Medicine & Health
RHODE ISLAND

Vol. 89 No. 3 March 2006

Special Issue: Pediatric Sleep Disorders

Cover: "Nora at Night," photograph, by Dwayne Richardson, a sleep-deprived father and photographer

Medicine & Health
RHODE ISLAND
Publication of the Rhode Island Medical Society

Volume 89, No. 3 March, 2006

COMMENTARIES

CONTRIBUTIONS

Pediatric Sleep Disorders: A CME Issue
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COLUMNS

Medicine and Health\Rhode Island *(USPS 464-820), a monthly publication, is owned and published by the Rhode Island Medical Society, 235 Promenade St., Suite 500, Providence, RI 02908, Phone: 401-331-3207. Single copies $5.00, individual subscriptions $50.00 per year, and $100 per year for institutional subscriptions. Published articles represent opinions of the authors and do not necessarily reflect the official policy of the Rhode Island Medical Society, unless clearly specified. Advertisements do not imply sponsorship or endorsement by the Rhode Island Medical Society. Periodicals postage paid at Providence, Rhode Island. ISSN 1086-5462. POSTMASTER: Send address changes to Medicine and Health\Rhode Island, 235 Promenade St., Suite 500, Providence, RI 02908. Classified Information: RI Medical Journal Marketing Department, P.O. Box 91055, Johnston, RI 02919, phone: (401) 383-4711, fax: (401) 383-4477, e-mail: rimj@cox.net*

Commentaries

Chemical imbalance or moral weakness? Personal responsibility in a time of brain science

William Bennett, Secretary of Education in the Bush senior administration, wrote a best selling book on morals. It was therefore of great public interest when he was outed as a pathological gambler. Of course, people who make a public point of educating the rest of us on ethics are like the people who lecture us on sexual issues. They are often people trapped by their fears and failings, part fox, part hen, wanting to guard your chicken coops (not theirs).

How much of behavior is "teachable?" Obviously we think that most is or we wouldn't be spending so much time doing it. We also know that behavior is a brain process, and that much depends on the various connections and proportions of the neurotransmitter "humors." The brain is, in simple terms, an organ ("my second most favorite organ," according to Woody Allen) that works along scientific principles, analogous to the lesser organs. Of course these are far more complex and include the most difficult to understand concept, self knowledge.

Brain alterations cause behavioral changes. Damage the frontal lobes and the ability to experience emotion is blunted or destroyed (frontal lobotomies). Stimulate one tiny region and you may create depression or mania, or cure severe obsessions. Brain diseases cause a variety of dysfunctions as do many medications that act on the brain. Crimes committed during active brain malfunctions are almost always considered the responsibility of the patient and not the disease. "Not guilty by reason of insanity" virtually never results in acquittal, except on television. A schizophrenic who kills someone while in the grip of a delusion usually is punished. Alcohol or drug intoxication does not exculpate responsibility.

Subtle personality alterations however are harder to address.

A relatively recent observation in my field, Parkinson's disease, was that dopamine agonists, a small group of drugs that have been increasingly used to treat the motor symptoms, may cause pathological gambling in people who had never been so inclined. When the medication is lowered, the behavior resolves. The patients, unaware that this is a potential medication effect, notice that they've become interested in this activity that had never interested them before. They do not experience this as a foreign or alien feeling. They are not intoxicated. They are not delirious. Their personality, memory, problem-solving abilities are all intact. It is perhaps analogous to someone deciding that they would like to pursue a new hobby, repairing old cars, starting to knit, becoming a watercolorist, etc. In fact, it is possible that some people on these medications may have begun doing these very things, since the drugs have induced rare cases of severe senseless repetitive behavior disorders. A recent article described a PD patient who had, indeed, developed a "calling" to oil painting. The authors thought that this medication was to "blame", but who knows if the patient may have developed such a calling even if she hadn't been on the medications, or developed PD, since they didn't stop the medication to determine if this was a medicine related behavior?

If the PD patient lost his house at Foxwoods, could he sue the drug company that made the drug for not having this information in the package insert? Could he sue me for not preparing him for this outcome? How much is the drug's fault, and how much is the patient's? Who's responsible? If the drug is responsible, then isn't it possible that compulsive gamblers not on these medications may simply have genetic abnormalities causing similar chemical imbalances that mimic this process? And if this is true, does it imply that the courts should be more lenient with them when they declare bankruptcy?

The question here, of course, is where does personal responsibility end and physiology begin? Are the PD patients who developed a desire to gamble different in some way from the PD patients taking equal amounts of drug; different in some tangible, physiological way? Do they metabolize the drug differently, or do they simply have a "weaker" id, a lesser ability to ward off impulses? Are they morally weaker than the others or do the others simply not have these impulses at all? They do not experience the urge to gamble as foreign. They experience the desire and the pleasure as new, but not alien. The PD patients who don't gamble usually chuckle when asked about gambling, and report that they have not felt any urge to buy scratch tickets, or go to the gambling tables. They've had no impulse to resist.

