fits into the new ACGME framework of attaining training milestones, a concept familiar to pediatricians who

K.R. Ross, M.D., M.S.
University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, OH, USA

C. Rosen, M.D. (✉)
Pediatric Sleep Center, Rainbow Babies & Children Hospital, University Hospitals Case Medical Center, Cleveland, OH, USA
e-mail: carol.rosen@case.edu

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routinely assess the developmental progress of their patients. These domains are more easily taught and assessed in clinical environments. The listing of domains will assist program directors and trainees to ensure adequate exposure to the necessary variety of patient ages and presenting complaints.

Table 17.2 gives some illustrations of educational objectives that can be assessed in clinical environments or with assessments such as essay questions. Most require the integration of factual knowledge with more practical skills usually conceptualized as the "art of medicine." Additional tools for assessing competence and milestones included in this chapter are a recall matching test, essay questions, and an IQ case.

Unique to the pediatric section of training in sleep medicine is the need for the trainee to demonstrate the ability to interact with children at developmentally appropriate level as well as their parents/caregivers when addressing sleep disorders. This skill should be assessed where relevant in the objectives and other assessment tools. Trainees whose primary background is not in pediatrics may require additional mentorship and direction to develop this competency.

Of special importance is the manner and environment for diagnostic testing. A "kid-friendly" facility will have features that create an inviting environment. Children notice different things than adults, including transference about the comfort level of the facility staff with children and their parent or other caregiver. There is also more need to "show and tell." Preparation for a test can be crucial, with aids like "storybooks" or a visit to the lab before the test being some of the more contemporary methods to reduce anxiety of the patient and the family. In our experience, making a sleep facility "kid-friendly" does not result in a place that is uncomfortable for the adult patient, but failure to address this issue by administration and the laboratory director will result in stress and reduced satisfaction with testing.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/pediatric-sleep-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 17.1 Cognitive Map of the Content Domains Relevant to Pediatric Sleep Medicine

	Knowledge	Skills	ACGME competency
I. *Epidemiology*	Yes	No	B, F
Developmental age			
Familial risk factors			
Special populations			

(continued)

(continued)

	Knowledge	Skills	ACGME competency
II. *Mechanisms of health and disease*	Yes	No	A, B
Social and family belief structure			
Neurodevelopmental aspects			
Circadian rhythm			
Upper airway structure			
Body and limb movements			
Comorbidity			
Sleep and neurocognition			
Hypersomnia			
III. *Risk factors*	Yes	No	A, B
Environmental			
Genetic			
Age-related			
IV. *Patient assessments*	Yes	Yes	A, C, D, E
Infant			
Pediatrics			
Special populations			
V. *Diagnostic measures and interpretation*	Yes	Yes	A, C, F
Sleep diary			
Actigraphy			
PSG criteria			
MSLT			
Self-report questionnaires			
VI. *Disease management*	Yes	Yes	A, E, D, F
Age-appropriate presentation of therapeutic options			A, F
Decisions on therapy			A, F
Family-centered follow-up			A, F
Multidisciplinary management			
VII. *Health and disease clinical pathways*	Yes	Yes	A, C, F
Response to public inquiry			
Psychological referrals			
PAP management			
ENT or craniofacial referral			
Special needs management			
Hypersomnia			
Code for ACGME competencies			
A. Patient care		D. Interpersonal skills	
B. Medical knowledge		E. Professionalism	
C. Practice-based learning and improvement		F. System-based practice	

Table 17.2 Examples of Topics with Educational Objectives

Item I. Epidemiology
- Describe the prevalence and risk factors for insomnia and night wakings in toddlers and school-aged children
- Compare the prevalence of OSA in children to adults
- Compare sleep requirements and typical architecture in infants, school-aged children, and adolescents (pre- and postpuberty)
- Describe the prevalence and risk factors for sleep problems and disturbances in neurodevelopmental syndromes including autism and autistic spectrum disorders

Item II. Mechanisms of health and disease
- Describe the pathophysiology for partial arousal parasomnias in childhood
- Describe the developmental features of sleep stages and the normal timing of the appearance of sleep EEG signatures (e.g., spindles, K complexes)
- Show the interaction between processes C and S on the features of behavioral insomnia of childhood
- Describe the behavioral consequences of sleep and sleep fragmentation in children
- Compare and contrast norms for sleep state progressions in infants and children
- Describe the potential consequences of REM deprivation on brain development
- Compare features of narcolepsy to that of Kleine-Levin syndrome in childhood

Item III. Risk factors
- Describe how environmental and behavioral factors may influence sleep onset and sleep complaints
- Analyze the effect of puberty on sleep in both genders
- Discuss the associations of obesity and sleep-disordered breathing in childhood OSA
- Discuss genetic syndromes that have prominent sleep pathology (CCHS, RETT, Down syndrome, Prader-Willi, etc.)
- Discuss craniofacial abnormalities that predispose to sleep-disordered breathing

Item IV. Patient assessments
- Compare the optimal office visit for a pediatric patient to that of an adult
- Differentiate organic from behavioral sleep problems by sleep history
- Relate how you would work up a child presenting with complaints of nocturia
- Describe when and how one would ask about a potential relationship between sleep problems and abuse
- Discuss the pros and cons of a sleep diary and compare this to the use of actigraphy

Item V. Diagnostic measures and interpretation
- List features of a child- and family-friendly sleep study
- Use age and developmentally appropriate language to explain to a school-aged child and caregiver what to expect at an overnight sleep study
- Compare scoring rules for respiratory events in infants, children, and adults
- Describe normal values for sleep latency, arousal indices, periodic limb movements, and breathing rate in infants, toddlers, school-aged children, and adolescents
- Distinguish the scoring definitions for respiratory events in children and adults
- Discuss the choices for editing the raw data and summary measures for the key elements in actigraphy that are used to assess sleep-wake patterns and direct treatment recommendations
- List the indications for polysomnography in children and how your strategy for interpreting the study might vary based on the indication

(continued)

(continued)

Item VI. Disease management

- List the principal outcome measures for treatment of sleep apnea in children
- Describe the key treatment strategies for delayed sleep-phase disorder in adolescents
- Discuss adenotonsillectomy for OSA, including diagnostic and follow-up guidelines
- Describe key elements to a multidisciplinary approach to night wakings in children with neurodevelopmental syndromes
- Compare the strategies used to treat the limit-setting type of behavioral insomnia of childhood with the sleep association type of behavioral insomnia of childhood
- Discuss the pharmacologic and nonpharmacologic strategies for treating hypersomnolence disorders in children

Item VII. Health and disease clinical pathways

- Propose a collaboration pathway with alternative and complementary medicine to improve sleep knowledge and the value placed on sleep for children and adolescents in the community
- Collect information on school start time in your community
- Create a knowledge system for prevention of sleepiness in adolescent drivers
- Plan an approach to assess and improve adherence to CPAP in adolescents
- List patient expectations vs. physician objectives in terms of outcomes in the management of pediatric insomnia

Matching Test

Questions

Associated with blunted ventilatory response and increased central apneas. ☐
Normal rhythmic event often seen with sleep initiation or reinitiation. ☐
Sleep history mnemonic. ☐
Common complaint in surveys of adolescent insomnia. ☐
A nonepileptic stereotypic parasomnia. ☐
Choreoathetotic movements and dystonic posturing in NREM (N2 sleep). ☐
Example of an environmental cause for insomnia. ☐
Paroxysmal fussing more than 3 h a day for more than 3 weeks, often including sleep onset. ☐
Present in the EEG at 24–28 weeks of conceptional age. ☐
Sometimes called 17-p syndrome, it has an inverted circadian rhythm of melatonin. ☐
Elfin facial appearance, along with a low nasal bridge, an unusually cheerful demeanor, and ease with strangers. ☐
Has not only sleep hypoventilation but also autonomic dysregulation. ☐
Questions to determine Owl-Lark phenotype. ☐

Answers

1. Behavioral insomnia of childhood, limit-setting type
2. Delayed sleep-phase disorder
3. Advanced sleep-phase disorder
4. Tourette's syndrome
5. RETT syndrome
6. Achondroplasia
7. Asperger's syndrome
8. Type II Chiari malformation
9. Hirschsprung's disease
10. Headbanging
11. Amphetamine
12. Cerebral palsy
13. BEARS
14. Sunday night insomnia
15. Blindness
16. Benzodiazepines
17. SIDS
18. Paroxysmal hypnogenic dystonia
19. REM behavior disorder
20. Cow's milk allergy
21. Clonidine
22. Clonazepam
23. Colic
24. Forbidden sleep zone
25. Delta brushes
26. Alpha-delta sleep pattern
27. Pierre-Robin
28. Prader-Willi
29. Smith-Magenis syndrome
30. Williams syndrome
31. Down syndrome
32. Kleine-Levin syndrome
33. CCHS
34. PHOX2b
35. Transitional objects
36. Sleep enuresis
37. Morning-eveningness preference
38. Adenotonsillectomy

Questions with Answers

Associated with blunted ventilatory response and increased central apneas. 8
Normal rhythmic event often seen with sleep initiation or reinitiation. 10
Sleep history mnemonic. 13
Common complaint in surveys of adolescent insomnia. 14
A nonepileptic stereotypic parasomnia. 19
Choreoathetotic movements and dystonic posturing in NREM (N2 sleep). 18
Example of an environmental cause for insomnia. 20
Paroxysmal fussing more than 3 h a day for more than 3 weeks, often including sleep onset. 23
Present in the EEG at 24–28 weeks of conceptional age. 25
Sometimes called 17-p syndrome, it has an inverted circadian rhythm of melatonin. 29
Elfin facial appearance, along with a low nasal bridge, an unusually cheerful demeanor and ease with strangers. 30
Characterized by sleep hypoventilation and autonomic dysregulation. 33
Questions to determine Owl-Lark phenotype. 37

Essay Questions

Case Study 1

Parasomnia

A 5-year-old otherwise healthy girl presents with complaints of night wakings. For the last year, she has episodes of waking suddenly and appearing extremely agitated and fearful. She is often sweating and breathing very heavily during these episodes. Her parents' attempts to console her are usually ineffective. In addition, they have found her wandering the house at night on a few occasions. She appears to be awake, but when she speaks to them she does not make much sense. She is easy to redirect back to bed during these wakings.

Questions

1. What is the differential diagnosis for this presentation? Briefly list the key additional historical points you need to know to determine the most likely diagnosis.
2. You elicit a history of moderate snoring. You decide to order a polysomnogram to evaluate the above behaviors and to rule out sleep-disordered breathing. What information would you include on the order to the lab?
3. The additional history you obtain from the parent strongly suggests these episodes are partial arousal parasomnias. The polysomnogram reveals mild snoring with no significant sleep-disordered breathing. She has an episode during slow wave sleep in which she sits up, cries out briefly, and then lies back down. The background EEG pattern during this event appears to be N3 sleep. What other findings should you look for in the EEG?
4. The child and parent follow up with you after the study. List the major bullet points of your discussion with them in terms of treatment. What would be indications for pharmacologic treatment?
5. The child's grandmother calls you the following week. She is very concerned that these episodes mean the child is being abused. There are no behavioral concerns during the day. The child has a very happy demeanor and is doing well in kindergarten. What do you tell the grandmother about the relationship between partial arousals and trauma?

Ideal Answers

1. Partial arousal parasomnia (night terror, sleep walking, confusional arousal) is the most likely diagnosis. Other things to consider include seizure disorder/nocturnal epilepsy, nightmares, and nighttime panic attacks.
   Historical elements:
   - Time of night they occur
   - Single or multiple episodes per night

- Recall of events
- Triggers for events
- Presence of repetitive or stereotyped movements, incontinence

Additional explanation: Partial arousal phenomena usually occur in the first third of the night out of slow-wave sleep, rarely occur more than once per night, do not include stereotyped movements, and rarely include incontinence. There is often a family history. Nocturnal epilepsy may occur more than once per night, occurs at more variable times during the night and more often with sleep-wake transitions, and usually includes stereotyped movements, drooling, or incontinence. There is often significant sleep fragmentation and subsequent daytime dysfunction, unlike partial arousal parasomnias. Children are usually amnesic to the events in both partial arousal phenomena and nocturnal epilepsy but have vivid recall of nightmares. Sleep deprivation commonly triggers partial arousal parasomnias and can trigger epilepsy. Nightmares usually occur in the last third of the night. Nighttime panic attacks are usually accompanied by daytime panic attacks, and there is recall of the events.

2. The indication for the study is both sleep-disordered breathing and parasomnia. If there are features in the history concerning for nocturnal epilepsy, you should consider ordering additional EEG sensors. It will be important to have good video and audio recording so you can examine any episodes that occur.
3. The background EEG should be examined for epileptiform discharges, including spike and slow wave and sharply contoured waveforms.

- Safety measures, including ways to notify parent of events, reducing chances of climbing out of windows, leaving the house, and falling down stairs
- Importance of adequate sleep to reduce frequency of events
- Appropriate response during an event – gently guiding child back to bed, not attempting to awaken the child, and avoiding next-day discussions
- Indications for pharmacologic treatment (frequent severe episodes, significant safety concerns)

4. Reassure the grandmother that these are common events in childhood and there is no evidence that they are caused by trauma or psychological problems.

Case Study 2

An 8-year-old boy presents with concerns about falling asleep during school. His mother is worried that he has sleep apnea, because her mother was diagnosed with sleep apnea after she started falling asleep a lot during the day. There is no snoring, but he is a restless sleeper and moves his legs a lot. He started falling asleep in school in the last year, and his teachers have been calling home regularly. They think he is lazy and have been sending him to the principal's office multiple times per week. His Epworth Sleepiness Score is 20. Prior to this year, he did very well in school and was a very active boy. He started gaining weight 1 year ago and now has a BMI above the 97th percentile for his age.

Questions

1. Is excessive daytime sleepiness typical for childhood sleep apnea? If not, what is the typical presentation in terms of daytime symptoms?
2. What is your differential diagnosis for this presentation? What additional questions will you ask to help determine the most likely diagnosis?
3. If he has narcolepsy, what are some key findings you might expect on his physical exam?
4. How will you evaluate him?
5. He has a PSG/MSLT. There is no evidence for sleep-disordered breathing. Total sleep time on the PSG is 8 h 45 min. He has significant sleep fragmentation with increased wakings and arousals. His sleep latency is short (5 min). He has increased periodic limb movements during sleep with associated arousals (PLMI of 15 and a PLMAI of 5). On the MSLT the following day, he naps in 4 out of 5 napping opportunities, his mean sleep latency is 5 min, and he has 3 sleep onset REM periods. How do you interpret these tests?
6. You see him for a follow-up in the clinic. What are your treatment recommendations? List some key points in counseling the family? How should you interact with his school?

Ideal Answers

1. Excessive daytime sleepiness is not a typical complaint in obstructive sleep apnea or other disorders that cause sleep fragmentation in school-aged children. School-aged children more often have attentional problems or hyperactivity as daytime consequences of OSA.
2. This degree of excessive daytime sleepiness strongly suggests a hypersomnolence disorder such as narcolepsy or idiopathic hypersomnia. You could also consider inadequate sleep, severe psychiatric disorders, head trauma, frequent nocturnal seizures, medication side effects, and ingestion of drugs. Kleine-Levin is a syndrome with recurrent episodes of hypersomnia that usually presents in adolescent boys. Additional historical elements would include usual sleep schedule, sleep hygiene, the presence of cataplexy, hypnagogic hallucinations, sleep paralysis, nocturnal wakings, automatic behaviors, medication history, presence of drugs in the home, history of trauma or serious illnesses, signs of early puberty present, and family history of sleep disorders especially hypersomnias.
3. In general, the physical exam in children with narcolepsy is often normal, although children are often overweight or obese, have an increased incidence of precocious puberty, and may fall asleep in the exam room.
4. PSG/MSLT, sleep diaries, and urine toxicology testing. Consider testing for the narcolepsy HLA haplotype (DQB1*0602). In rare cases, CSF hypocretin-1 may be ordered as well as brain imaging.
5. The PSG and MSLT are consistent with narcolepsy. Increased periodic limb movements can be seen in narcolepsy, although they can also be associated with decreased iron stores so a serum ferritin should be ordered. There is often significant nocturnal sleep fragmentation in narcolepsy as seen on this study.

His mean sleep latency and the number of SOREM's meet ICSD-2 criteria for narcolepsy. The normal mean sleep latency in prepubertal children is higher than it is in adults, so all prepubertal children with hypersomnolence disorders may not meet these criteria. You would decide if he had narcolepsy without cataplexy or narcolepsy with cataplexy based on the history.