A doctor with Parkinson's disease acts irresponsibly with a patient of the opposite sex. He loses his license. Is it a medication-related problem? Can he practice again if his PD medications are altered? Who's to blame? How do you detect a problem that does not seem out of place? How do we decide if a behavioral change is part of a disease process, due to the treatment, or simply intrinsic to the person's personality? Most people who gamble, pathologically or not, do not have Parkinson's disease. None of them take the offending drug. There are many paths to the same outcome.

I believe that people are responsible for their actions. I believe, however, that there are different levels of responsibility, so that some brain disorders should mitigate punishment. A post-seizure patient who, in a confused state, hurts a bystander trying to help him, is not responsible for his actions, at least not if he's been compliant taking his medications. A patient who acts out dream behavior and does something bad while asleep can't be deemed responsible, unless he had refused treatment for this problem. But with these very rare exceptions, most others are indeed responsible for their actions. Sometimes that responsibility is shared with the doctor providing the medicine.

Most of the time no one knows how irrational, pathological, or "alien" behaviors originate. The fact that some of these can be induced by medications that appear to produce exquisitely isolated behaviors, such as gambling, but not other impulsive or compulsive behaviors, suggests that our personalities and habits may be governed more by a multitude of rather simple chemical relationships than by years of ethical teaching. Of course, the education may produce the harmonious chemical balance underlying the state of appropriate grace, but a mild perturbation of one neurotransmitter in an enormously complex soup may put the whole system out of balance.

It is a true observation, but daunting, for it undermines our confidence in the very notion of personal responsibility. The chemical imbalance for sanctimonious hypocrisy has not yet been identified.

Joseph H. Friedman, MD

A Bat out of Hell

The word *reservoir* generally denotes a storage space where something may accumulate for a specified future use. The word thus possesses three attributes: first, it defines a place [such as a tank or a lake], second, a substance to be collected [such as water], and third, a purpose [such as irrigation].

Those concerned with the dynamics of infectious disease have often been perplexed by where certain germs accumulate [or hide] during the off-season when things are quiet and no one appears acutely ill. And for want of a better name, epidemiologists have designated those creatures which harbor a particular human pathogen as the disease-reservoirs. With some infectious diseases which are readily communicable, smallpox for example, the reservoirs are solely other humans. And thus if there are no humans acutely sick with smallpox in the immediate vicinity, the likelihood of contracting smallpox is very small. [The sole exception being bed-clothing recently used by smallpox victims which may carry infective material for days and thus may act as a temporary reservoir].

To establish effective barriers to the spread of many infectious diseases, public health officials need to know the answers to two critical questions: First, where do the germs hide when not infecting humans [that is, where is their reservoir?]. And second, how do these germs travel from the reservoir to the next potential victim? [And if these germs are carried by an independent creature such as a mosquito, as in the case of malaria, then the carrier is referred to as a the vector.]

If, as with smallpox and measles, the reservoirs are other acutely infected humans, and the means of communication are by physical contact or by an air-borne route through sneezing or coughing, then the cycle of communicability can be interrupted by isolating the acutely ill patients – a process called quarantine. If, on the other hand, the infection is carried by ticks and the reservoirs are feral deer, as with Lyme disease, then quarantining becomes of little practical value.

In the remote past, infectious diseases, primarily of domesticated animals, may have crossed over to infect humans; and over the many centuries these diseases have been adapted to humans; then the means of communication became principally or exclusively human-to-human. The animal reservoir was no longer needed to initiate the process of infectivity. But there are infectious disorders, generally viral in character, which still need an animal reservoir as the only continuing infective source. Rabies, for example, was considered to be caused by the bite of a rabid animal, typically a dog or a wolf. And yet there were confirmed cases of rabies not associated with any rabid dog. A search finally indicted bats as an alternative reservoir of rabies, with the bite of the bat as the means by which the virus is transmitted to humans. In this case then, the bat is both the reservoir and the vector of the disease.

Bats are global in their distribution. They may resemble birds but they are mammals with modified forelimbs facilitating flight. Bats are so clearly distinguishable from other animals that each culture has viewed them as variously harbingers, as symbols of malevolent creatures or even as surrogates of celestial or satanic forces. In Mosaic law, they were classified as unclean beasts and symbolic of pagan idolatry. Pliny, on the other hand, considered their blood to be aphrodisiac and hence, to him, they symbolized eroticism. In Chinese cosmology, the bat portrayed longevity and good fortune. And Taoist belief endowed the bat with great wisdom and a heavy brain [thus explaining why bats roosted upside down.] And Victor Hugo, for unclear reasons, declared the bat to be an accursed creature which personified atheism. This nocturnal creature, therefore, arrives upon the epidemiological stage with a closetful of myths, perceptions and alleged powers.