6. Alerting agents would be recommended. Modafinil and armodafinil do not have pediatric labeling but may be used. Long-acting amphetamines may also be used, sometimes with additional short-acting doses depending on the child's response and symptoms. Medications for cataplexy include SSRIs and sodium oxybutate:
   - Narcolepsy is a lifelong condition that responds well to treatment; it cannot be cured.
   - Cataplexy and other features may develop later so the family should observe the child for them.
   - Good sleep hygiene with a regular sleep schedule is very important.
   - Scheduled brief naps once or twice a day may be helpful.
   - Weight management is important.
   - Treat any comorbid sleep conditions to reduce sleep fragmentation.
   - The sleepiness is not under the patient's control – it is not laziness or oppositional behavior and should not be punished.
   - Direct communication with the school is often needed – most educators have little experience with this condition.
   - Family members with EDS should be tested (genetic component).

Case Study 3

JB is a 16-year-old girl who presents to the sleep clinic with a complaint of trouble falling asleep. She first started noticing she was having trouble falling asleep when she started 10th grade. She is currently in 11th grade, and she feels it is getting worse because she has recently started being late to school because she has trouble getting up in time. She reports a lot of fatigue during the school day, but is not actually falling asleep during school. However, she often dozes off when she is trying to do her homework. Her Epworth Sleepiness Score is 12/24.

Questions

1. List your differential diagnosis and some additional elements in the history that will help you in the evaluation.
2. You elicit the following sleep schedule: she goes to bed at 11 p.m., falls asleep around 2 a.m., and has her alarm set for 6 a.m.. She often oversleeps and does not remember her alarm going off. On weekends, she goes to bed at 1:30, falls asleep in 20–30 min, and gets up between 10 and 11. What does this schedule suggest?

3. She does not snore. She denies symptoms of restless legs or growing pains. She reports a few episodes of sleep walking as a younger child but not for several years. She denies cataplexy, hypnagogic hallucinations, and sleep paralysis. What testing if any would you order?
4. List some strategies you will recommend as treatment.
5. She returns to the clinic in 2 months and has not been successful in implementing the strategies you suggested. Her schedule has now shifted even later, and she routinely falls asleep around 3 a.m. What other option do you have to reset her clock?

Ideal Answers

1. Delayed sleep-phase disorder, psychophysiologic insomnia, insomnia due to medical or psychiatric condition, restless legs syndrome, sleep apnea, poor sleep hygiene, school avoidance, psychiatric disorder, hypersomnolence disorder. The most important elements in the history will be a detailed sleep schedule history, including sleep latency, schedule shifts between weekdays/weekends, total sleep, and sleep hygiene issues including screen time in the evenings. Additional helpful historical elements include the presence of snoring/leg symptoms, screening for psychiatric history, medical history, school performance, and problems at school (bullying, etc.).
2. Strongly suggests delayed sleep-phase disorder because sleep latency is normal when she sleeps during her preferred schedule. The sleep inertia (not hearing alarm) would be expected at 6 a.m. if her preferred schedule is to sleep from 2 to 10.
3. Sleep diaries to confirm her schedule would be helpful. If there are discrepancies between her report and the parent's report or she has difficulty describing her sleep schedule, actigraphy could be helpful. A PSG is probably not necessary, but could be considered to rule out unrecognized sleep apnea or movement disorder.
4. Anchoring wake time, phase advancement, bright light therapy, melatonin at phase shifting dose 5–7 h before desired bedtime, sleep hygiene, and avoiding naps.
5. When the difference between the desired and current sleep time is more than 3 h, phase delay (chronotherapy) may be necessary. This involved delaying the bedtime and wake time by 2–3 h every 1–2 days. If her current bedtime is 3 a.m., the first night she would stay up until 6 a.m. and sleep until 2 p.m., advancing forward until the desired schedule is achieved. Chronotherapy requires significant motivation and support from the family to accomplish. It should be timed during a vacation if possible to avoid missing school.

IQ Case

IQ Case for Student

Goal: The evaluation of the child for sleep-disordered breathing involves assessments beyond that of the patient and sensitivity to the risk factors, diagnostic, prognostic, and outcome found in this population, as compared to adult presentations.

Case Vignette

A 7-year-old girl with a past medical history significant for trisomy 21 was referred to you by her primary care physician for complaints of difficulty sleeping. Her mother reports that she goes to bed at around 8:00 p.m. and falls asleep quickly but wakes up multiple times through the night and often comes into the parent's bedroom. They have observed loud snoring, especially when she sleeps on her back. In the last several months, they have also observed her to stop breathing and then gasp and choke. She is not sleepy during the day, but she has been having some behavioral problems recently with difficulty concentrating and doing tasks she used to do well. She has also started to wet the bed after being dry at night for a few years. Her mother describes that she has always been a "little chubby," but the pediatrician has been concerned about excessive weight gain in the last 1–2 years.

In terms of her development, she is described as a "high functioning" Down syndrome patient. She attends a regular school with extra help from an aide. She speaks fairly clearly and is cooperative with your exam. On PE, her weight is at the 95th percentile and her height is at the 50th percentile using a Down syndrome-specific growth curve. Her BMI is above the 97th percentile. She has facial features typical of trisomy 21, including a small midface, crowded oropharynx, and a tongue that is large relative to her mouth. Her tonsils are 3+. Her nasal turbinates are edematous. The lungs, heart, and abdominal exams are normal. Her extremities are warm and well perfused without edema. On neuro exam, she has mild hypotonia but is otherwise normal.

You order a polysomnogram. Your child-friendly sleep lab has a child life worker who helps with the set up, and with the mother's help they are able to apply all the sensors. The polysomnogram shows the following: waking RR is 18, SpO2 is 98 %, ETCO2 is 42, and TCCO2 is 44 mmHg. Sleep onset latency is 10 min. Sleep efficiency is 75 %. Sleep maintenance efficiency is 77 %. The child spends 15 % of the night in N1 sleep, 70 % of the night in N2 sleep, 5 % of the night in N3 sleep, and 10 % of the night in REM sleep. She has 32 wakings and her arousal index is 25. Moderate continuous snoring observed. Frequent obstructive hypopneas and occasional obstructive apneas in NREM sleep. Frequent obstructive apneas in REM sleep. Occasional central apneas post arousal and in REM. The overall OAHI is 41. The REM OAHI is 63. There are periods with sustained oxygen saturations in the high 80s with ETCO2s in the low 50s without scoreable respiratory events.

During REM, there are oxygen desaturations to the high 70s with respiratory events. The 3 % oxygen desaturation index is 50. The child spends 50 % of the night with oxygen saturations below 90 %. ETCO2 values are above 50 mmHg for 30 % of the night and TCCO2 values are above 50 mmHg for 55 % of the night. Mean heart rate is 110 bpm during sleep; the rhythm is sinus tachycardia with rare PVCs. There are no excessive periodic limb movements during sleep.

She undergoes adenotonsillectomy the following week. Her evaluation for pulmonary hypertension prior to anesthesia is normal. Her snoring improves. You repeat the PSG 6 weeks later and the OAHI is 15. Her oxygenation is improved, but she still spends 10 % of the night with oxygen saturations below 90 %. Her ETCO2 and TCCO2 are improved, with 20–25 % of the night with values above 50 mmHg. Mild sleep fragmentation is present. A CPAP titration study shows good control of sleep apnea with CPAP 8 cm H_2O but there is limited supine REM sleep captured. She is placed on autoPAP and returns to the clinic after 1 month. The CPAP download shows some use on 80 % of nights, but use for more than 4 h on only 35 % of nights. You elicit additional history from the mother and discuss strategies to improve adherence.

IQ Case for Facilitator

Goal: The evaluation of the child for sleep-disordered breathing involves assessments beyond that of the patient and sensitivity to the risk factors, diagnostic, prognostic, and outcome found in this population, as compared to adult presentations.

Learning Objectives

A. List the characteristics of this patient that contribute to her risk of sleep-disordered breathing.
B. Discuss what makes a sleep lab "child-friendly."
C. Interpret the polysomnogram findings in terms of sleep architecture and respiratory findings.
D. Discuss the potential consequences of untreated sleep apnea in children.
E. Describe the treatment options and the risk factors for residual OSA in this child after adenotonsillectomy.
F. Discuss barriers to adherence to CPAP in children and general strategies you would recommend.

Case Vignette

A 7-year-old girl with a past medical history significant for trisomy 21 was referred to you by her primary care physician for complaints of difficulty sleeping. Her mother reports that she goes to bed at around 8:00 p.m. and falls asleep quickly but wakes up multiple times through the night and often comes into the parent's bedroom. They have observed loud snoring, especially when she sleeps on her back. In the last

several months, they have also observed her to stop breathing and then gasp and choke. She is not sleepy during the day, but she has been having some behavioral problems recently with difficulty concentrating and doing tasks she used to do well. She has also started to wet the bed after being dry at night for a few years. Her mother describes that she has always been a "little chubby," but the pediatrician has been concerned about excessive weight gain in the last 1–2 years.

Probing Questions

1. What is the most likely diagnosis?
2. What are the risk factors for this diagnosis in this patient?

Ideal Answers

1. Obstructive sleep apnea is the most likely diagnosis due to the history of snoring, fragmented sleep, and secondary enuresis.
2. Risk factors include the small midface, relatively large tongue, and large neck that are typical of trisomy 21, hypotonia typical of trisomy 21, and recent weight gain.

In terms of her development, she is described as a "high functioning" Down syndrome patient. She attends a regular school with extra help from an aide. She speaks fairly clearly and is cooperative with your exam. On PE, her weight is at the 95th percentile and her height is at the 50th percentile using a Down syndrome-specific growth curve. Her BMI is above the 97th percentile. She has facial features typical of trisomy 21, including a small midface, crowded oropharynx, and a tongue that is large relative to her mouth. Her tonsils are 3+. Her nasal turbinates are edematous. The lungs, heart, and abdominal exams are normal. Her extremities are warm and well perfused without edema. On neuro exam, she has mild hypotonia but is otherwise normal.

Probing Questions

3. What is the next step to confirm the diagnosis?
4. What special considerations are there in proceeding due to her history of trisomy 21?

Ideal Answers

3. An overnight polysomnogram is indicated.
4. She is "high functioning" and cooperative with your exam, so it is reasonable to expect that an experienced child-friendly lab should be able to accomplish this test. The ordering physician should do everything they can to prepare the child and family for what to expect to help things run smoothly. This can include a pamphlet or brochure with pictures of the process or a visit to the lab ahead of time. Child life professionals are often very helpful in these situations.

You order a polysomnogram. Your child-friendly sleep lab has a child life worker who helps with the set up, and with the mother's help they are able to apply all the sensors. The polysomnogram shows the following: waking RR is 18, SpO2 is 98 %, ETCO2 is 42, and TCCO2 is 44 mmHg. Sleep onset latency is 10 min. Sleep

efficiency is 75 %. Sleep maintenance efficiency is 77 %. The child spends 15 % of the night in N1 sleep, 70 % of the night in N2 sleep, 5 % of the night in N3 sleep, and 10 % of the night in REM sleep. She has 32 wakings and her arousal index is 25. Moderate continuous snoring observed. Frequent obstructive hypopneas and occasional obstructive apneas in NREM sleep. Frequent obstructive apneas in REM sleep. Occasional central apneas post arousal and in REM. The overall OAHI is 41. The REM OAHI is 63. There are periods with sustained oxygen saturations in the high 80s with ETCO2s in the low 50s without scoreable respiratory events. During REM, there are oxygen desaturations to the high 70s with respiratory events. The 3 % oxygen desaturation index is 50. The child spends 50 % of the night with oxygen saturations below 90 %. ETCO2 values are above 50 mmHg for 30 % of the night and TCCO2 values are above 50 mmHg for 55 % of the night. Mean heart rate is 110 bpm during sleep; the rhythm is sinus tachycardia with rare PVCs. There are no excessive periodic limb movements during sleep.

Probing Question

5. How do you interpret these results?

Ideal Answer

5. Severe obstructive sleep apnea with sleep fragmentation. Obstructive hypoventilation in addition to scored respiratory events. Severe hypoxemia. Sinus tachycardia, which may be due to OSA but should also prompt evaluation for pulmonary hypertension as a consequence of untreated OSA.

She undergoes adenotonsillectomy the following week. Her evaluation for pulmonary hypertension prior to anesthesia is normal. Her snoring improves. You repeat the PSG 6 weeks later and the OAHI is 15. Her oxygenation is improved, but she still spends 10 % of the night with oxygen saturations below 90 %. Her ETCO2 and TCCO2 are improved, with 20–25 % of the night with values above 50 mmHg. Mild sleep fragmentation is present. A CPAP titration study shows good control of sleep apnea with CPAP 8 cm H_2O but there is limited supine REM sleep captured. She is placed on autoPAP and returns to the clinic after 1 month. The CPAP download shows some use on 80 % of nights, but use for more than 4 h on only 35 % of nights. You elicit additional history from the mother and discuss strategies to improve adherence.

Probing Questions

6. What is the first-line therapy for OSA in children?
7. Is it different in children with trisomy 21 compared with healthy children?

Ideal Answers

6. Adenotonsillectomy is the first-line treatment if the child is a surgical candidate based on assessment by a pediatric otolaryngologist.
7. Children with trisomy 21 are at increased risk for residual OSA, so repeating the PSG after surgery is necessary. CPAP is the next line, but adherence can be challenging in special populations and often requires a multidisciplinary approach.

IQ Case Handout/Objectives

Goal: The evaluation of the child for sleep-disordered breathing involves assessments beyond that of the patient and a sensitivity to the risk factors, diagnostic, prognostic, and outcome found in this population, as compared to adult presentations.

Learning Objectives

A. List the characteristics of this patient that contribute to her risk of sleep-disordered breathing.
B. Discuss what makes a sleep lab "child-friendly."
C. Interpret the polysomnogram findings in terms of sleep architecture and respiratory findings.
D. Discuss the potential consequences of untreated sleep apnea in children.
E. Describe the treatment options and the risk factors for residual OSA in this child after adenotonsillectomy.
F. Discuss barriers to adherence to CPAP in children and general strategies you would recommend.

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Chapter 18
Sleep and Aging

Nikolaus Netzer and Kingman P. Strohl

Introduction

The demographic changes of the population in Western countries such as the USA are now becoming visible in the daily medical practice. More and more elderly persons with ages over 70 years (most research in the USA defines >65 years as elderly) frequent doctors' offices, including sleep clinics. Whereas sleep disorders have been long underestimated in the elderly population and medicine concentrated on middle-aged population groups such as the Wisconsin cohort, recent research has recognized a high prevalence of sleep disorders in the elderly with impact on frailty and the overall cost for the health system. The foundation is now in place so that training in sleep medicine must include an appreciation of sleep disorders in the elderly. The ACGME requirements for a Sleep Medicine Fellowship (http://www.acgme.org/acWebsite/downloads/RRC_progReq/520_sleep_medicine_07012012.pdf: last accessed 2/22/12) state that trainees must demonstrate comprehensive knowledge of the aging effects on the physiology and pathophysiology related to sleep. This is most clearly stated in the Medical Knowledge competency, though elements of this topic can be found in other competencies as well.

For this chapter, the content and competency examples were developed through discussions with sleep faculty and fellows, review of existing literature in the

N. Netzer, M.D., Ph.D. (✉)
Research Program for Hypoxia and Sleep Medicine Research,
Research Program of the Paracelsus Medical University, Hermann Buhl Institute and Clinic Ghersburg for Geriatric Rehabilitation, Ghersburgstr. 9,
83043 Bad Aibling, Germany
e-mail: nikinetzer@yahoo.com

K.P. Strohl, M.D.
Case Western Reserve University, Cleveland, OH, USA

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fields of interest, and examination of the ACGME requirements. The ACGME requirements list comprehensive knowledge in a number of physiologic domains, though some of these (i.e., basic neurological mechanisms of sleep, respiratory physiology during sleep) are covered in other chapters in this book and will not be addressed here. This chapter will focus on the effect that aging has on sleep and the specificities of diagnostic and treatment options of sleep disorders in the elderly with ages of 70 years and up.

This chapter is not designed to be an all-inclusive review of the literature in this field of study, but rather to highlight important findings expected to be part of a sleep practitioner's knowledge base as well as to provide specific examples of how topics in this area could be taught and then assessed for competency. Table 18.1 provides a cognitive road map of content domains showing how subtopics may be related to the ACGME general competencies for training in sleep medicine. Medical Knowledge is the competency most applicable to the topic of sleep and aging, though there are areas where patient care and other general competencies can be addressed and assessed. Table 18.2 lists examples of content-specific questions from which learning objectives can be formulated and then assessed. These questions can also be used as essay questions, spur journal club discussions, or form the basis of a lecture on the particular issue raised by the question. The goals of these lectures are to provide standardized content from which the program can evaluate the learner's knowledge through mechanisms listed below as well as to provide direction for the trainee for further self-learning.

Intertwined with the content delivery, as organized and discussed above, is the need to assess competency of the learner in these areas. This chapter provides specific case examples of how this can be accomplished. We include examples of traditional knowledge assessment tools utilizing matching tests to review factual knowledge of sleep and aging. As more data becomes available in this field, these questions can be modified and additions can be made. Essay questions attempt to assess a more comprehensive understanding of the issue posed. These can be provided as either closed or, if self-directed learning is the goal, open book written questions. However, the most useful method to gauge the learner's comprehension of the topic might be to pose these types of questions as open discussion questions in a one-on-one session. This allows the evaluator to change the direction of the discussion to assess particular subtopics as well as allows the evaluator to judge the learner's ability to "think on their feet." And finally, IQ cases offer examples of group exercises, in which the learning objectives are disclosed only after the fact, requiring the learners to seek and evaluate information that they believe will achieve the learning objectives of the case. These group discussions are helpful for the learners in that they can share knowledge and hopefully improve their learning techniques. The IQ cases are probably best used to obtain an overall assessment of where the group or program is in their training. There are inherent limitations to performing individual assessments with this tool.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/geriatric-sleep-disorders.html). It may be reviewed by the student and the program or discussed in a group format before or after the essay questions or IQ case.

Table 18.1 Cognitive Map of the Content Domains Relevant to Sleep and Physiology[a]

	Knowledge	Skills	ACGME competency
I. *Epidemiology*	Yes	No	B, F
Age			
Risk factors			
Special populations			
II. *Mechanisms of health and disease*	Yes	No	A, B
Circadian rhythm system			
Autonomic nervous system			
Cardiovascular			
Respiratory			
Endocrine			
Immunologic			
Cognitive function			
III. *Risk factors*	Yes	No	A, B
Environmental			
Genetic			
Age-related			
IV. *Patient assessments*	Yes	Yes	A, C, D, E
Adult			
Special populations			
V. *Diagnostic measures and interpretation*	Yes	Yes	A, C, F
Hemodynamic measurements			
Cognitive function testing			A, C
Long-term pulse oximetry			
Brain transmitter measures			
Patient-based testing			A, B, F
VI. *Disease management*	Yes	Yes	
Presentation of therapeutic options			A, E, D, F
Decisions on therapy			A, F
Follow-up			A, F
VII. *Health and disease clinical pathways*	Yes	Yes	A, C, F
Cardiovascular assessment			
Cognitive function assessment			
Sleep deprivation, circadian rhythms, and endocrinological diseases			
Sleep and host susceptibility			
Insomnia			
Parkinson-specific assessment			

Code for ACGME competencies

A. Patient care	D. Interpersonal skills
B. Medical Knowledge	E. Professionalism
C. Practice-based learning and improvement	F. System-based practice

[a]Basic neurological mechanisms of sleep and respiratory physiology are covered in the chapter on sleep-disordered breathing

Table 18.2 Examples of Topics with Educational Objectives for Sleep and Aging

Item I. Epidemiology

- Compare the prevalence of sleep-disordered breathing and insomnia in the elderly to other age groups
- List frailty grades and how they may be connected to sleep quality
- Give an assumption of the connection between SDB and stroke risk in the elderly
- Discuss the difference of importance of high blood pressure during daytime between the elderly and middle-aged persons

Item II. Mechanisms of health and disease

- Propose a mechanism by which changes in daily behavior and activities of daily living increase insomnia in elderly people
- Suggest a pathophysiology based on airway collapsibility for the increase of sleep-disordered breathing with aging
- Make a table that details how changes in neurological mediators with aging alter sleep function. How could the reduction of acetylcholine in elderly with Alzheimer's dementia influence REM sleep?
- Show the interaction between processes of Parkinson's disease on the central level of sleep generation
- Describe feedback loops in the interaction of melatonin on the sleep-wake cycle and circadian and seasonal rhythms that could be changed with aging and what the reasons for those changes could be (e.g., reduction in light sensitivity of the retina and overall light exposure, calcification of the pineal gland). What would that impose on the thermoregulation of elderly people?

Item III. Risk factors

Name reasons for an impaired respiratory drive in sleep after a stroke

- Discuss the pros and cons of wearing complete and partial dentures at night in regard to its effect on pharyngeal structure
- What forms of arterial hypertension would you consider to be more clearly related to sleep-disordered breathing in the elderly than others (SDB as the risk factor)?
- Explain the advanced sleep phase and the delayed sleep phase syndrome in examples implying the daily living behaviors of seniors
- Why could generalized anxiety disorder (GAD) play an even greater role in affecting sleep in the elderly than in younger people?

Item IV. Patient assessments

- The ONSI and the Essen Inventory are an SDB and a daytime sleepiness questionnaire developed especially for elderly people. Compare the advantages of a questionnaire specific for elderly people with sleep disorders to the general questionnaires like Epworth, Berlin, and Pittsburgh Sleep Quality of Life Index
- Select the most important geriatric assessments that should accompany a patient interview for sleep problems and sleep behavior in elderly patients
- Relate how you would link fall injuries to a senior's sleep problems
- When would you do brain imaging in elderly patients with sleep problems?

Item V. Diagnostic measures and interpretation

- What measures would you take to distinguish different movement disorders RLS (restless legs syndrome) and RBD (REM sleep behavior disorder) at first hand in patients whose relatives complain about their interrupted nights?

(continued)

(continued)

- Which types of apnea (obstructive, central, mixed) or hypopnea would you expect to see more often in elderly patients with sleep apnea?
- Lay out the higher prevalence of some organic diseases in the elderly and their link to sleep apnea
- In order to establish the diagnosis of insomnia in an elderly person
- Describe pretest probability and posttest uncertainty for diagnostic testing for insomnia
- Explain sensitivity and specificity for clinical outcomes
- Discuss how you would combine cognitive function assessment with assessment for sleep disorders in the elderly
- Discuss what the major weaknesses of these assessment tools are in a clinical and psychological context

Item VI. Disease management

- Discuss the actual data on CPAP adherence in elderly and why research data might be different from clinical experience
- Advise an elderly patient with insomnia on non-drug-related treatment options such as behavioral therapy
- Describe the interaction of different sleep and sedative medication with its possible effects on sleep quality
- Discuss the effect of oxygen therapy as a possible alternative to CS CPAP in patients with Cheyne-Stokes respiration and heart failure and extend this discussion to non-CPAP compliant patients with OSAS
- Discuss how anti-dementia drugs might have effects on sleep
- List the effects of a treatment with melatonin and drugs with effect on melatonin metabolism in elderly patients
- Compare that to light therapy
- Imagine novel approaches

Item VII. Health and disease clinical pathways

- Propose a collaboration pathway in assessing patients with sleep movement disorders and sleep and breathing disorders
- Analyze the effect of sex hormone replacement on sleep in both genders
- Describe the principles in the initiation of therapy
- Now that a patient has responded to therapy, list the factors for management of apnea as a chronic disease in elderly patients
- List patient expectations vs. physician objectives in terms of outcomes

Matching Test

Questions

Decreases linear with age. ☐

Decreases in aged men influencing circadian rhythm via hypothalamic-pituitary-adrenal axis. ☐

How influences reduced acethylcholine REM in Alzheimer's patients? ☐

The decreased hypocretin/orexin levels in the elderly lead to…. ☐

Loop gain in the elderly is most likely to…. ☐

Which would mean that…. ☐
But upper airway resistance is higher in the elderly most likely due to…. ☐
Therefore the Pcrit in the elderly is…. ☐
The diurnal blood pressure curve with a dipping of BP at night (10–20 % lower than average daytime BP) in many (60 %) elderly is …. ☐
The relationship between stroke and OSA in the elderly appears to be…. ☐
The mortality in stroke patients who develop SDB within 24 h after the incident is …. ☐
Besides their strong correlation to all forms of SDB, cardiovascular disorders in the elderly often lead to …. ☐
Among the sleep phase shift syndromes, more often in the elderly is…. ☐
In the elderly ASPS is rather than to a shortened circadian period more likely related to…. ☐
The recommended treatment for ASPS in all age groups in principle of practice parameters is…. ☐
The sleep-wake amplitude and the body core temperature amplitude in the elderly are…. ☐
The simple and inexpensive lab parameters to accompany the diagnostic procedure in elderly patients with RLS (restless legs syndrome) are…. ☐
REM sleep behavior disorder (RBD) is often related in elderly patients to…. ☐
Besides the neurodegeneration as cause for RDB in Parkinson's patients, the onset of the parasomnia is also linked to …. ☐
Besides its slightly higher prevalence in the elderly compared to middle-aged adults, RLS in the elderly is more often…. ☐
Of the different psychiatric disorders leading to insomnia in the elderly, the vast majority belongs to …. ☐
Because of their reduced drug abuse and dependency potential as well as reduced cardiovascular side effects in the elderly. ☐
The prevalence of insomnia in the elderly (>65) is estimated by objective major studies (National Sleep Foundation Survey, Upper Bavarian Field Study, National Institute on Aging) to be …. ☐
Regarding a gender preference for the prevalence of insomnia that is between middle-aged adults and seniors. ☐
Compared to healthy elderly persons, Alzheimer's patients show a reduction of the following polysomnographic parameters. ☐
Besides circadian and sleep architectural changes in Alzheimer's patients with advancing dementia have a significantly higher prevalence for…. ☐
Because regular chrono-medication with melatonin or usual light therapy with light boxes are less practical in severe dementia patients, a more practical form of therapy is…. ☐
Treatment of SDB with CPAP and medication with cholinesterase inhibitors in Alzheimer's patients improve. ☐

Answers

1. Melatonin
2. TSH, LH, testosterone
3. REM decreases
4. Increased daytime sleepiness and daytime naps
5. Slightly decrease with aging
6. A high respiratory drive is not playing a major role in predisposing the elderly for severe sleep apnea
7. Lower pharyngeal muscle tension, less stability in the soft tissue, and increased pharynx length
8. Increased
9. Flattened, the dipping attenuated
10. Bidirectional
11. Highly increased
12. Insomnia
13. Advanced sleep phase syndrome (ASPS)
14. Behavior and lifestyle changes including a shorter and less exposure to bright light
15. Chronotherapy, timed melatonin, and light therapy
16. Decreased
17. Iron and ferritin
18. Parkinson's disease
19. Higher daily doses of dopaminergic medications
20. Underdiagnosed
21. Generalized anxiety disorder (GAD)
22. Melatonin and long-acting melatonergic agents (ramelton, agomelatine) have been found to be clinically useful drugs against depression and insomnia in this age group
23. Between 23 % and 36 %
24. No difference. Women prevail significantly independent of age
25. SWS, REM, and sleep spindles
26. Sleep-disordered breathing (SDB)
27. Room light therapy
28. Cognitive function

Questions with Answers

Decreases linear with age. 1
Decreases in aged men influencing circadian rhythm via hypothalamic-pituitary-adrenal axis. 2
How influences reduced acethylcholine REM in Alzheimer's patients? 3
The decreased hypocretin/orexin levels in the elderly lead to…. 4
Loop gain in the elderly is most likely to…. 5
Which would mean that…. 6
But upper airway resistance is higher in the elderly most likely due to…. 7
Therefore the Pcrit in the elderly is…. 8
The diurnal blood pressure curve with a dipping of BP at night (10–20 % lower than average daytime BP) in many (60 %) elderly is …. 9
The relationship between stroke and OSA in the elderly appears to be…. 10
The mortality in stroke patients who develop SDB within 24 h after the incident is …. 11
Besides their strong correlation to all forms of SDB cardiovascular disorders in the elderly often lead to …. 12
Among the sleep phase shift syndromes, more often in the elderly is…. 13
In the elderly ASPS is rather than to a shortened circadian period more likely related to…. 14
The recommended treatment for ASPS in all age groups in principle of practice parameters is…. 15
The sleep-wake amplitude and the body core temperature amplitude in the elderly are…. 16
The simple and inexpensive lab parameters to accompany the diagnostic procedure in elderly patients with RLS (restless legs syndrome) are…. 17
REM sleep behavior disorder (RBD) is often related in elderly patients to…. 18
Besides the neurodegeneration as cause for RDB in Parkinson's patients the onset of the parasomnia is also linked to …. 19
Besides its slightly higher prevalence in the elderly compared to middle-aged adults, RLS in the elderly is more often…. 20
Of the different psychiatric disorders leading to insomnia in the elderly, the vast majority belongs to …. 21
Because of their reduced drug abuse and dependency potential as well as reduced cardiovascular side effects in the elderly. 22
The prevalence of insomnia in the elderly (>65) is estimated by objective major studies (National Sleep Foundation Survey, Upper Bavarian Field Study, National Institute of Aging) to be …. 23
Regarding a gender preference for the prevalence of insomnia that is between middle-aged adults and seniors. 24
Compared to healthy elderly persons, Alzheimer's patients show a reduction of the following polysomnographic parameters. 25
Besides circadian and sleep architectural changes in Alzheimer's patients with advancing dementia have a significantly higher prevalence for…. 26

Because regular chrono-medication with melatonin or usual light therapy with light boxes are less practical in severe dementia patients, a more practical form of therapy is…. 27

Treatment of SDB with CPAP and medication with cholinesterase inhibitors in Alzheimer's patients improve. 28

Essay Questions

Pharyngeal Structure

Case Study

A 78-year-old female patient in the geriatric clinic unit has been observed by her roommate with loud snoring and apneas. The patient is in the clinic for post hip replacement rehabilitation. The patient is treated for hypertension with the ACE inhibitor ramipril and a low dose ß-blocker. Otherwise she has no history of a stroke, chronic heart failure, or any other cardiovascular disease. Polysomnographic (PSG) results reveal an obstructive sleep apnea with an AHI of 56/h, an ODI of 48/h, and moderate REM and SWS reduction. The patient refuses CPAP. The patient has full dentures and sleeps regularly without them. For a second PSG night, the patient is asked to keep the dentures in at night. In this PSG night, without CPAP, the AHI and ODI are significantly reduced to 6/h and sleep stages are within normal limits.

Questions

1. Why would the recommendation to keep the dentures in overnight been useful also in the case of CPAP acceptance?
2. What causes pharyngeal instability in the elderly?
3. How does a decrease in loop gain with aging adversely affect obstructive sleep-disordered breathing in the elderly?

Answers

1. CPAP leakage is a major problem for patients with full dentures or upper jaw dentures, who sleep without their dentures, because CPAP masks do not seal well without the resistance from the upper jaw teeth. A possible solution can be nasal pillow masks for these patients. The positive effect of full and partial denture wearing at night against obstructive sleep apnea and snoring is controversially discussed in the literature with two major studies presenting opposite results.
2. The change in genioglossus muscle fibers towards less elasticity with aging is speculated to be one major reason for collapsibility. The increased size and numbers of fat pads, which replace muscle tissue and elastic tissue in the elderly, is another. Upper airway length increases with age and correlates with sleep apnea in postmenopausal women.
3. The lower loop gain is in conjunction with a decreased respiratory drive in the elderly. Thus, the effect of ventilatory instability with major cyclical oscillations in the respiratory curve and obstructive events are attenuated or reduced. However, central events are increased with the lower respiratory drive.

Parkinson's and Dementia

Case Study

A 75-year-old male presents to the sleep clinic with the complaint of violent dreams resulting in injuries to the head. The violent dreams are progressing over the last years and the patient indicates that he would on occasions hit his bed partner. In the PSG night there was an increase in limb movement in REM and on one occasion the patient would play with his cell phone during REM. Although the patient was for a while successfully treated with clonazepam against REM sleep behavior disorder, the patient developed over the next years' deficits in attention and memory and neuropsychological assessment revealed mild to moderate dementia. Bradykinesia and decreased postural reflexes finally led to the diagnosis of Parkinson's disease.

Questions

1. What is the prevalence of RBD in elderly Parkinson's patients compared to normal elderly persons?
2. Parkinson's is affecting the GABA "sleep switch" through degeneration in the VLPO (ventrolateral preoptic nucleus). What are the more common and less spectacular sleep complaints caused by this progressive neurodegeneration?
3. How can light therapy help dementia patients with circadian rhythm disorder?
4. Besides light therapy, which drug intervention could be useful in dementia patients with circadian rhythm disorder and excessive daytime sleepiness?