Rabies in vampire bats is largely confined to the Latin American nations although rabid bats have been found elsewhere. Rabies in cattle, however, constitutes a major economic problem. It is estimated that about 500,000 head of Mexican cattle are destroyed each year by the rabid bite of vampire bats. Mexico also has recorded as many as 170 human rabies fatalities per year attributable to bat-bites.

In recent decades, bats have been demonstrated to be reservoirs for such viral illnesses as West Nile fever. Japanese B encephalitis, St. Louis encephalitis, and possibly, Lassa fever. [Lassa is a highly fatal viral infection first recognized in nurses working in the Nigerian township of Lassa. Since then there have been sporadic outbreaks in Sierra Leone, Liberia and a number of other west-central African nations.]

Marburg fever, a viral disease first recognized in 1967, is thus far limited to west Africans and those working with primates derived from west Africa. There have been outbreaks in numerous villages in central Africa and until recently it was presumed that rain forest primates were the sole reservoir of the virus. But then there arose clusters of cases in adventuresome Europeans exploring caves in east-central Africa. The role of bats in this disease, sometimes called green monkey fever, has yet to be proven; but the cave-exploring cases strongly suggest that bats may indeed be one of the principal reservoirs of Marburg fever. In recent months an outbreak in Angola resulted in 376 confirmed cases with 315 deaths [mortality rate of 83.8%].

Ebola fever derives its name from the Ebola river, a small tributary of the northern branch of the great Congo River. It was in this region that the first cases of hemorrhagic fever were first encountered. A filoform virus has since been isolated from human victims suggesting that it is closely related to the Marburg virus. And in November, 2005, virologists in the west African nation of Gabon demonstrated the existence of the virus in numerous bats captured from the region, thus confirming the suspicion that the reservoir of many of the fatal hemorrhagic fevers of central Africa is the bat.

When the witches of Macbeth concocted their evil brew ["Eye of newt, and toe of frog, Wool of bat, and tongue of dog, Adder's fork, and blind-worm's sting"] little did Shakespeare appreciate the reservoir of malevolence within the bat.

Stanley M. Aronson, MD

Introduction: Topics in Pediatric Sleep Medicine

JUDITH A. OWENS, MD, MPH

I am delighted to introduce the readers of *Medicine & Health/Rhode Island* to this special issue on topics in pediatric sleep medicine. The recognition of the importance of these topics and of the field itself reflects the progress we have made over the past decade in clinical work, research, education, and advocacy in pediatric sleep. It also represents the hard work and dedication of many individuals, including a number in the Brown medical and research community, like Drs. Mary Carskadon and Richard Millman. An increased understanding of normal sleep development across childhood and adolescence, the recognition of the potential neurocognitive and neurobehavioral impact of sleep disorders, and a growing appreciation of the health consequences of inadequate sleep in the pediatric population have all helped both to bring these issues into the public spotlight and to necessitate the development of continuing medical educational initiatives such as this special issue.

It is particularly fitting, given the emergence of pediatric sleep medicine as a new and exciting field, that all of the articles in this issue were contributed by students and trainees at Brown. Furthermore, the diverse disciplines represented by the authors (developmental/behavioral pediatrics, pulmonary medicine, child psychology, human biology) are representative of the basic trans-disciplinary nature of the field and the breadth of knowledge it encompasses. The selection of topics is equally broad and ranges from fundamental pathophysiologic and clinical differences in sleep-disordered breathing between children and adults to the clinical challenges of evaluating and treating sleep problems in special pediatric populations to the use of evidence-based behavioral treatment strategies for managing bedtime problems and night wakings in infants.

We hope that this issue will not only highlight exciting research developments in pediatric sleep, but will also provide the clinician with insight into the causes and consequences of sleep problems in children and provide guidance regarding recognition and management in clinical practice. The most important "take home" message for the practicing physician is that screening for, diagnosing, and successfully treating sleep disorders in infants, children, and adolescents not only is our responsibility as health care providers, but is likely to have a significant positive impact on the health and well-being of both children and families.

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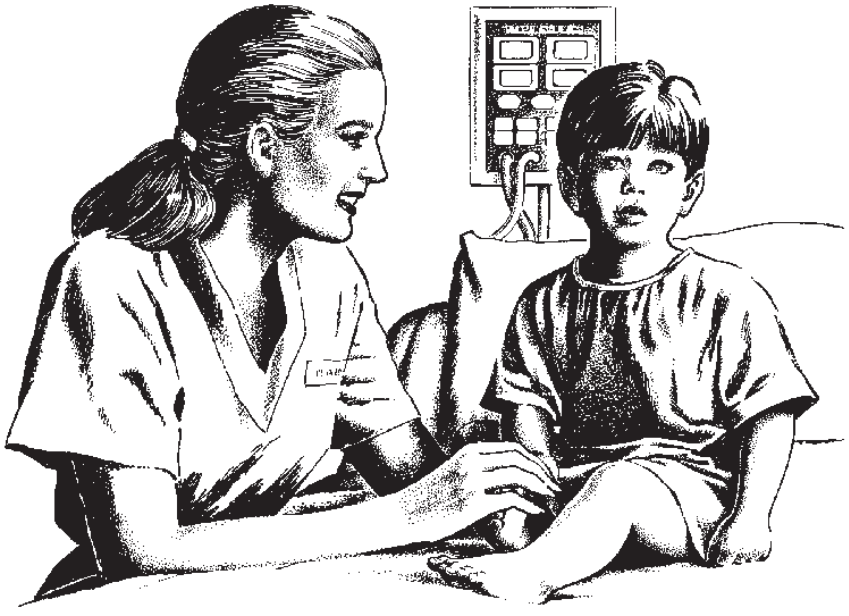