Answers

1. Whereas 0.5 % of the healthy elderly population develops idiopathic RBD, 33 % of newly diagnosed Parkinson's patients have reported to have RBD: The numbers are even higher for patients with Levy body dementia. Parkinson's-related degeneration of cells in the peri-locus coeruleus area is believed to interrupt the regular inhibition of alpha motor neurons and the REM sleep muscle atonia.
2. Insomnia and daytime sleepiness are affecting almost every Parkinson's patient. The distinction of the neurodegenerative effects and side effects of the aminergic drug treatment with dopamine and dopamine agonists causing insomnia is not always easily distinguishable. More distinguishable treatment forms for severe progressed Parkinson's with deep brain stimulation or apomorphine delivered via subcutaneous syringe and a pump might be an exit strategy from this dilemma.
3. Intensive blue light during daytime can be used as a chronotherapy to activate melatonin production in the pineal gland via signals from the suprachiasmatic nucleus. The timing of the light exposure can synchronize wake and sleep cycles.
4. Melatonin and MT receptor agonists such as ramelton and agomelatine.

IQ Cases

Cardiovascular Stroke for Student

Goal: Understand the effect of brain lesions caused by stroke at different brain levels on the sleep-wake cycle and respiration during sleep.

Case Vignette

A 70-year-old man is referred to the sleep clinic from neurology for evaluation of hypersomnolence and neurological impairment after a stroke. The patient had a history of hypertension and diabetes mellitus, and the actual event was his second stroke with a history of dysarthria and facial paralysis. A head CT 2 days after the actual acute event, which came with a status of unresponsiveness and positive Babinski reflexes, showed symmetric bilateral thalamic lesions suggestive of a hypoxemic cause. Cardiologic counseling revealed a now existing hypertensive heart disease with atrial fibrillation. The patient required continuous anticoagulation therapy. His breathing was regular.

The polysomnogram was performed at the stroke unit for a period of 17 h. TST was 11.5 h and total wake time 5.5 h. The longest wake periods had been an hour of duration. REM was 68 min and SWS 293 min (42 % of TST). REM latency was 202 min and sleep spindles had not been identified. At one time during wakefulness, the patient became suddenly unresponsive with immediate NREM 2. Epileptiform activity was not observed, neither were central or obstructive apneas or hypopneas with an AHI of more than 3/h.

The patient is diagnosed with hypersomnia with paroxysmal sleep, classified as hypersomnia of central origin. The patient received anti-cardiovascular risk treatment with antihypertensive medication, antidiabetes treatment, anticoagulation with rivaroxaban 15 mg twice daily, and post stroke rehabilitative treatment with speech therapy, behavioral therapy, and physical therapy.

Thalamic infarction results in markedly different clinical syndromes of their location. Paramedian thalamic infarctions are associated with supranuclear palsy, hypersomnolence, and neurological as well as memory impairments. Bilateral infarcts may lead to long-term recovery and an unfavorable outcome. The occlusion of the artery of Percheron should be considered as a main cause for such lesions.

The patient recovers with some memory impairment and speech problems quite well. A repeated PSG after a year shows a more normal sleep-wake relationship and more regular latencies. No major SDB is detected. In the interdisciplinary conference discussing the development of this patient, a young neurologist asks you he/she has heard that humans could have a total loss of dreaming after stroke.

Cardiovascular Stroke for Facilitator

Goal: Understand the effect of brain lesions caused by stroke at different brain levels on the sleep-wake cycle and respiration during sleep.

Objectives (Revealed at the End of the Session):

A. List the lesions at different major brain levels (3–5) a stroke can cause and the possible impairment of brain functions associated with each brain level.
B. Interpret the bidirectional relationship between sleep disorders and stroke.
C. Discuss the sleep-related therapeutic interventions after a stroke (noninvasive ventilation, medication, oxygen).
D. Discuss imaging for sleep disorders appearing after a stroke.
E. Propose an interdisciplinary collaboration pathway between faculties to avoid overseeing of crucial sleep problems after stroke.

Case Vignette

A 70-year-old man is referred to the sleep clinic from neurology for evaluation of hypersomnolence and neurological impairment after a stroke. The patient had a history of hypertension and diabetes mellitus, and the actual event was his second stroke with a history of dysarthria and facial paralysis. A head CT 2 days after the actual acute event, which came with a status of unresponsiveness and positive Babinski reflexes, showed symmetric bilateral thalamic lesions suggestive of a hypoxemic cause. Cardiologic counseling revealed a now existing hypertensive heart disease with atrial fibrillation. The patient required continuous anticoagulation therapy. His breathing was regular.

Probing Questions

1. What would you expect in regard to neurological impairment regarding the thalamic lesions?
2. What are the patient's expectations for recovery after his second stroke and how could they be improved through sleep medicine interventions?
3. What are his risk factors for different sleep disorders?
4. Why would you perform a sleep study although the breathing seems to be normal?

The polysomnogram was performed at the stroke unit for a period of 17 h. TST was 11.5 h and total wake time 5.5 h. The longest wake periods had been an hour of duration. REM was 68 min and SWS 293 min (42 % of TST). REM latency was 202 min and sleep spindles had not been identified. At one time during wakefulness, the patient became suddenly unresponsive with immediate NREM 2. Epileptiform activity was not observed, neither were central or obstructive apneas or hypopneas with an AHI of more than 3/h.

Probing Questions

5. What does the sleep study show? How would you interpret the distribution of sleep studies?
6. Why has the patient no sleep breathing disorder in knowledge of the CT scan results?
7. If the patient would have had sleep epilepsy, in which sleep stage would one expect to have the events happened?

The patient is diagnosed with hypersomnia with paroxysmal sleep, classified as hypersomnia of central origin. The patient received anti-cardiovascular risk treatment with antihypertensive medication, antidiabetes treatment, anticoagulation with rivaroxaban 15 mg twice daily, and post stroke rehabilitative treatment with speech therapy, behavioral therapy, and physical therapy.

Thalamic infarction results in markedly different clinical syndromes of their location. Paramedian thalamic infarctions are associated with supranuclear palsy, hypersomnolence, and neurological as well as memory impairments. Bilateral infarcts may lead to long-term recovery and an unfavorable outcome. The occlusion of the artery of Percheron should be considered as a main cause for such lesions.

Probing Questions

8. What can you tell the relatives of the patient about the cause for his hypersomnolence and how would you reduce their fear?
9. Where would you have expected stroke lesions, if the patient would have had post stroke sleep-disordered breathing (SDB)?
10. Is it possible that this patient despite showing no acute signs of SDB might be seen with SDB at a later time point and how could this be related to normalization of his sleep stage distribution?

The patient recovers with some memory impairment and speech problems quite well. A repeated PSG after a year shows a more normal sleep-wake relationship and more regular latencies. No major SDB is detected. In the interdisciplinary conference discussing the development of this patient, a young neurologist asks you he/she has heard that humans could have a total loss of dreaming after stroke.

Probing Questions

11. Name the syndrome that the young colleague was referring to?
12. Where is the focal lesion and which artery is involved in that syndrome x, which eventually (discussed controversially if it really exists) leads to total dream loss?

Cardiovascular Stroke Handout/Objectives

Goal: Understand the effect of brain lesions caused by stroke at different brain levels on the sleep-wake cycle and respiration during sleep.

Objectives (Revealed at the End of the Session):

A. List the lesions at different major brain levels (3–5) a stroke can cause and the possible impairment of brain functions associated with each brain level.
B. Interpret the bidirectional relationship between sleep disorders and stroke.
C. Discuss the sleep-related therapeutic interventions after a stroke (noninvasive ventilation, medication, oxygen).
D. Discuss imaging for sleep disorders appearing after a stroke.
E. Propose an interdisciplinary collaboration pathway between faculties to avoid overseeing of crucial sleep problems after stroke.

IQ Case. Circadian Rhythm Disorder/Dementia for Student

Goal: The group is encouraged to study the impact of neurodegeneration on the sleep-wake cycle and learn about medical and behavioral possibilities to deal with its implications for the patient and his social interactions.

Case Vignette

A 78-year-old female nonobese and clinically healthy except for a mild hypertension, treated with the ACE inhibitor ramipril 5 mg/daily, comes with her daughter and son-in-law to your sleep clinic. The daughter is the main caregiver and has the power of attorney for her mother who is suspected to have Alzheimer's dementia with increasing memory loss and disorientation. However, the patient is functioning with moderate help at all activities of daily living and only leaves the house accompanied by family members. Your geriatric short assessment reveals a moderate dementia with two points in the Shulman clock test and seven points in the MMSE, of which parts are not performable because of noncompliance; the patient knows her birth date but cannot answer to any other quality (time, location, address). The relatives complain that the mother is mostly sleepy during daytime, has given up on watching her favorite TV shows, and starts to wander around in the house after 2 a.m. handling stuff in the kitchen and lately almost burning down the house using the gas stove. The shift in the sleep-wake cycle of the patient has affected the family around her, the grandchildren complain about daytime tiredness and difficulties performing, and the daughters- and sons-in-law's sexual lives and marriage are in jeopardy.

You perform a PSG in the patient's house from 6 p.m. to 2 p.m. the next day with a device that allows remote data transfer via Bluetooth signal, so that the patient can wander around at night. Family members have been instructed how to repost removed or fallen-off electrodes. Your PSG reveals a total TST of 12.7 h distributed over four sleep periods from 8.30 p.m. to 2 a.m., 5.20 a.m. to 920 a.m., 11 a.m. to 13.20 p.m., and 2 p.m. to 2.50 p.m. The sleep stage distribution for the whole TST is SWS 6 %, REM 4 %, NREM 2 78 %, and NREM 1 12 %, and no sleep spindles

are seen; REM latency in the first sleep period was 4.4 h; in the third sleep period, 2 h; and in the second and fourth periods no REM was seen. The PSG results confirm your suspicion of a dementia-related circadian change, and the changes seen in sleep structure are in concordance with Alzheimer's-related PSG findings.

You discuss the results with the patient's family. The relatives decide to care for grandma in the house for a while longer, preparing the house so that the patient can wander around in the house but not harm herself or the family. Except for the antihypertension therapy, the patient has still not received any other medication from the family's general physician.

IQ Case. Circadian Rhythm Disorder/Dementia for Facilitator

Goal: The group is encouraged to study the impact of neurodegeneration on the sleep-wake cycle and learn about medical and behavioral possibilities to deal with its implications for the patient and his social interactions.

Objectives (Revealed at the End of the Session):

A. Give a short overview of your understanding of Alzheimer's disease.
B. Discuss why sleep is important for cognitive function.
C. Review the potential consequences of interrupted sleep in dementia patients.
D. Describe treatment forms of circadian disorders which pop up in to your mind as possible options for dementia patients.
E. Discuss how treatment interventions in dementia patients could affect caregivers.

Case Vignette

A 78-year-old female nonobese and clinically healthy except for a mild hypertension, treated with the ACE inhibitor ramipril 5 mg/daily, comes with her daughter and son-in-law to your sleep clinic. The daughter is the main caregiver and has the power of attorney for her mother who is suspected to have Alzheimer's dementia with increasing memory loss and disorientation. However, the patient is functioning with moderate help at all activities of daily living and only leaves the house accompanied by family members. Your geriatric short assessment reveals a moderate dementia with two points in the Shulman clock test and seven points in the MMSE, of which parts are not performable because of noncompliance; the patient knows her birth date but cannot answer to any other quality (time, location, address). The relatives complain that the mother is mostly sleepy during daytime, has given up on watching her favorite TV shows, and starts to wander around in the house after 2 a.m. handling stuff in the kitchen and lately almost burning down the house using the gas stove. The shift in the sleep-wake cycle of the patient has affected the family around her, the grandchildren complain about daytime tiredness and difficulties performing, the daughters- and sons-in-law's sexual lives and marriage are in jeopardy.

Probing Questions

1. Besides your immediate suspicion of a dementia-related shift of the sleep-wake cycle, which differential diagnoses do you have to consider?
2. Which diagnostic tools do you want to use to confirm your suspicion in consideration of the patient's age and the overall dementia-related situation?
3. How do you include the patient's family in your medical care processes and how would you explain them why it makes sense to take care of the sleep problem?
4. How would you define the postulation of Borbely that "the management of the sleep-wake cycle in consciousness, and its volitional perturbation, can best be expressed as the interaction between two opponent processes" in view of Alzheimer's dementia?

You perform a PSG in the patient's house from 6 p.m. to 2 p.m. the next day with a device that allows remote data transfer via Bluetooth signal, so that the patient can wander around at night. Family members have been instructed how to repost removed or fallen-off electrodes. Your PSG reveals a total TST of 12.7 h distributed over four sleep periods from 8.30 p.m. to 2 a.m., 5.20 a.m. to 9.20 a.m., 11 a.m. to 13.20 p.m., and 2 p.m. to 2.50 p.m. The sleep stage distribution for the whole TST is SWS 6 %, REM 4 %, NREM 2 78 %, and NREM 1 12 %, and no sleep spindles are seen; REM latency in the first sleep period was 4.4 h; in the third sleep period, 2 h; and in the second and fourth period no REM was seen. The PSG results confirm your suspicion of a dementia-related circadian change and the changes seen in sleep structure are in concordance with Alzheimer's-related PSG findings.

Probing Questions

5. What role do these changes in the sleep structure play in regard to the patient's memory consolidation?
6. Which of the Alzheimer's-related neuronal transmitter changes do you consider the most influential on the sleep structure?
7. Could one have received the same information on the patient's sleep problems from actigraphy?

You discuss the results with the patient's family. The relatives decide to care for grandma in the house for a while longer, preparing the house so that the patient can wander around in the house but not harm herself or the family. Except for the antihypertension therapy, the patient has still not received any other medication from the family's general physician.

Probing Questions

8. What can you tell the family about the further development of the sleep-wake cycle changes?
9. Would you warn the family about the effects that the proceeding dementia could have on their family life?
10. You consider a start with chronotherapy. What are your most practical approaches?
11. Describe the benefits, as they relate to sleep, an anti-dementia treatment with donepezil or a different cholinesterase inhibitor could have.

IQ Case. Circadian Rhythm Disorder/Dementia Handout/ Objectives

Goal: The group is encouraged to study the impact of neurodegeneration on the sleep-wake cycle and learn about medical and behavioral possibilities to deal with its implications for the patient and his social interactions.

Objectives (Revealed at the End of the Session):

A. Give a short overview of your understanding of Alzheimer's disease.
B. Discuss why sleep is important for cognitive function.
C. Review the potential consequences of interrupted sleep in dementia patients.
D. Describe treatment forms of circadian disorders which pop up in to your mind as possible options for dementia patients.
E. Discuss how treatment interventions in dementia patients could affect caregivers.

Selected References

1. Kramer M. Dreaming and dreaming disorders in the elderly. In: Sandi–Perumal SR, Monti JM, Monjan AA, editors. Geriatric sleep medicine. Cambridge University Press; New York (US published) 2010.
2. Canet T. Sleep and stroke. In: Culebras A, editor. Case studies in sleep neurology. Cambridge University Press; New York 2010.
3. Harper DG. Sleep and circadian rhythm disturbances in Alzheimer's disease. In: Pandi-Perumal SR, Monti JM, Monjan AA, editors. Principles and practice of geriatric sleep medicine. Cambridge University Press; New York 2010.

Chapter 19
Ethical, Legal, and Social Issues in Sleep Medicine

Salim Surani

Introduction

Sleep medicine over the past few decades has evolved significantly. In this chapter, we focus on ethical and legal issues pertaining to sleep medicine. AASM-accredited facilities are required to follow the Code of Medical Ethics of the American Medical Association, which was adopted as an official policy in 1998. While more often evident in questions and dilemmas pertaining to the end of life care, e.g., balancing the principle of beneficence and non-maleficence, ethical questions arise in the daily practice of sleep medicine, such as releasing the patient with narcolepsy for driving, preventing harm posed by patients with rapid eye movement (REM) behavior disorder, or prescribing wake-promoting substances for patients with sleep deprivation.

Very little has been written about ethics pertaining to sleep medicine, as opposed to specific rule making, policy, and regulations. Ethics is also a neglected topic in fellowship training, though the ACGME, in Sect. IV.A.2.b.1.m of program requirements, states the need for competence in medical ethics and its application in sleep medicine, and Sect. IV.A.2.b.1.n requires competencies regarding the legal aspects of sleep medicine. Section IV.A.2.e requires the demonstration of professionalism.

In this chapter we will address topics on ethical, legal, and social issues in sleep medicine that prove challenging to fellows, faculty, and those practicing in the community. We will focus on:

- Conflicts between patient confidentiality and public responsibility in sleep medicine
- Rules and regulations, including Stark's law and federal compliance
- The issue of drowsy driving in commercial and noncommercial drivers
- Ethical principles from cases of REM behavior disorder and narcolepsy

S. Surani, M.D., MPH, MSHM, FACP, FCCP, FAASM (✉)
Department of Pulmonary, Critical Care & Sleep Medicine, Texas A&M University,
7613 Lake Bolsena, 78413 Corpus Christi, TX, USA
e-mail: srsurani@hotmail.com

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For this chapter, content domains were developed through the examination of relevant ACGME requirements, discussions with sleep medicine specialists and prior fellows about current and/or best practices, and collection of existing relevant training material.

The delivery of this content should be through a variety of avenues to accomplish the educational objectives. It should be delivered to impart knowledge, skills, and attitudes that a fellow should be able to exhibit following instruction in the content areas. Following training the fellows should be assessed for competencies in the areas shown in Table 19.1.

Illustrations of Content Delivery

Recall matching answer sets (RMAs) are designed to match a concept or function with its "name." Many of the terms in the content domains of ethics, law, and the social aspects of sleep medicine are listed in the left column of the Matching Test section. The learner is asked to match these items with those in the right column that contain related laws or principles.

Some of the essay questions may be related to straightforward definitions, while others may be presented in case-based or descriptive formats. Essay questions (EQs) cover content delivered in any format and can be given before or after the presentation or at intervals during the program. Their objective is to let the learner synthetize the material and reform it in his/her own words. In this instance, in the section of essay questions, four relevant essay questions are provided. The fellows will first provide their best responses to these questions. Ideal answers are provided and a discussion may ensue.

Case study questions are designed around a brief case, which are followed by questions. These can serve either as the basis of a discussion or for implementing learning objectives of the key elements. The case study can be covered in 1 h with more time allocated for a follow-up discussion. It is presented in IQ Cases. On-site or outside experts can be invited to moderate the discussions.

Lectures and presentations are available online at www.competenciesinsleep-medicine.weebly.com, especially if there is no in-house expert on the topic of ethics and law in sleep medicine. Also, a faculty member can acquire an off-the-shelf presentation and moderate it with comments on not only its content but also its conceptual framework. One of the presentations on fraud and abuse is cited and has been created by the value option group, which is available on web at http://www.valueoptions.com/providers/Compliance/FraudandAbuse.pdf. The goal is to introduce the topic and provide illustrations of the utility of the content. Other than providing your objectives at the beginning and the end of the presentation, and asking at the end whether these objectives were met, there is no individual assessment of the lecture content.

Table 19.1 Content Covered and Competencies Assessed Examples

Topics	Objectives	Competency achieved
I. Ethics of medicine	To understand the different medical ethical principles	
	To understand the scenarios when conflict among ethical principles arises	
	To understand the exceptions when public or other persons' safety supersedes the patient confidentiality	
II. Rules and regulations for patient referral	To understand the CMS rules and regulations that pertain to referral of sleep studies and patient referral	
III. Stark's law	To understand Stark's law, its exceptions, and penalties	
IV. Rules and regulations for CPAP setup and compliance	To understand the CMS rules for CPAP setup and compliance	
	To understand the rules that apply if patients fail to comply	
V. Regulations on drowsy driving	To understand the law as it pertains to drowsy driving and fatigue law	
VI. Law regarding commercial drivers	To be familiar with the laws pertaining to commercial driving license and sleep apnea	
VII. Ethical principles pertinent to REM behavior disorder and narcolepsy	To understand the ethical principles applicable to situations arising from REM behavior sleep disorder	
	To understand the law pertaining to narcoleptic patients	
VIII. Quality Assurance (QA) law	To understand the laws pertaining to QA for the sleep center	
IX. Compliance law	To understand the seven elements of federal compliance	

Matching Questions

Questions

It would be covered by CMS for AHI if the physician feels it is necessary. ☐
Fatigue law. ☐
Informed consent as an example. ☐
First, do no harm. ☐
Patient-physician privilege. ☐
It would be covered by CMS if AHI is greater than 15. ☐
Act of killing someone during an episode of sleep walking. ☐
Concerns the distribution of scarce health resources and the decisions on who gets what treatment (fairness and equality). ☐
Prohibits physicians from making self-referrals. ☐
The patient has the right to refuse or choose his/her treatment. ☐
A practitioner should act in the best interests of the patient. ☐
The patients (and the person treating the patients) have the right to be treated with dignity. ☐

Answers

1. Autonomy
2. Beneficence
3. Non-maleficence
4. Justice
5. Dignity
6. Truthfulness and honesty
7. Confidentiality
8. CPAP
9. Continuous Quality Assurance
10. Homicide somnambulism
11. Stark's law
12. Maggie's law

Questions with Answers

It would be covered by CMS for AHI if the physician feels it is necessary. 9
Fatigue law. 12
Informed consent as an example. 6
First, do no harm. 3
Patient-physician privilege. 7
It would be covered by CMS if AHI is greater than 15. 8
Act of killing someone during an episode of sleep walking. 10
Concerns the distribution of scarce health resources, and the decisions on who gets what treatment (fairness and equality). 4
Prohibits physicians from making self-referrals. 11
The patient has the right to refuse or choose his/her treatment. 1
A practitioner should act in the best interests of the patient. 2
The patients (and the person treating the patients) have the right to be treated with dignity. 5

Essay Questions

Case Study 1

Sleep Apnea and Driving Law

A 42-year-old male with a history of hypertension, diabetes, and obesity and with a BMI (Body Mass Index) of 38 presented with a complaint of excessive daytime sleepiness. He intends to start working as a commercial driver. He denies any previous history of any car accident.

Part 1

Questions

1. What is currently required for Commercial Driver's License (CDL) medical certification regarding OSA?
2. What are the ethical, legal, and social concerns for commercial driving with OSA?
3. How can body mass index (BMI) and neck size affect your CDL medical certification?
4. Should this driver be disqualified from driving based only on his BMI of 38?

Ideal Answers

1. Currently, the Department of Transportation requires for CDL holders to answer brief questions regarding OSA. Examiners are not required to screen for the condition if the drivers respond that they are symptom free.
2. As commercial drivers they are concerned about their livelihood and their life. Under current CDL medical restrictions, commercial drivers with moderate to severe OSA that interferes with safe driving can be disqualified for CDL, if a state licensed medical examiner determines that they should not drive. The lifestyle of commercial drivers can also lead to higher rates of obesity, which in turn lead to increased risk of hypertension, diabetes, and arrhythmia, to name a few.
3. In 2008, a health panel recommended to the Medical Review Board that CDL medical certification be conditional based on the BMI. They recommended that commercial drivers with a BMI of 30 or higher should be required to undergo testing for OSA. A neck circumference is considered large at 16″ in women and 17″ in men.
4. Currently fleet owners use a BMI of 39 or higher to screen and disqualify driver applicants.

Part 2

The patient was seen by a medical examiner.

Questions

1. What diagnostic tests need to be performed by the medical examiner?
2. What treatment modalities should be offered?
3. When can the person return to work after the CPAP treatment?
4. When can the person return to work after treatment with oral appliances?
5. When can the person return to work after treatment with surgery or weight loss?

Ideal Answers [1]

1. Diagnosis should be made by a physician and confirmed by a polysomnography study, preferably in an accredited sleep laboratory or by a certified sleep specialist. A full night study should be done unless a split night is indicated (severe OSA after at least 2 h of sleep). Alternatively, home sleep testing can be performed.
2. The first-line treatment of the prospective commercial driver with OSA should be via continuous positive airway device or bi-level positive airway device. The device should be able to record the duration of use. The minimum average time of use of CPAP is 4 h within a 24-h period. The drivers should also be advised to undergo a longer treatment as that may be more beneficial to them. It is also suggested that treatment be started as soon as possible or within 2 weeks of study. They should be followed up with a sleep specialist after 2–4 weeks of treatment with CPAP. If the patient cannot tolerate CPAP, then oral appliance for mild and moderate OSA may be considered. Surgical therapy is reserved for cases that do not fall in that category (details are beyond the scope of this chapter).
3. At a minimum of 2 weeks after therapy with CPAP, but within 4 weeks, the driver should be reevaluated by the sleep specialist and compliance and BP assessed. An AHI of <5 should be merely documented, or if the AHI is less than or equal to 10, then the clinical features should be documented. If the driver is compliant and the BP shows improvement, then the driver can return to work but should be certified for no longer than 3 months.
4. Oral appliance should only be used as a primary therapy if AHI < 30. Prior to resuming work, the driver must have a follow-up NPSG study, demonstrating an AHI of <5 or less than or equal to 10 while wearing an oral appliance if he has no symptoms of excessive daytime sleepiness or high blood pressure.
5. Patient could return to work after surgery provided prior to resuming work the patient has completed a follow-up NPSG study, demonstrating an AHI of <5 or less than or equal to 10 while wearing an oral appliance if he has no symptoms of excessive daytime sleepiness or high blood pressure.

Case Study 2

Essay on Ethical Principles

The physician-patient relationship is based on the principles of ethics. These principles apply to every facet of one's life. Knowledge of medical ethics plays a very important role in a physician's profession, as the values and judgments derived from it form the basis for honoring the sanctity of life and the dignity of the human person while making patient-care decisions.

Part 1

Questions

1. What are the six values that commonly apply to medical ethics?
2. Describe each one in detail.

Ideal Answers

1. Autonomy, beneficence, non-maleficence, justice, dignity, and truthfulness and honesty
2. These are:
   (a) Autonomy: It is the patient's right to refuse treatment (Voluntas aegroti suprema lex). It determines the right of an individual for self-determination.
   (b) Beneficence: The practitioner should act in the best interest of the patient (salus aegroti suprema lex). It refers to an action that promotes the well-being of others.
   (c) Non-maleficence: "First do no harm" (primum non nocere). This focuses on the balance between benefits and the side effects. A physician may use a treatment that he/she feels may benefit patients without taking into consideration the side effects and that may result in harm.
   (d) Justice: It implies the distribution of scarce health resources fairly and equally. It addresses the principle of fairness and equality.
   (e) Dignity: Patient and provider should be treated in a dignified manner.
   (f) Truthfulness and honesty: It implies that the physicians should be honest and truthful to their patients.

Part 2

Question

1. What does "double effect" refer to in the ethics, and what are the examples of conflict between different ethical principles?

Ideal Answer

1. Double effect refers to two types of consequences, one positive and the other negative, which can be produced by a single action. For example, the use of morphine can be an essential component in easing pain, but at the same time, it can suppress respiration.

Sometimes the principle of autonomy can come in conflict with the principle of beneficence, as in the case of a patient who may refuse blood transfusion because of religious reasons, whereas the physician may want to perform transfusion that would benefit the patient in case of gastrointestinal bleeding.

Question

2. What are the exceptions to the principle of patient confidentiality?

Ideal Answer

2. Exception 1: Concern for the safety of the other person. The HPIAA (Health Insurance Portability and Accountability Act) Law has placed significant emphasis on patient confidentiality under the 1974 Federal Privacy act and subsequent acts. On the one hand, physicians were charged with the responsibility of protecting patients' rights and confidentiality but on the other hand were also entrusted with the duty to protect other identifiable individuals from any serious threat or harm if they could. An example is the case of a patient who shares specific plans with the physician or psychotherapist to harm a particular individual.

   Exception 2: Concern for public welfare. In most cases, physicians are required by state law to report certain communicable diseases to the public health authorities. In these cases the duty to protect public health outweighs the duty of maintaining patient confidentiality.

Case Study 3

Essay Questions Pertaining to the Stark's Law

A 36-year-old male was referred to the sleep center for evaluation of possible OSA. Patient polysomnography revealed the patient had an AHI of 35. At 14 cm of H_2O, most of the respiratory events were eliminated. Referral was made to the durable medical equipment company for setting up CPAP.

Questions

1. What is Stark's law?
2. What factors should a physician consider to avoid Stark's law violation?
3. Who are the immediate family members?
4. Who falls under the designated health services?

5. Can a physician refer a request to DME supplier who is leasing space from him in his own building? If so, what are the factors that should be considered? If not, what are the reasons?
6. Can a physician refer the DME equipment request to the DME company which is owned by his son-in-law?
7. Can a physician refer the request to the DME company of which he is a part owner? If not, can he include his company in the list he provides the patient of all DME companies?
8. What are the Stark's law compensation exceptions?

Ideal Answers

1. Stark's law applies to physicians' self-referrals. It generally prohibits physicians from making self-referrals. Stark's law was amended in 1993 to extend to entities other than clinical laboratories. The amendment, which was effected in 1993, introduced the concept of "designated health services" (DHS). It was then dubbed as Stark II. It took effect in 2002, which was called Stark II, phase 1 rule. The second rule took effect in 2004 and was known as Stark II, phase II rule.
2. If a physician or her/his immediate family members have a financial relationship with an entity, then the physician may not make a referral to the entity for furnishing DHS for which payment may come from Medicare/Medicaid or any other payer of Federal Government.
3. Immediate family members can be a husband or wife, natural or adoptive parents, child or sibling, stepparents, stepchild, stepbrother and sister, father-in-law, mother-in-law, son-in-law, daughter-in-law, brother-in-law, sister-in-law, grandparent or grandchild, and spouse of a grandparent or grandchild.
4. Designated health services encompass:

   (a) Inpatient and outpatient hospital services
   (b) Home health services
   (c) Clinical laboratory services
   (d) Radiation and certain outpatient imaging services
   (e) Physical and occupational therapy and speech pathology services
   (f) Nutritional equipment suppliers
   (g) Durable medical equipment and supplies
   (h) Radiation therapy supplies and equipment
   (i) Outpatient prescription drugs
   (j) Prosthetic, orthotics, and prosthetic devices and supplies

5. If a sleep center or physician rents space to a DME supplier, the physician can refer the patient to the supplier if the rental agreement complies with the applicable Stark's law and anti-kickback statue exceptions on safe harbor.
6. No, he cannot, without violating Stark's law.
7. No; Yes, with full disclosure.

8. The following are the Stark's law compensation exceptions:

   (a) Nonmonetary compensation of up to $300
   (b) Fair market value compensations
   (c) Physician payments for items and services
   (d) Rental of office space; rental of equipment
   (e) Bona fide employment relationship
   (f) Reimbursement unrelated to provisions of DHS
   (g) Personal service arrangements
   (h) Physician recruitment
   (i) Isolated transactions

Case Study 4

Essay Questions to Cover the Seven Elements of Compliance

A sleep center affiliated with a University has been audited by the Federal Government to ensure that it complies with federal laws. The surveyors were very pleased with the quality of patient care, as well as the knowledge and attitude of the staff toward patient care. They ranked the center very high in their customer and patient satisfaction programs. The surveyors inquired if the program was fulfilling the seven elements of compliance to combat fraud and abuse. They felt that this was a magic recipe for enforcing ethics and compliance with federal laws.

Part 1

Questions

1. What are the seven elements of the compliance program the surveyor is referring to?
2. Provide a very brief description of each element.

Ideal Answers

Elements of Compliance

1. (a) Standards of conduct
   (b) Compliance officer designation
   (c) Education and training of employees
   (d) Reporting/complaint hotline
   (e) System to respond to allegations of improper/illegal activities
   (f) Auditing
   (g) Enforcement and discipline

2. (a) Standards of conduct: It has been described as crucial to the company's ability to create a culture of integrity by setting up standards and procedures to which all employees can adhere to. They are also referred to as the organization code, which serves as a guide for expected behavior on the part of the employee and the institution.
   (b) Compliance officer designation: The Office of Inspector General (OIG) has emphasized that in order to promote integrity and ethics, the program needs a strong leader such as a compliance officer, who can oversee the operations of the institution and ensure proper standards of conduct.
   (c) Education and training of employees: In addition to having standards of conduct, the institution should ensure continuation of education and training of employees in this regard.
   (d) Reporting/complaint hotline: Mechanisms should be in place to empower any employee of the organization to report any discrepancies without the fear of retaliation.
   (e) System to respond to allegations of improper/illegal activities: Reporting and prevention should be an integral part of the compliance program. In addition to having policies and procedures in place, the organization should have a system to respond to any allegations and prevent it from recurring.
   (f) Auditing: Organization should deploy a system of constant internal auditing and monitoring to verify compliance.
   (g) Enforcement and discipline: In addition to setting up the compliance rules, there could be an effective system to enforce the rules and to discipline and take action against those who violate the rules. Sentencing guidelines state specifically that enforcement should be consistent with appropriate disciplinary action.