Sleep and ADHD: A Review

Kristin Bartholomew and Judith Owens MD, MPH

Attention deficit/hyperactivity disorder (ADHD), the most common childhood psychiatric disorder, affects between 5 and 10% of school-age children in the United States. [1] Approximately four times more boys than girls are diagnosed with ADHD; this finding may be partially due to referral bias, but probably also reflects a true gender difference. Although the clinical presentation varies somewhat with age and gender, the cardinal features of the disorder are both behavioral (hyperactivity, impulsivity) and cognitive (inattention, difficulty focusing, distractibility) in nature. Deficits in "executive functions" (e.g,., working memory, response inhibition), controlled by the prefrontal cortex, are also a hallmark of the disorder. Dysfunction in any of these areas can lead to social and family difficulties, academic underachievement, and impaired occupational functioning.[2] In the majority (upwards of 60%) of children diagnosed with ADHD, functional impairment continues into adulthood.

Although a number of "objective" measures of inattention (e.g., **computerized performance tasks (CPT)**) may be helpful in the evaluation of a child with ADHD symptoms, the diagnosis remains essentially a clinical one. Positive identification of 6 out of 9 DSM-IV-R inattention or hyperactivity/impulsivity characteristics in two or more settings is required; ADHD subtypes include primarily inattentive (approximately 25%), primarily hyperactive/impulsive (15%) and combined (60%).[3] Symptoms must be present before the age of 7, persist for at least 6 months, and significantly impair academic, social, or occupational functioning. Other important considerations are that the child's symptoms are viewed in a developmental framework, (i.e., based on what is expected of others in the same age group and of the same cognitive level and evaluated in the context of the individual child's cognitive potential.

Upwards of 65% of children with ADHD may have a co-morbid psychiatric disorder, such as oppositional defiant disorder (ODD; 40-60%), learning disabilities (40%), anxiety disorders (30%), conduct disorder (14%), and chronic motor tic disorders (11%). ADHD may contribute to substance abuse disorders in adolescents and adults,[4] although studies suggest that treatment with psychostimulants appears to mitigate, rather than increase, the risk of, substance abuse in ADHD. Co-morbid conditions complicate the diagnosis and treatment of ADHD, and many children with co-morbidities may benefit from additional psycho-social interventions.[5]

"...all children presenting to health care practitioners with learning, attention, behavioral, or emotional concerns, especially ADHD, should be carefully assessed for underlying or comorbid sleep disorders as part of the routine evaluation."

One of the more recently recognized co-morbid conditions in childhood ADHD is sleep disorders.[5] Clinical experience suggests that sleep problems in children with ADHD are not only common, but may exacerbate symptoms of inattention and behavioral dyscontrol. Although precise figures are unavailable, a number of research studies have also suggested that sleep problems are a common co-morbid condition with ADHD.[6] Some studies have assessed the prevalence of neurobehavioral deficits in clinical populations of children with diagnosed primary sleep disorders; the pediatric sleep disorders most frequently studied from this perspective are discussed below and are sleep disordered breathing conditions including **obstructive sleep apnea (OSA)** and snoring, **Restless Legs Syndrome/ Periodic Limb Movement Disorder (RLS/PLMD)** and narcolepsy.[7] Conversely, other studies have examined the prevalence of sleep problems in pediatric populations identified with learning, behavioral, attentional, or academic problems compared to control populations.[8] Finally, a number of studies which have examined the effects of both acute and chronic partial sleep deprivation (sleep restriction) in older children and adolescents under experimental conditions have documented relative deficits in a number of neurobehavioral and neurocognitive domains, including behavioral signs and subjective reports of sleepiness, attention, reaction time, memory, and problem-solving ability and creativity (so-called "executive" or higher level cognitive processes).[9] For example, early rise times in fifth graders have been associated with self-reported difficulties in attention and concentration. [10]

ADHD and Primary Sleep Disorders

Obstructive sleep apnea affects roughly 2% of children ages 3 to 7. [11] Adenotonsillar hypertrophy is considered the most prevalent risk factor in childhood, but OSA is frequently identified in children who are overweight and obese. Most pediatric studies have supported a similar range of deficits in children with ADHD and with **sleep-disordered breathing (SDB**) in terms of attention, memory, and executive functions, as well as an increase in subjective sleepiness and mood disturbance. [12-15] A higher prevalence of parent-reported externalizing behavior problems, including impulsivity, decreased attention span, hyperactivity, aggression, and conduct problems has been frequently reported in studies of children with either polysomnographically-diagnosed OSA or symptoms suggestive of SDB, such as frequent snoring. Furthermore, studies which have looked at changes in behavior and neuropsychological functioning in children following treatment (usually adenotonsillec-

tomy) for OSA/SDB have also documented significant improvement in daytime sleepiness, behavior, and academic performance post-treatment.[16-18] In addition to these more subjective reports of improvement, there were objective improvements in neuropsychological measurements of attention, vigilance and reaction time, and cognitive functions.