The institution deployed the seven elements of compliance, but due to budget and financial constraints, the compliance department barely existed with no compliance officer. They were subjected to an audit by the federal agencies [2].

Part 2

Question

1. If the federal agencies find the institution noncompliant with their compliance program, what penalties can be assessed?

Ideal Answer

1. The penalties can range from $27,500 per day for each day of noncompliance to criminal prosecution [2].

IQ Cases

Case I. Case Study on Law About CPAP for Student

Goal: To become familiar with the law pertaining to initiation and setup of CPAP

Vignette

A 42-year-old patient was referred to the sleep center for nocturnal polysomnography for the possibility of OSA. The patient had been feeling tired and had fatigue and excessive daytime sleepiness for the past 6 months. He had gained 20 lbs. weight over a period of 6 months. He did have a history of hypertension, diabetes, and obesity with a BMI of 34. The patient was evaluated by his primary care physician and was referred for nocturnal polysomnography study. The patient was found to have OSA with AHI of 10.5.

The patient received the CPAP device for a trial period. He had a difficult time in tolerating the CPAP. Both the physician and the patient felt that it could be beneficial.

Case I. Case Study on Law About CPAP for Facilitator

Goal: To become familiar with the law pertaining to initiation and setup of CPAP

Vignette

A 42-year-old patient was referred to the sleep center for nocturnal polysomnography for the possibility of OSA. The patient had been feeling tired and had fatigue and excessive daytime sleepiness for the past 6 months. He had gained 20 lbs. weight over a period of 6 months. He did have a history of hypertension, diabetes, and obesity with a BMI of 34. The patient was evaluated by his primary care physician and was referred for nocturnal polysomnography study. The patient was found to have OSA with AHI of 10.5.

Part 1

Questions

1. What information is needed by the sleep center per CMS law for proceeding with the study?

2. In the current study, does the patient with the AHI of 10.5 qualify for the CPAP? If yes, why? If not, what are the reasons which make him not qualify for CPAP.
3. What are the criteria for qualification for CPAP?

The patient received the CPAP device for a trial period. He had a difficult time in tolerating the CPAP. Both the physician and the patient felt that it could be beneficial.

Part 2

Questions

1. What is the criterion which makes the patient pass the trial period under CMS law?
2. If patient fails the initial trial, what needs to be done to qualify the patient for a second trial?

Discussion

Medicare has issued very specific criteria for allowing DME companies to issue CPAP which is outlined in great detail in the website listed [3]. The patient needs to have the following: (a) face-to-face interaction with the clinician prior to the sleep study; (b) AHI > than 15/h or > 5 or equal to 14/h with at least 10 documented events, along with excessive daytime sleepiness, impaired cognition, mood disorder or insomnia or hypertension, ischemic heart disease, or stroke; and (c) the patient or caregiver has received instructions from the supplier of CPAP device and accessories in the care and proper use of equipment.

Continued coverage beyond the 3 months requires that treating physician must conduct a reevaluation to assess the effectiveness of the therapy. The adherence to CPAP is defined as use of positive airway pressure device of ≥4 h/night on 70 % of the nights.

Case II. Case Study on Drowsy Driving for Student

Goal: To understand the ethical principles relating to drowsy driving and understand the pertinent reporting law in different states

Vignette

A 30-year-old male presented to your office with the complaint of being tired and suffering from fatigue and excessive daytime sleepiness. He reported the weight gain

of approximately 30 lbs. over a period of 1 year. His laboratory data was within normal limit. His TSH was borderline. He stated that over the past 1 month, he had been falling sleepy behind the wheel, especially when his vehicle was at the stoplight. He did report his car frequently swaying from one lane to the other when he was on the highway for an extended period of time. He also crashed his car to a tree due to falling asleep while driving. His significant other does give the history of him having been very sleepy, especially over the past month. She stated that he snored loudly and had pauses in breathing. He also dosed off while watching television and sometimes even during conversations. He worked as a commercial driver. On examination the patient was found to have a blood pressure of 160/90 mmHg, BMI of 35, and very crowded pharyngeal space with a Mallampati score of 4. The patient was clinically diagnosed with borderline hypothyroidism, obesity, hypertension, and OSA. Patient was given counseling on weight loss and sleep hygiene. He was scheduled for the polysomnography. Earliest date when he could undertake the polysomnography was 1 week later. Patient was instructed to avoid driving till he underwent the polysomnography and adequately treated for his problem.

Patient stated that he had to deliver a very important consignment to a destination 2,000 miles away and he must drive. You advised the patient against it and mentioned that you would document this in his medical record. You are informed by your nurse that patient mentioned about delivering the commercial goods in his 18-wheeler truck regardless.

The patient refrained from driving and underwent polysomnography studies 2 days later. He was found to have severe obstructive sleep apnea with AHI of 41 and underwent CPAP trial, and at 15 cm H_2O most of the respiratory events were eliminated. The patient was counseled again regarding weight loss and sleep hygiene. He was started on CPAP at 15 cm of H_2O. Patient desired to return to work the very next day.

The patient followed your advice and refrained from driving and returned 1 week later. He stated that he was compliant with the CPAP therapy, and the smart card reader confirmed CPAP average use of 7.5 h per night with the AHI of 3.5 and no desaturation. He still complained of excessive daytime sleepiness. He was started on modafinil. Patient returned to your office a week later. At this time he stated that he was feeling much better and was using CPAP religiously. Smart card data confirmed that and he denied excessive daytime sleepiness.

He stated that his employer needed a definite clearance and objective data from you certifying that he was not sleepy during the daytime.

Case II. Case Study on Drowsy Driving for Facilitator

Goal: To understand the ethical principles relating to drowsy driving and understand the pertinent reporting law in different states

Case Vignette

A 30-year-old male presented to your office with the complaint of being tired and suffering from fatigue and excessive daytime sleepiness. He reported the weight gain of approximately 30 lbs. over a period of 1 year. His laboratory data was within normal limit. His TSH was borderline. He stated that over the past 1 month, he had been falling sleepy behind the wheel, especially when his vehicle was at the stoplight. He did report his car frequently swaying from one lane to the other when he was on the highway for an extended period of time. He also crashed his car to a tree due to falling asleep while driving. His significant other does give the history of him having been very sleepy, especially over the past month. She stated that he snored loudly and had pauses in breathing. He also dosed off while watching television and sometimes even during conversations. He worked as a commercial driver. On examination the patient was found to have a blood pressure of 160/90 mmHg, BMI of 35, and very crowded pharyngeal space with a Mallampati score of 4. The patient was clinically diagnosed with borderline hypothyroidism, obesity, hypertension, and OSA. Patient was given counseling on weight loss and sleep hygiene. He was scheduled for the polysomnography. Earliest date when he could undertake the polysomnography was 1 week later. Patient was instructed to avoid driving till he underwent the polysomnography and adequately treated for his problem.

Patient stated that he had to deliver a very important consignment to a destination 2,000 miles away and he must drive. You advised the patient against it and mentioned that you would document this in his medical record. You are informed by your nurse that patient mentioned about delivering the commercial goods in his 18-wheeler truck regardless [4].

Part 1

Questions

1. If you inform the Department of Motor Vehicles (DMV) about the patient's health status, what ethical principle are you violating, if any?
2. If you inform the DMV, what ethical justification will you use?
3. What are the state laws in your area regarding voluntary and mandatory reporting?
4. What are the state laws in your region regarding drowsy driving?

The patient refrained from driving and underwent polysomnography studies 2 days later. He was found to have severe obstructive sleep apnea with AHI of 41 and underwent CPAP trial, and at 15 cm H_2O most of the respiratory events were eliminated. The patient was counseled again regarding weight loss and sleep hygiene. He was started on CPAP at 15 cm of H_2O. Patient desired to return to work the very next day.

Part 2

Questions

1. Is it appropriate for the patient to return to work the very next day? Why or why not?
2. Is it ethical to give him a stimulant and allow him go to work with the instruction that he must sleep at least 8 h per day and avoid driving when sleepy?

The patient followed your advice and refrained from driving and returned 1 week later. He stated that he was compliant with the CPAP therapy, and the smart card reader confirmed CPAP average use of 7.5 h per night with the AHI of 3.5 and no desaturation. He still complained of excessive daytime sleepiness. He was started on modafinil. Patient returned to your office a week later. At this time he stated that he was feeling much better and was using CPAP religiously. Smart card data confirmed that he denied excessive daytime sleepiness.

He stated that his employer needed a definite clearance and objective data from you certifying that he was not sleepy during the daytime.

Part 3

Questions

1. Would you give the patient a clean bill of health? Why or why not?
2. What objective tests you can do and what are the limitations of those tests?

Comment: The answers to some of the above questions can vary depending on the state where one practices. The questions require an application of ethical principles, which can lead to an interesting discussion.

Case III. Case Study on REM Behavior Disorder for Student

Goal: This case deals with the principles of ethics, mainly on patient confidentiality versus public or another person's safety. This case will help to understand the different ethical principles and exceptions to the physician-patient confidentiality.

Case Vignette

A 42-year-old male presented to your office with the compliant that her spouse is stating that he had tried to smother her with the pillow on several occasions over the past month. Patient's wife is not accompanying the patient. He stated that he was in good relation with his wife and no marital conflict existed. He also mentioned that this was exacerbated when he was sleep deprived and it happened in the later part of

the night. His spouse stated that it lasted for 20–30 min at any given time. On the basis of his history, you clinically concluded that he was suffering from REM behavior disorder (RBD). He was counseled to ensure that he slept in a separate room away from his wife and was given the information about the REM behavior disorder as well as the possibility that he was suffering from it. He was scheduled for the nocturnal polysomnography.

Case III. Case Study on REM Behavior Disorder for Facilitator

Goal: This case deals with the principles of ethics, mainly on patient confidentiality versus public or another person's safety. This case will help to understand the different ethical principles and exceptions to the physician-patient confidentiality.

Case Vignette

A 42-year-old male presented to your office with the compliant that her spouse is stating that he had tried to smother her with the pillow on several occasions over the past month. Patient's wife is not accompanying the patient. He stated that he was in good relation with his wife and no marital conflict existed. He also mentioned that this was exacerbated when he was sleep deprived and it happened in the later part of the night. His spouse stated that it lasted for 20–30 min at any given time. On the basis of his history, you clinically concluded that he was suffering from REM behavior disorder (RBD). He was counseled to ensure that he slept in a separate room away from his wife and was given the information about the REM behavior disorder as well as the possibility that he was suffering from it. He was scheduled for the nocturnal polysomnography.

Part 1

Question

Do you think the physician should inform the spouse or the law enforcing agency about this patient's condition?

Patient returned to you the following week. The NPSG study did confirm REM behavior. He stated that at one instance he went out of his house in his sleep. Immediately on arousal he felt that he was about to kill his wife, as he had a knife in his hand. He stated that she was not aware of it and would like this part specifically to be treated as confidential, protected by patient-physician confidentiality, and not to disclose this to his wife. He was very concerned that if this information was revealed to her, it could lead to significant challenges in his marital life. You were very concerned that he might harm his wife.

Part 2

Question

What are the exceptions under which it is reasonable to break the patient-physician confidentiality?

Comment: The sleep physicians sometimes come across this type of scenarios, which place them in an ethical dilemma, caught between the duty to preserve confidentiality and the duty to prevent harm. It would be appropriate to have an ethicist in the discussion to elucidate the ethical principles and their applications [5].

Case IV. Case Study of Patient Confidentiality for Student

Goal: To understand the importance of patient confidentiality

Case Vignette

A 28-year-old female presented to the sleep clinic with symptoms consistent with insomnia. The patient stated that she was under significant stress, which she was trying to cope with. On physical examination, the patient was found to have numerous bruises on her back and extremities. She was also found to have healing right clavicular fracture. She also had a couple of healing scars following injuries inflicted from a sharp object. She also had indication of blunt trauma on the head. On your insistence she informed you that she was being abused by her husband, but wanted you not to inform anyone. She stated that this was her private issue and she was going to solve it herself.

Case IV. Case Study of Patient Confidentiality for Facilitator

Goal: To understand the importance of patient confidentiality

Case Vignette

A 28-year-old female presented to the sleep clinic with symptoms consistent with insomnia. The patient stated that she was under significant stress, which she was trying to cope with. On physical examination, the patient was found to have numerous bruises on her back and extremities. She was also found to have healing right clavicular fracture. She also had a couple of healing scars following injuries inflicted from a sharp object. She also had indication of blunt trauma on the head. On your

insistence she informed you that she was being abused by her husband, but wanted you not to inform anyone. She stated that this was her private issue and she was going to solve it herself.

Questions [6]

1. What is/are the ethical problem/s that her case presents?
2. Is it allowable by law for you to report this incident?
3. You reported this to the law enforcement agency. Patient has now sued you for breaking patient-physician confidentiality. Is the law on her side?
4. What defense would your attorney provide?

Case V. Case Study on Stark's Anti-kickback Law for Student

Goal: To learn about the law pertaining to the Stark's anti-kickback law

Case Vignette

A 52-year-old patient was referred by the sleep specialist to the IDTF (Independent Testing Facility) for nocturnal polysomnography for the diagnosis of sleep apnea. The IDTF facility has been very generous to the specialist and has been helping his children by providing them comfortable jobs at the IDTF. He receives on and off gifts from this IDTF.

The patient inquired from the physician if he had any relationship to the facility. Trying to avoid any trouble, he decided to refer the patient to another IDTF facility and informed the patient that neither he nor his family had any financial relationship with the facility that the patient would be referred to, except that in the past year, he had received gifts from them of $260 value and that he was not compensated by the IDTF for any referral.

Case V. Case Study on Stark's Anti-kickback Law for Facilitator

Goal: To learn about the law pertaining to the Stark's anti-kickback law

Case Vignette

A 52-year-old patient was referred by the sleep specialist to the IDTF (Independent Testing Facility) for nocturnal polysomnography for the diagnosis of sleep apnea. The IDTF facility has been very generous to the specialist and has been helping his children by providing them comfortable jobs at the IDTF. He receives on and off gifts from this IDTF.

Part 1

Questions

1. Would this still fall under Stark's law violation?

The patient inquired from the physician if he had any relationship to the facility. Trying to avoid any trouble, he decided to refer the patient to another IDTF facility and informed the patient that neither he nor his family had any financial relationship with the facility that the patient would be referred to, except that in the past year, he had received gifts from them of $260 value and that he was not compensated by the IDTF for any referral.

Part 2

Questions

1. Does that constitute Stark's law violation?
2. What are the criteria for a physician to be subjected to Stark's anti-kickback laws?
3. What are the penalties under the law for kickbacks under Stark's law?

Case VI. Case Report on the Ethics of Wake-Promoting Substance for Student

Goal: To understand the effects and limitations of wake-promoting substances and the ethical dilemmas around it

Case Vignette

A 56-year-old neurosurgeon colleague, with no significant past medical history, presented to you with the complaint of having excessive daytime sleepiness. On further examination, he revealed that his partner had been out on sick leave and had been up without sleep for almost 96 h. He informed you that he would like to have a prescription for modafinil, as he had four long and complicated routine cases for the following day. He felt that, because of his severe exhaustion, he may not be able to perform this complicated surgery without the wake-promoting substance. He also informed that he would like to keep this discussion very confidential as part of the physician-patient relationship of confidentiality.

Case VI. Case Report on the Ethics of Wake-Promoting Substance for Facilitator

Goal: To understand the effects and limitations of wake-promoting substances and the ethical dilemmas around it

Case Vignette

A 56-year-old neurosurgeon colleague, with no significant past medical history, presented to you with the complaint of having excessive daytime sleepiness. On further examination, he revealed that his partner had been out on sick leave and had been up without sleep for almost 96 h. He informed you that he would like to have a prescription for modafinil, as he had four long and complicated routine cases for the following day. He felt that, because of his severe exhaustion, he may not be able to perform this complicated surgery without the wake-promoting substance. He also informed that he would like to keep this discussion very confidential as part of the physician-patient relationship of confidentiality.

Part 1

Question

1. What would you do and why? What ethical principles would you apply to decide on what you would do?

You decided not to give him the wake-promoting drug and instead explained to him the limitation of the wake-promoting agent. He was not happy with your explanation and answers and decided to visit your other colleague. The other colleague on the medical staff decided to give him modafinil so he could proceed with his four complex routine surgeries. You also happen to be the Chief of Staff of the facility.

Part 2

Questions

1. What are your legal and ethical responsibilities to the patients as the Chief of Staff?
2. What are your responsibilities to the neurosurgeon as your patient?
3. What ethical principles will you apply in deciding your course of action?

Comment: This case also provides an opportunity to have a good discussion about different ethical issues, especially on the issue of conflict between patient

confidentiality and public safety. Having an on-site or remote ethicist can provide an environment for an informed discussion.

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Chapter 20
Administration and Delivery of Sleep Medicine

Shyam Subramanian

Introduction

Industry experts and market research firms project the sleep industry reached $32.4 billion in the USA in 2012. The estimates are an 8.8 % year-over-year increase since 2008, inclusive of everything from pills, products, and medical devices to "sleep consultants" to hospitals, labs, and sleep centers, and to deluxe mattresses. The options for a bed are no longer just box springs and a mattress. At one full-spectrum mattress store chain, a salesperson receives 180 h of training in product specifications, construction, and special features, covering regular beds, water beds, specialty foam, and air-filled sleeping platforms. Boutiques focused on sleep are now in malls and offer a variety of items including noise canceling machines, slippers, scented candles, special pillows, bedding, and lighting elements to simulate dawn and dusk. So sleep is big, maybe less than the alertness market (coffee, tea, energy drinks, etc.) but monetarily significant.

Therapy for sleep problems is a significant market. More over-the-counter sleep aids are bought than any other OTC drug, and 25 % of us take a sleep medicine every year. The more popular include Nytol, Benadryl, Sominex, Tylenol PM, Advil PM, and Nyquil. In 2010, 1 in 20 adults took prescribed sleeping pills, and more than 56 M prescriptions were dispensed in 2009 for sleep. There is a wristband and app combo that will calculate how long it took you to fall asleep, how often you woke up during the night, and how many hours and minutes you slept. It can send data to your iPhone all night, and the company will offer you a consultation with a sleep coach.

The National Sleep Foundation says that more than 50 million Americans will suffer from a sleep disorder at some point in their lives. The medicine side of

S. Subramanian, M.D., M.B.A. (✉)
Department of Pulmonary Critical Care and Sleep Medicine,
Mercy West Hospital, 6540 Winton Road, Cincinnati, OH 45224, USA
e-mail: shyammd@gmail.com

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business, specifically the testing for sleep disorders and disturbances, including pediatric sleep issues, has grown rapidly. The major disorder in which testing is indicated is sleep apnea. 100 million people worldwide are thought to suffer from obstructive sleep apnea, and a majority is probably still undiagnosed. CPAP devices, or those providing continuous positive airway pressure, are estimated to be issued at a rate of about 1,000/month in the Cleveland area. US-based companies have a major share of the global sleep apnea market.

This chapter is presented to introduce the models for care provision. It is complementary Chap. 19 which addresses some ethical and legal aspects of sleep medicine. Table 20.1 maps the content to the ACGME competencies. All domains are knowledge. The listing of domains may help trainees to consider options and opportunities to practice sleep medicine after the fellowship.

Table 20.2 gives examples of topics with educational objectives that can be assessed in clinical environments or with assessments such as essay questions. Most require the integration of factual knowledge.

An additional tool for assessing competence and milestones included in this chapter is essay questions. There is no IQ case.

Table 20.1 Cognitive Map of the Content Domains Relevant to Administrative Sleep Medicine

		Knowledge	Skills	ACGME competency
I.	*Patient assessments*	Yes	Yes	A, C, D, E
	Clinic			
	Laboratory testing			
	Special populations			
II.	*Diagnostic measures and interpretation*	Yes	Yes	A, C, F
	Cost-effectiveness			
III.	*Disease management*	Yes	Yes	
	Accountable care act			A, E, D, F
	Multidisciplinary management			
IV.	*Health and disease clinical pathways*	Yes	Yes	A, C, F
	Co-consultants			
	Code for ACGME competencies			
	A. Patient care		D. Interpersonal skills	
	B. Medical knowledge		E. Professionalism	
	C. Practice-based learning and improvement		F. System-based practice	

Table 20.2 Examples of Topics with Educational Objectives

Item I. Patient assessments
• Compare the costs for an office visit for a pediatric patient to that of an adult
• Describe the functions of a utilization management firm targeted on PSG testing
Item II. Diagnostic measures and interpretation
• Compare the time and equipment costs of OOCST and PSG approaches to managed care
• List the environmental features need to present a child and family-friendly sleep program
Item III. Disease management
• List the principal outcome measures for accountable care organizations
• Explain the sleep elements in the Physician Quality Reporting System
• Compare items needed for a business plan for a sleep laboratory to that for a sleep center
Item IV. Health and disease clinical pathways
• What are the elements to negotiate in incorporating a dental practitioner into a sleep medicine practice
• List the elements needed for an Independent diagnostic testing facility

Matching Test

Questions

A voluntary reporting program that can lead to incentive payments. ☐
Authorized by the 3022 Affordable Care Act. ☐
Banks and lending companies. ☐
Current ratio and quick ratio. ☐
Elements are segmentation, targeting, and positioning. ☐
Elements are strengths, weaknesses, opportunities, and threats. ☐
Examples are inventory turnover ratio and total asset turnover ratio. ☐
Has 17 standards and requirements and a separate Medicare number. ☐
Includes C corp, S corp, and LLC. ☐
One of the out-of-center sleep testing (OOCST). ☐
Total Assets – Total Liabilities = Equity. ☐

Answers

1. Independent diagnostic testing facility (IDTF)
2. Performance standards
3. Physician office model
4. Sole proprietorship
5. General partnership
6. Limited liability partnership
7. Incorporated practice
8. Angel investor
9. Private equity/venture capital
10. SBA programs
11. Commercial lenders
12. SWOT analysis
13. Vision statement
14. Balance sheet
15. Cash flow
16. Activity ratio
17. Liquidity ratio
18. Marketing strategy
19. Utilization management firms
20. CMS
21. AASM
22. Joint commission
23. NBRC
24. BRPT
25. ABSM
26. Physician Quality Reporting System
27. HST
28. Integrated services model
29. Accountable care organization

Questions with Answers

A voluntary reporting program that can lead to incentive payments. 27
Authorized by the 3022 Affordable Care Act. 30
Banks and lending companies. 12
Current ratio and quick ratio. 18
Elements are segmentation, targeting, and positioning. 19
Elements are strengths, weaknesses, opportunities, and threats. 13
Examples are inventory turnover ratio and total asset turnover ratio. 17
Has 17 standards and requirements and a separate Medicare number. 1
Includes C corp, S corp, and LLC. 8
One of the out-of-center sleep testing (OOCST). 28
Total Assets – Total Liabilities = Equity. 15

Essay Questions

Case Study 1

You are approached by a practice management firm to set up a corporation for provision of sleep services in a rural location in the vicinity of where you live.

Questions

1. In formulating a business plan for this venture, what factors will you consider to be critical in evaluating the feasibility?
2. How will you decide on the ideal setting – hospital based or IDTF and size of the lab?
3. What measures might you need to consider in framing the operational strategy to minimize risk of running afoul of OIG advisory opinion?

Ideal Answers

1. There are some basic steps in evaluating the feasibility of a new practice venture, and these include location, demographic profile, competition, how is the venture going to be funded, what is the financial status of the firm that wishes to partner with you, who are the investors and what is their prior track record, what is the nature of the relationship and how much financial risk and liability are you going to assume, and how much control over the operational aspects of the practice are you going to have. The AMA provides a template that can be accessed at https://catalog.ama-assn.org/MEDIA/ProductCatalog/m1400084/Starting%20a%20Medical%20Practicech01.pdf as well as a more thorough guide that is accessible to members at http://www.ama-assn.org/resources/doc/rfs/preparing-practice-toc.pdf
2. A hospital-based lab provides for greater access to more specialist evaluations, facilitates a multidisciplinary format, provides for higher remuneration, and can support higher acuity of care for high-need patients such as those with tracheotomies. An IDTF does not have the constraints of space and resource utilization, has a less complex administrative structure, and allows for non-physician ownership where the physician need not assume direct financial risk and liability.
3. OIG analyzed relationships between hospitals and sleep service providers and concluded that "per-click fee structure" does not meet the safe harbor requirement and are "inherently reflective of the volume or value of services ordered and provided." Steps the physician can take to reduce risk would include the following: (a) Sleep testing services are ordered and interpreted by physicians without a direct or indirect financial interest in the Facility. (b) Fees under the proposed agreement are consistent with fair market value in an arm's-length transaction. (c) Fees are not determined in a way that would take into account the value or volume of referrals or other business generated between the parties. (d) The hospital assumes business risk and contributes substantially to furnishing the sleep testing services for which it bills, including providing necessary space, equipment, a medical director, and administrative services. (e) The fees the facility charges for equipment, marketing, and other services and supplies are set in advance.

Case Study 2

A 57-year-old male is assessed by you as a sleep medicine specialist and you suspect sleep apnea on the basis of loud snoring, observed pauses during sleep, daytime sleepiness (ESS 13/24), and restless sleep. On examination, the patient has enlarged tonsils and nasal polyps. There is no indication of cardiopulmonary disease. Your request to perform a polysomnography is denied by the insurance company, and a utilization management firm representing the insurance company sends you a list of providers for home sleep testing.

Questions

1. What is the function of a utilization management firm?
2. Discuss the pros and cons of this approach to outpatient management.
3. What elements could you point to that might persuade the insurer to proceed first to polysomnography?

Ideal Answers

1. A utilization management firm conducts a review of the proposed site of service and a review of the health-care resources required or the proposed procedure or treatment. Such organizations assist in discharge planning, catastrophic case management, and other health-care review or benefit coordination services. Based on the information provided at the time of the review, the utilization management organization advises the claim administrator if the service meets the applicable health benefit plan's health-care review requirements.
2. Some measures to manage the cost of health care are necessary. Appropriately implemented, utilization management may be able to balance the clinical needs of the patients with cost-containment objectives. There are a large number of utilization management organizations, but they vary widely in terms of organizational structure and quality. From the clinician's point of view, many utilization management reviewers are intruding into clinical practice in a way that has a negative effect on quality of care by disturbing the potentially fragile treatment alliance, by compromising confidentiality, and by inappropriately mixing fiscal and medical treatment concerns.
3. For this patient there may be the opportunity for a surgical approach to the management of obstructive sleep apnea. The AASM guidelines are for a full polysomnography prior to surgery (or oral appliance) so that sleep-disordered breathing is assessed in all positions and sleep stages.

Case Study 3

You as a sleep medicine specialist are approached by the local hospital to become involved in an accountable care organization.

Questions

1. What is an accountable care organization (ACO)?
2. What are your negotiating strengths and weaknesses?
3. How will you place this in a business plan?

Ideal Answers

1. ACOs are a group of doctors, hospitals, and other health-care providers who come together (voluntarily) to give coordinated, high-quality care to Medicare patients. Coordinated care is designed to help the chronically ill get the right care at the right time, with the goal of avoiding unnecessary duplication of services and preventing medical errors. When an ACO succeeds in delivering high-quality care and lower spending of health-care dollars, it is to share in the savings it achieves for the Medicare program.
2. You have a specialized knowledge and skill set in the management of common chronic sleep disorders, such as sleep apnea and insomnia, as well as uncommon conditions like REM behavioral disorder which are more common in older Medicare parents. Daytime sleepiness, inadequate sleep time, insomnia, and other sleep disorders place a significant burden on the health-care system through increased utilization of the health-care system. Billions of dollars are spent each year in the USA on the direct costs of sleep loss and sleep disorders. These medical costs include expenses associated with doctor visits, hospital services, prescriptions and over-the-counter medications. In 1995, the direct cost of insomnia in the USA was estimated to be $13.9 billion. Patients with excess sleepiness and individuals with sleep-disordered breathing are associated with a 10–20 % increase in utilization. However, the perceived importance of care provided in sleep medicine is quite different, compared to cardiovascular or cancer care. How to place a value on your time and the testing that might be required for a Medicare population is not well known. Finally, the competition for sleep medicine access will vary by region. For these reasons a negotiation may be difficult.
3. One could outline strategies for streamlining the large-scale screening of sleep disorders, particularly sleep apnea, in the cohort of patients the ACO covers in a cost-effective and efficient manner and demonstrate the savings in both direct and indirect costs, as well as the projected savings in terms of reductions in health-care utilization costs.

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Chapter 21
Professional Training: Fellows and Faculty as Teachers

Clint W. Snyder

Introduction

The ACGME recognizes the role of faculty and fellows in the teaching mission of graduate medical education programs and requests that programs develop a plan to improve skills in education. For over four decades, the medical education literature has reported on the central role that fellows play in the education of medical students and residents [11]. Especially in university-based residency and fellowship training programs, this contribution is significant. It is an expectation that residents and fellows actively participate in the education of medical students and their fellow residents, and one study reports that residents commit up to 25 % of their time in the education and evaluation of medical students and their graduate medical education colleagues [1].

In spite of the centrality of teachers to our training of the next generation of physicians, medical schools and residency training programs frequently do not prepare fellows or faculty to become effective teachers. Both struggle to balance their own educational needs with the needs of their learners, while simultaneously attempting to provide competent patient care [2]. In Sleep Medicine, a focus on educational competency is often lost in the 1-year program.

The two major accrediting bodies for medical education in the United States, the Liaison Committee on Medical Education (LCME) and the Accreditation Council for Graduate Medical Education (ACGME), have both asserted the importance of preparing residents for their role as educators. In LCME Standard ED-24, residents/fellows in the role as teachers are specifically addressed (Liaison Committee on Medical Education 2012). This standard calls for medical schools and clinical

C.W. Snyder, Ph.D., M.B.A. (✉)
Department of Family Medicine and Community Health,
Case Western Reserve University School of Medicine,
10900 Euclid Avenue, Cleveland, OH 44106-5036, USA
e-mail: cws4@case.edu; clint.snyder@case.edu

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departments to provide enhancement of teaching and evaluation skills of residents through formal workshops and teaching resources. Likewise, the ACGME and its Outcomes Project addressed the need for preparation of residents/fellows as teachers [3]. Under the competency of Practice-Based Learning and Improvement, program directors are called upon to prepare residents for their roles to "educate patients and families" and to "facilitate the learning of students and other health care professionals" [4, 5]. The process of skill development in teaching for medical education is transferable to teaching patients, families, and caregivers.

However, Sleep Medicine programs feel constrained in their ability to fulfill these calls for preparation of fellows and faculty for their roles as teachers and evaluators. Many resident as teacher programs include content area such as teaching in an inpatient setting, teaching to the level of the learners, giving feedback, and the "One-Minute Preceptor" [6]. Without faculty members formally trained in education, many program directors feel ill-prepared to present formal sessions addressing these topics. Furthermore, while the principles are similar, the Sleep Medicine program is primarily an outpatient practice, and adjustments are needed.

However, reliance on the literature can give program directors the support they need to present teacher improvement programs. In particular, three areas for faculty development programs will be discussed: teaching in the inpatient setting, assessing the level of the learner using the RIME framework, and the "One-Minute Preceptor." RIME describes the progress of trainees from "Reporter" to "Interpreter" to "Manager" and "Educator" and the arc to clinical competency. The five skills – commitment, determination of supporting evidence, teaching of general rules, reinforcement what was done correctly, and correction of mistakes [7] – are very relevant to sleep behavior.

The purpose of this chapter is to present the general principles for the educational interaction and start the process of self-development of skills. In any given ACGME program, one should expect support for this line of work [3].

Teaching Inpatient Interactions

In the programs from which Sleep Medicine fellows accrue, the inpatient setting is the most common place where they initially have experienced opportunities for teaching. As they progressed to more senior status in their training programs, they supervised inpatient services with a variety of learners, from medical students to junior residents to trainees from other health professions. However, the time constraints of supervision of clinical care, patient care obligations, and documentation requirements may have made that a daunting learning environment for a new physician educator. Subha Ramani offers a structure to help guide teaching efforts, offering twelve tips to improve bedside teaching [8].