Alternatively, the prevalence of SDB symptoms in children with identified attentional, behavioral, and academic problems has also been examined. One sample of first graders performing academically in the lowest 10th percentile found a prevalence of 18% of significant SDB symptoms.[17] Several recent reports have documented a significant increase in OSA symptoms specifically in children being evaluated for or diagnosed with ADHD, and have suggested that as many as 25% of ADHD diagnoses may be linked to symptoms of sleep-disordered breathing such as habitual snoring.[14]

Significant neurobehavioral consequences may also occur related to RLS/PLMD, and may present as symptoms of ADHD.[19, 20] **Restless legs syndrome (RLS)** is characterized by what is often described as uncomfortable "creeping" or "crawling" sensations occurring primarily in the lower extremities and during periods of rest or inactivity (e.g.,, sleep onset), which are relieved by movement. There is frequently a familial component, and exacerbating factors include increased caffeine intake and iron deficiency (low ferritin). Although the prevalence of RLS in the pediatric population is unknown, approximately 10% of adults in the US has the disorder, and retrospective reports given by these adults suggest that symptoms (such as restless sleep and "growing pains") frequently first appear in childhood. [21] Approximately 80% of patients with RLS also have repetitive rhythmic kicking movements of the lower extremities during sleep called periodic limb movements. RLS is a clinical diagnosis; the diagnosis of PLMD requires polysomnography to detect the characteristic rhythmic movements of the tibialis anterior muscle group and frequent arousals. The symptoms of RLS appears to reflect decreased dopaminergic activity. Furthermore, treatment of these children with dopamine antagonists has been shown to result not only in improved sleep quality and quantity, but also in improvement in "ADHD" behaviors previously resistant to treatment with psychostimulants.

Is Sleep in Children with ADHD "Different"?

Studies of children with ADHD have largely used either parental (or self-report) surveys or **polysomnography (PSG)** to examine the relationship between sleep architecture, sleep patterns and behaviors, and sleep disturbances and ADHD. While results have been mixed and at times contradictory, some features of sleep in children with ADHD appear to be relatively consistent across studies. First, most of the "objective" studies have failed to find consistent significant differences in sleep architecture and patterns between children with ADHD and controls.[22] Second, although actigraphy studies using lightweight activity monitors,[23] which presumably capture more "naturalistic" sleep wake patterns across time (3 to 5 nights), have also failed to demonstrate striking, consistent differences between children with ADHD and controls on the typical actigraphic sleep parameters (sleep onset, sleep duration, sleep efficiency, night wakings), they have suggested there may be two other distinctive features of sleep in these children. Activity during sleep in children with ADHD has been shown to be higher in several actigraphy studies, both in terms of frequency and duration of movements; this finding is also supported by a study which utilized infrared video recordings to assess nocturnal movements in children with ADHD.[24] Several more recent studies examined not only the average of the actigraphic sleep parameters across the 5 day monitoring period, which was not different from controls, but also the night-to-night variability.[25] The authors concluded that the instability of sleep patterns in children with ADHD set them apart, and postulated that this variability might reflect a fundamental impairment in arousal regulation in ADHD.

Finally, somewhat counter-intuitively, these studies consistently suggest that children with ADHD, although their sleep parameters are comparable, may actually be "sleepier" (as measured by the number and rapidity of sleep onsets on MSLT) than normal children.[26, 27] This raises the intriguing possibility that ADHD is associated with *hypo-* rather than *hyper*arousal, and that, at least for some children with ADHD, hyperactivity is an adaptive behavior that counteracts the effects of underlying daytime sleepiness. This hypothesis also provides an explanation for the seemingly paradoxical effectiveness of psychostimulants in treating this disorder.