Teaching in the inpatient setting should be thought about in three components, parallel to clinical care [8]. First, in clinical teaching think of the "pre-round" component, which in Sleep Medicine is the "pre-clinic" component. During this

stage, the clinical teacher should prepare for teaching. Drawing a "roadmap" of what is to be achieved as a destination during a teaching session is vital, as is the orientation of learners to the plan. Negotiation of expectations for learning assures that all members of the team are in agreement. The second stage, one that is termed "rounds," is the teaching that occurs in the presence of the patient. Clinical teaching in this setting means that the fellow is a role model for the physician-patient encounter, including taking the responsibility of introducing the entire team to the patient. During the encounter in the presence of the patient, it is important that a "teacher" step back from clinical interactions with the patient to observe learners in action. The use of empathy in challenging the learning and correcting mistakes while in the presence of the patient is vital. While still with the patient, the suggestion is to summarize what has been learned to help the team connect with the patient and conclude the encounter. Finally, the "post-rounds" or "post-clinic" component allows for debriefing. This is a time for both teacher and learners to reflect on what has gone well, what needed to be approached differently, and for all to gain clarification. This reflection is important for the teacher, as the next opportunity to teach is generally in the next patient interaction.

The structure set out by Ramani does not require any particular educational expertise [8]. Rather, it provides a structure for the clinical teacher during three stages of the learning process in the inpatient setting. Identifying these "tips" for our resident teachers can help them to structure learning and become adept at integrating teaching in their inpatient care.

The RIME Framework

A challenge for even the most skilled physician teachers is adjusting the level of learning and the expectations of learners to the myriad of clinical learners. For many, remembering the skill and knowledge set of an early third-year medical student, for example, challenges clinical teaching, as the level of instruction ends of being far above the abilities of the learner. Effective clinical teachers adjust instruction to meet the appropriate level and expectation of their learners, yet doing that is often a difficult task.

Lou Pangaro provided a straightforward approach to categorizing learners and their abilities and thereby directing teaching [9]. The RIME Framework [9] places learners into one of four categories: Reporter, Interpreter, Manager, and Educator. The first stage, Reporter, sets out characteristics of learners at the most junior level. Like a reporter for a newspaper, these learners should be taught and assessed for an accurate gathering and communicating of clinical facts. These learners will have basic skills and knowledge of what to look for and how to gather relevant information. They can distinguish abnormal findings, but not necessarily have the ability to understand the cause(s) of the abnormality. Professional behaviors and attitudes are expected at this level. Interpreters, like those in a business organization, translate information with meaning. Learners at this level are able to interpret data, identify

and prioritize clinical problems, and may offer a relatively robust differential diagnosis. These learners are able to match diagnostic testing to clinical problems and provide for an appropriate follow-up. However, they are not yet at the level of patient management. For the Manager, the "what is next" questions are the issue. Learners at this level are able to determine plan of action based on a fund of knowledge and a deeper understanding of the patient and his/her condition. They can establish a plan of action that includes multiple options, and they are able to adjust a course of action to some degree depending upon the patient, practice environment, and resources available. The final level, one that not all learners achieve, is that of Educator. The Educator is a self-directed learner who is keenly aware of evidence behind therapies and diagnostic testing. They are able to identify researchable or unanswered questions related to the clinical encounter, patient or condition, and are consistently superior in knowledge, patient care, and care management.

Having a structure such as the RIME Framework helps the clinical teacher understand where they are and where others are in order to create an appropriate learning environment. Remembering the abilities and skills at each level assists the clinical teacher in setting expectations for the teaching encounter. This can help make the learning more effective and efficient, as well as leading to higher levels of satisfaction for both teacher and learner.

The One-Minute Preceptor

Having a structure for a one-on-one teaching encounter helps physician teachers navigate the teaching encounter in light of their busy clinical practices. Being efficient and effective in clinical teaching is vital if one is to give equal importance to the care of the patient and the care of the learner. Many clinical teachers become overwhelmed with balancing two important priorities such as these, and most frequently, teaching takes a back seat to the care of the patient.

Jon Neher and colleagues conceptualize the clinical teaching encounter using the "One-Minute Preceptor" approach in order to integrate five important "microskills" [7]. Like the clinical encounter, the One-Minute Preceptor encourages looking at the teaching encounter in two groups: behaviors to diagnose the learner and behaviors for teaching (Fig. 21.1). To diagnose the learner, there are two microskills. First, the clinical teacher should "get a commitment." To do this, the clinical teacher should have learners articulate their diagnosis or question for the teaching encounter. The learner should commit to an answer, an approach, or a plan even if it turns out to be wrong. This behavior allows the teacher to understand the clinical reasoning of deficits of the learner. The second behavior is to "probe for supporting evidence and reasoning." This approach allows the clinical teacher to evaluate the learner's knowledge and clinical reasoning. Moving beyond the current clinical presentation with hypothetical scenarios allows the teacher to work with the learner on broader and deeper answers to the current clinical situation. The subsequent three skills focus on teaching the learner. "Teach to general rules" is a reminder that teaching so

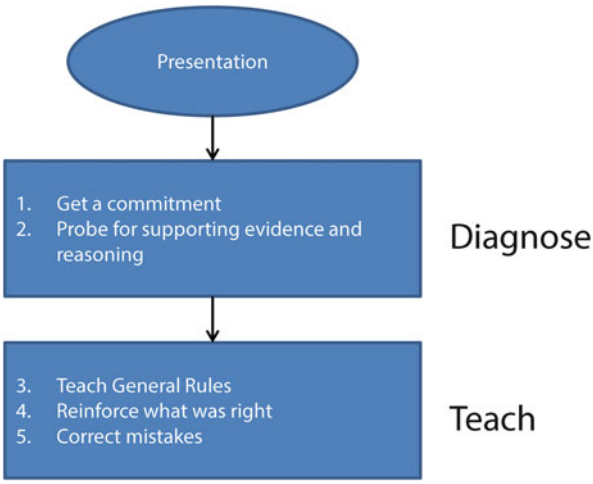

Fig. 21.1 The clinical teacher ideally at presentation of the opportunity would have learners articulate their diagnosis or question for the teaching encounter using five microskills

specific to the current case that it cannot be easily generalized to other situations by the learner is not an effective strategy. Looking for exceptions in the current case or distilling a pearl of wisdom for other cases like this is an effective approach to helping learners generalize the teaching to a future case. The final two teaching skills revolve around feedback. "Reinforce what was done well" calls on the clinical teacher to provide positive feedback to the learner. This not just increases the confidence and comfort of the learner, but it assures that behaviors appropriate for the current clinical situation are repeated in the future. Conversely, "correct errors" to provide negative feedback. This constructive approach helps learners to correct errors in judgment and clinical practice, and it affords them the opportunity to make changes in behavior or remediate deficits in knowledge.

Particular to the final two behaviors, it is feedback that receives additional attention. Feedback is one of the most basic of teaching behaviors, and it is one that clinical learners, both medical students and residents, most often feel is lacking. A straightforward checklist like the one offered by Bergquist and Phillips [10] can be very effective for junior teachers. These are simple descriptive statements regarding feedback that serve as both a guide and reminder for clinical teachers. Feedback is descriptive rather than evaluative, and it should be specific and detailed. It is well timed, and it has a limited amount of information at one time. It should focus around sharing information rather than giving advice, and it should be pointed toward a behavior that the learner can improve. This approach of giving a list of characteristics of appropriate feedback will help junior teachers improve their feedback, and it is a reminder of how central this teaching behavior is.

Having an explicit and standard plan in a busy clinical setting is vital for our residents and fellows as they strive to fulfill both teaching and clinical supervision roles. An approach such as the One-Minute Preceptor allow resident and fellow teachers to use a structure familiar from clinical care to help them break their

Table 21.1 Illustrations of objectives for installation of teaching activities in a fellowship program

• Describe the "diagnose" and "teach" components of the clinical teaching encounter relevant to sleep disorders for a resident and medical student
• List five microskills that can be used to teach clinical learners
• Prepare a plan for clinical teaching using the five microskills model
• Compare and contrast different levels of learners in the clinical medicine
• List the four categories of the RIME approach and apply to your teaching style
• Contrast the four levels of learners and the impact this has on your clinical teaching
• Describe an overall concept of teaching in multidisciplinary patient settings
• Organize the plan for teaching into pre-clinic, clinic, and post-clinic segments

teaching down into discrete, easily achievable components. This will help residents and fellows be more comfortable with their new roles as teacher and be effective in helping their junior colleagues learn and grow (Table 21.1).

Having formal preparation for residents and fellows in teaching is required by the undergraduate and graduate medical education accrediting bodies in the United States. But more importantly, it is an important component to professional development of junior colleagues and faculty. Assuring that our fellows and medical students receive high-quality teaching in Sleep Medicine is important. But benefits also result to those residents who are formally prepared for their roles as teachers. Those residents who have preparation for these roles have a higher level of enthusiasm for teaching, and they also exhibit greater job satisfaction [5]. Resident as teacher programs can be modest or robust, but the importance of providing basic skills and knowledge to these clinical teachers is undeniable.

An illustrative PowerPoint is presented in a PDF format on the companion website (http://competenciesinsleepmedicine.weebly.com/professional-training.html). It may be reviewed by the student and the program or discussed in a group format before or after the Essay Questions or IQ case.

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Appendix Material

Purpose and Process for the Essay Questions

Essay Questions (EQs) were inspired by best practices in our medical school curriculum. These questions require students to demonstrate understanding of the material and their ability to synthesize – i.e., apply to new situations – the concepts that they are learning. EQs should be written by content specialists.

- Students can be given a choice between two EQs pertaining to the week's learning objectives to answer in one page or less by the end of the week. At the end of the week, "ideal" answers to the EQs written by the specialists should be available. Students may compare their answers to "ideal answers" and self-evaluate. In addition, faculty could review students' answers and provide feedback.
- In given a timeframe, the EQ can be one method to evaluate whether the fellow takes a serious approach to deadlines and to the process.
- Students may confer with specialists who wrote the questions, work in groups, and use all references available to them to learn the material asked in the EQ. The EQ is intended as a formative learning experience.
- Though they may work in groups to study and review the material, **their answers to EQs should ultimately** *represent their own synthesis of the information and concepts in their own words*.
- While it is tempting for students to copy and paste their answers verbatim from various online sources, this practice should be identified as inappropriate and discontinued. It defeats the purpose of the SEQ assignment, students lose the learning opportunity, and it also wastes IQ faculty time. If the copied material is not attributed appropriately, then it is plagiarism. For all of these reasons, the practice of copying and pasting answers to EQs is unprofessional behavior.
- It is best for IQ faculty to take a proactive approach to this by reinforcing expectations for students' EQ answers simply by saying:
    - Write your answers in your own words as part of this learning assignment.

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- Copying and pasting answers verbatim from resources defeats the purpose of the assignment and undermines your learning. If you copy and paste and do not appropriately quote and reference your sources, it is plagiarism.

Feedback and Assessment for IQ Group Facilitators

The IQ Group facilitator participates in Feedback and Assessment.
Instructions and details are listed in the following pages.

During a session, the IQ Group facilitator will:

1. *Observe and document students' behaviors. See "Daily Observation Sheet" that follows. (This may be handed out to the participants.)*
2. *Review each student's Synthesis Essay Question (SEQ) weekly, compare answers to the "ideal" answers, and provide feedback/comments.*
3. *Assessment of student participant.* See following pages for instructions.

Introduction to the IQ Group Process

The purpose of the IQ group is to develop skills in learning with an iterative process of question development through a structured Case Study, concept learning and development though self-study, and articulation of concepts in a group learning format. The learners and the facilitator need to be open, flexible, and willing to give and take.

Note that the domains being assessed are not related to acquisition of specific skills or knowledge, but are process oriented. There is no answer, and each person has his/her own learning styles and preferences. The facilitator is to assist the learner to recognize personal strengths, consider alternative modes of thought and learning, and appreciate interpersonal differences inherent in problem solving.

Behaviors being assessed	Strengths	Areas for improvement and further learning
Contributions to the group content and process		
• Contributes to identifying learning issues in cases and to selecting group learning points that need further study		
• Provides supportive and constructive feedback to group members		
• Asks questions that reflect outside reading, and stimulate group discussion and thinking		
Skills at critical appraisal of resources		
• Uses a variety of references and critically appraises them		

(continued)

Behaviors being assessed	Strengths	Areas for improvement and further learning
• Analyzes and applies relevant studies, sources, and facts		
• Generates and considers alternative perspectives		
• Carefully weights evidence and refrains from drawing conclusion too quickly		
• Makes links with prior relevant readings, experience, or knowledge		
Professional behaviors		
• *Arrives on time, stays, does not leave early*		
• *Listens to others respectfully and attentively*		
• *Accepts constructive feedback and modifies behavior based on that feedback*		
• *Acknowledges the limits of one's own knowledge*		
• *Demonstrates accountability to self and group members for mastery of learning objectives*		
• *Completes tasks as negotiated within the group; is dependable*		
• *Identifies own strengths and weaknesses*		
• *Maintains composure during difficult group interactions*		

The group should set its priorities, procedures, and plan in the initial 10 min of a session or at the beginning of the 1-year fellowship. At the end of each session, a 10-min period is set aside for each person to comment on his/her own participation and on the behavior of the group.

Observation Sheet

Case number: _____ Date: _____
Facilitator: _____

Variables of interest

1. *Contributions to group content*: asks questions, weights evidence, makes links, analyzes, and prioritizes
2. *Contributions to group process*: completes tasks, identifies strengths, weaknesses, provides comments
3. *Professionalism:* listens to others respectfully, demonstrates accountability
4. *Attendance:* (absences, tardies) attends each session, does not arrive late or leave early

Student name	Observations

Self- and Group Evaluation

The Quick Overview: Four Steps for the Final IQ Group Evaluation

1. "Before we start our Final Self and Group Evaluation discussion, I would like you to take 3 minutes (I'll time you). Think about 2 things – your self-evaluation and your group evaluation. Write down for yourself one thing you think you have done well as an IQ group member and one area where you could improve. Write down one way that the group has functioned well and one way it could improve." *Hand out the IQ Group and Self-Evaluation Form at the end of this packet.*
2. "Let's go around the room and start with our self-evaluations. Tell how you think you have contributed to the group over the past weeks. Tell one thing you have done well as an IQ group member and one area where you could improve."
3. "Now let's think about how our group has worked together over the block. Let's go around and each comment on one way our group has functioned well and on a way we could improve."

4. "What do you think the first week of your new IQ group will be like?" Try to help students identify the need to be open, flexible, and willing to give and take. With each block, the students bring more and more prior experience to the new group – a strength and a challenge.

   *Nothing needs to be officially written down and handed in

A Detailed Facilitator Guide for the Final IQ Group Evaluation

Think of 10 min as a check out. It is a chance for each student (and for you) to reflect on his/her own contribution and role in the group and well as on the group itself.

Suggested Way to Begin the Final Self- and Group Evaluation

> Take 3 minutes and think about 2 things – your self-evaluation and your group evaluation. Write down at least one thing you think you have done well as an IQ group member and at least one area where you could improve. Write down at least one way that the group has functioned well and at least one way it could improve.

Self-Evaluation Discussion

> Let's go around the room and start with our self-evaluations. Tell one thing you have done well as an IQ group member and one area where you could improve.

Once an individual has shared one strength and one area for improvement, let the group concur or add additional insights. This is a nonthreatening way to do peer-to-peer evaluations.

Group Evaluation Discussion

> Let's go around and each comment on one way our group has functioned well and on a way we could improve.

Again, let the group add to the conversation.

Case Inquiry (IQ) Group Facilitator Assessment of Student Participant: Mid Fellowship

Student:_____

Preceptor(s):_____

Block: 1 2 3 4 5 6 Period: first ½ second ½

May Insert Student Picture Here

Please use examples you have observed to comment on the student's behaviors during Case Inquiry Group discussions.

Behaviors	Strengths	Areas for improvement and further learning
Contributions to the group content and process		
• Contributes to identifying learning issues in cases and to selecting group learning points that need further study		
• Provides supportive and constructive feedback to group members		
• Asks questions that reflect outside reading, and stimulate group discussion and thinking		
Skills at critical appraisal of resources		
• Uses a variety of references and critically appraises them		
• Analyzes and applies relevant studies, sources, and facts		
• Generates and considers alternative perspectives		
• Carefully weights evidence and refrains from drawing conclusion too quickly		
• Makes links with prior relevant readings, experience, or knowledge		
Professional behaviors		
• *Arrives on time, stays, does not leave early*		
• *Listens to others respectfully and attentively*		
• *Accepts constructive feedback and modifies behavior based on that feedback*		
• *Acknowledges the limits of one's own knowledge*		
• *Demonstrates accountability to self and group members for mastery of learning objectives*		
• *Completes tasks as negotiated within the group; is dependable*		
• *Identifies own strengths and weaknesses*		
• *Maintains composure during difficult group interactions*		

1 Meets criteria *2* Does not meet criteria

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