In contrast to studies which have utilized more objective measures, parental report studies have almost universally reported a high frequency of significant sleep problems in children with ADHD. These include difficulty falling asleep, night wakings and restless sleep, at prevalence rates and/or at levels of intensity that are generally two-three fold that of control group children.[28, 29] More recent studies have suggested that many of these sleep disturbances may be attributable to either medication-related effects, primarily from psychostimulants, or from common psychiatric co-morbid conditions such as Oppositional Defiant Disorder, rather than to ADHD per se.[30, 31]

The etiology of sleep disturbances associated with ADHD in childhood, thus, is likely to be multi-factorial and to vary across patients. As noted above, several studies have suggested that pharmacologic treatment (primarily stimulants) side effects may play an important role;[32] for example, one study demonstrated subjective parental perception of increased (three-fold) severe sleep difficulties including sleep onset delay and night wakings in children on psychostimulants for ADHD. Stimulants increase the monoamines in presynaptic clefts by blocking reuptake of dopamine and norepinephrine and enhancing their release. [33, 34] Results of studies assessing objective (PSG) measures of psychostimulant effects are more variable; some have demonstrated evidence of delayed sleep onset, shorter sleep duration, and delayed onset REM. Stimulants may also have a "rebound" effect when wearing off at the end of the day, resulting in an increase in arousal and hyperactivity above baseline.[35]

In addition to medication-related sleep effects, there appears to be an important influence on sleep behavior of such common co-morbid condi-

tions as oppositional defiant disorder, depression, and anxiety disorders. Virtually all psychiatric disorders in children may be associated with sleep disruption as well as daytime sleepiness, fatigue, abnormal circadian sleep patterns, disturbing dreams and nightmares, and movement disorders during sleep. For example, sleep complaints, especially bedtime resistance, refusal to sleep alone, increased nighttime fears, and nightmares are common in children with anxiety disorders. Children with oppositional and defiant behavior may be more likely to demonstrate problems with limit setting and bedtime resistance. Conversely, growing evidence suggests that "primary" insomnia (i.e., insomnia with no concurrent psychiatric disorder) is a risk factor for later developing psychiatric conditions, particularly depressive and anxiety disorders.

However, the question remains as to whether at least some children, possibly a subgroup, with ADHD have more "intrinsic" settling problems at bedtime that are unrelated to either extrinsic factors, co-morbid psychiatric conditions, pharmacologic treatment, or primary or co-morbid sleep disorders.[36, 37] Some authors have postulated a catecholamine-mediated "hyperarousal" mechanism that prevents or delays settling at bedtime, while others have suggested that at least some of these children may have a melatonin-mediated, circadian-based sleep phase delay that results in bedtime resistance when these children are required to fall asleep earlier than their physiologic sleep onset time. An additional possibility is that some intrinsic sleep-wake regulatory dysfunction in these children results in unpredictable or erratic sleep onset latency.

Management

An important treatment goal should be evaluation of any comorbid sleep problems, followed by appropriate diagnostically-driven behavioral and/or pharmacologic intervention.[38, 39] Difficulty falling asleep related to psychostimulant use may respond to adjustments in the dosing schedule, because in some children the sleep onset delay is due to a "rebound"effect of the medication wearing off coincident with bedtime, rather than a direct stimulatory effect of the medication itself.

The use of other pharmacologic agents as an alternative to psychostimulants might be considered in children for whom medication-related insomnia is a problem; atomoxetine (Strattera®), is a non-stimulant, highly selective inhibitor of presynaptic norepinephrine reuptake which does not appear to have deleterious effects on sleep [(40)] .

It cannot be emphasized enough that all children presenting to health care practitioners with learning, attention, behavioral, or emotional concerns, especially ADHD, should be carefully assessed for underlying or comorbid sleep disorders as part of the routine evaluation. Parents, even the children, may not connect behavioral and learning disorders to sleep problems, and thus may fail to spontaneously volunteer such information. Furthermore, because parents of older children and adolescents may not be aware of any existing sleep difficulties, it is also important to question the patient about sleep.

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Sleep in Children with Developmental Disabilities

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An increasing number of studies over the past decade have examined the extent and severity of sleep disturbance in children with developmental delays and cognitive impairments. Rates of sleep problems in this broadly defined population range from 13-86%.[1] These children have shown difficulties with initiation and maintenance of sleep, irregular sleep patterns, shortened sleep duration, and early morning awakenings.[2] This paper will review research on several diagnostic groups.

Sleep in Heterogeneous Groups of Developmentally Disabled Children

Much of the sleep research in children with special needs has used heterogeneous diagnostic groups, rather than isolating the sleep patterns of children with specific diagnoses. High prevalence rates for sleep problems in this population, ranging from 13-85%, may be related to any number of factors, including intrinsic abnormalities in sleep regulation and circadian rhythms, sensory deficits, and medications used to treat associated symptoms. Reported rates of sleep disturbance also vary depending on age, type of sleep problem, living environment, measures used, and perception/tolerance levels of caregivers. Evidence has been mixed on whether severity of sleep disturbance is related to severity of mental handicap, although more evidence appears to point to a positive correlation. [1,3]

Richdale and colleagues studied the sleep behaviors of 52 children with mild to profound intellectual disabilities, compared with those of 25 typically developing children. Children in the intellectually disabled group had the following disorders: Down Syndrome, autism, Fragile X, unspecified developmental delay, and "other known disorders" which included cerebral palsy. Results indicated a significantly higher frequency of both past and present sleep problems amongst the disabled children versus the control group. The most commonly reported sleep problems in the former group included frequent night waking, problems settling to sleep, snoring, bed-wetting, and yelling at night. Level of intellectual disability was not generally associated with the frequency of occurrence of past or present sleep problems. There was, however, a relationship between sleep disturbance and increased behavioral problems.[4]

"... children with autism often have difficulty falling asleep, frequent awakenings, and restless sleep."

In a longitudinal study of 200 children ages 1-18 years with severe mental retardation, 51% had settling difficulties, while 67% had frequent nighttime awakenings. At three-year follow-up, 50-75% of the children who initially presented with sleep disorders continued to have these difficulties. In this sample, sleep problems were significantly associated with the following child characteristics: poor academic skills, poor self-help skills, poor communication skills, incontinence, and daytime behavior problems. The children with a sleep disturbance showed significantly more impairment in these areas than did children with no sleep disturbance. There was an additional strong association between children's sleep problems and maternal stress. A path model indicated that a deficit in child communication skills influenced the frustration of parents attempting to teach their children to engage in more socially appropriate behavior, such as settling at bedtime.[5]

Sleep in Children with Autistic Spectrum Disorders

Prevalence estimates for sleep disorders in this specific population range from 44-83%.[6] As in the heterogeneous participant groups described above, children with autism often have difficulty falling asleep, frequent awakenings, and restless sleep.[7] One study found that parents of children with autism reported their kids as having sleeping problems significantly more often than did parents of children with general mental retardation.[8]

Some researchers have hypothesized that parents of children with autism are oversensitive to their children's sleep behaviors and, therefore tend to report more problems with sleep than do parents of typically developing children.[9] In one study, the sleep of eight autistic children whose parents had identified them as having sleep problems was monitored via 72-hour actigraphy: with the exception of an approximate 1-hour earlier wake time, these children had sleep patterns similar to those of non-autistic children. However, the results of this study have limited generalizability given the small sample size.

A larger-scale study by Wiggs and Stores included both subjective and objective measures collected on 69 children, ages 5-16, with autism spectrum disorders. Parents were asked to complete an interview and detailed questionnaires, as well as 2-week sleep diaries. The children wore actigraphs for five nights. Parents reported sleeplessness in 64% of the children, with behavioral sleep disorders featured most prominently. Anxiety-related sleep problems and sleep-wake cycle disorders were also identified. The objective sleep quality of all children

seemed compromised, with sleep/wake times abnormally early or late, sleep latency abnormally high, and sleep efficiency (defined as: time asleep/time in bed) abnormally low. Sleep patterns as measured by actigraphy did not differ between those autistic children with or without reported sleeplessness. The authors suggested that those children identified as having problematic sleep might have differed from the others only in the degree to which they could soothe themselves back to sleep without involving a parent. While some children signal to their parents that they are awake, others may not.[10] Some parents of autistic children may also respond more often to their children's movements or cries at night, knowing that these children tend to be more reactive to changes in the environment. In responding, these parents may inadvertently wake children who are asleep (and perhaps having a nightmare), thus increasing report of sleeplessness.[8]

Sleep problems have also been linked with increased symptoms of autism. Schreck, Mulick, and Smith evaluated 55 children ages 5-12 years with autism. They found that fewer hours of sleep per night predicted overall autism scores, social skills deficits, and stereotypic behavior. Children who awoke screaming were more likely to experience higher rates of stereotyped behaviors and to have more communication abnormalities.[11] Although the direction of this association is unclear, it is possible that interventions for nighttime problems will positively affect daytime functioning, or at a minimum help children to benefit further from daytime therapies.

Assessment and Treatment of Sleep Problems

Prior to developing an effective intervention for a developmentally disabled child with a sleep disorder, the clinician must first evaluate possible contributing and maintaining factors. This may be accomplished through the use of questionnaires, interviews, and sleep diaries. A functional assessment of sleep problems, in which parents are asked to track the antecedent and consequence of each disruptive nighttime behavior, can also be performed. The latter approach has shown that the nighttime behaviors of children with developmental disabilities may be maintained by social consequences, such as parent attention in the form of comfort, play, or even verbal warnings. This is not to say that children's sleep problems necessarily emerge as a function of parent behaviors, but that parents may be reinforcing them once the initial cause (e.g., flu or ear infection) is no longer present. Compared with typically developing children, those with developmental disabilities may have more difficulty recovering from interruptions to their sleep patterns, and therefore require more intervention from caretakers. Once a novel interaction is established at bedtime, such as a parent sitting with a child night after night until she falls asleep, it may be all the more challenging to alter it in this population. Functional assessment to evaluate this hypothesis can contribute to effectiveness of treatment. Once this reinforcement is identified and removed, whether through graduated or immediate extinction, night time disruptive behaviors often improve.[12]

In addition to extinction, other behavioral interventions have been shown as effective in treating various sleep problems within this special population, including circadian rhythm disturbances. These include positive attention/rewards for desired bedtime behaviors, stimulus control, improving sleep hygiene, gradual distancing, sleep-wake scheduling, bedtime fading, chronotherapy, and light therapy.[1, 13] Of course, all these strategies involve commitment and consistency from parents. Families with disabled children face challenges on a daily basis, and caregivers may be hesitant to disrupt established patterns of home behavior for the sake of intervening with their children's sleep problems. Clinicians should discuss any such concerns before asking families to initiate a behavioral plan. Educating parents about the link between decreased daytime functioning and disrupted sleep[11],and providing ongoing support, are two ways to help parents.[13]

Another option for treatment of circadian rhythm sleep disorders in developmentally disabled children is the use of medication. There is some evidence that natural production of melatonin may be reduced in this population, and that replacement of melatonin subsequently improves sleep in some children. No major side effects have been reported in the use of melatonin for pediatric sleep treatment, and short-term therapy with melatonin can be safer than the use of hypnotics. However, melatonin is most effective when used in combination with behavioral interventions.[14]

Finally, some children with developmental disabilities will not respond to either behavioral intervention and/or the use of melatonin for their sleep disorders. As a second-line treatment option, clonidine has been shown to be effective in improving the sleep of children with mental retardation and autistic spectrum disorders, with minimal side effects.[15]

Summary

Sleep disturbances are more common in children and adolescents with developmental disabilities than in non-disabled individuals. Given the potential benefit of improved sleep for a patient's daytime functioning, it is important that clinicians who work with this population query caretakers about sleep problems and offer intervention, whether behavioral or pharmacological. Sleep problems in children with developmental disorders often fail to improve spontaneously, as may be the case in typically developing children, which can lead to further distress, disappointment, and frustration for families.[15] Attempting to resolve sleep difficulties as they arise can benefit not only the patient, but also the patient's caretakers.

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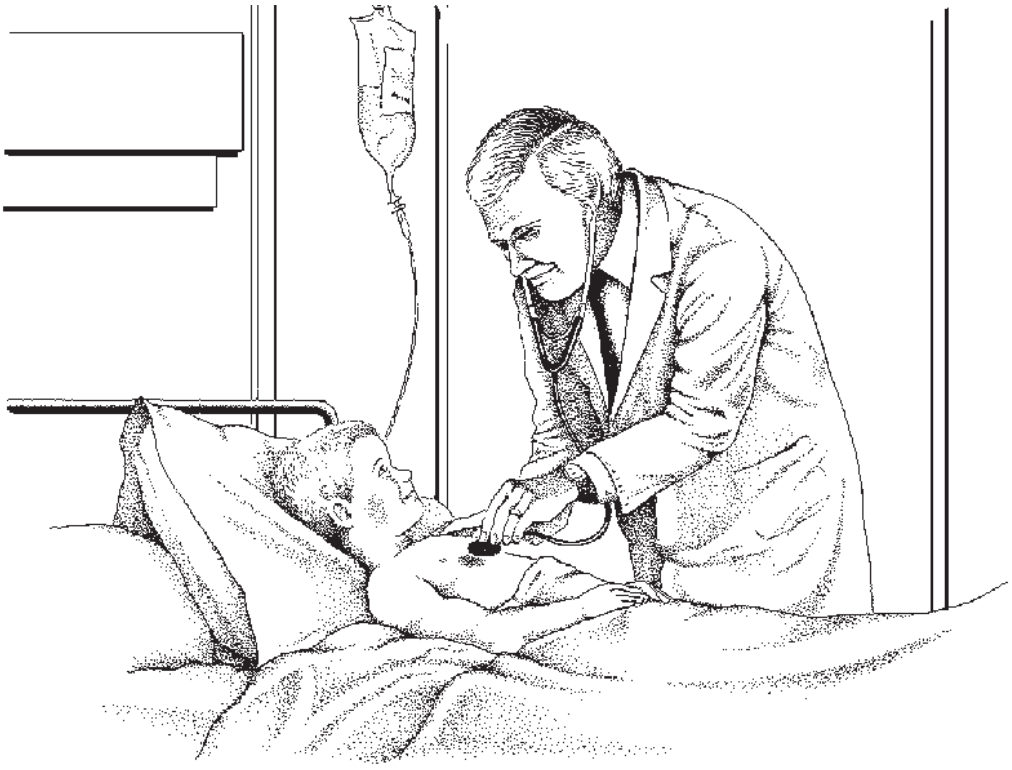

Behavioral and Massage Treatments for Infant Sleep Problems

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The regulation and consolidation of sleep are major developmental tasks of infancy and usually occur by six to nine months of age. By that time, 70% of infants will have developed a consistent sleep pattern and "sleep through the night" as defined by a continuous period of sleep from midnight to 5:00 am. Although it is normal to have brief nighttime awakenings at this age, most infants are able to self-soothe, i.e. go back to sleep without assistance. However, research suggests that 30-40% of infants either fail to learn self-soothing techniques or develop new sleep problems in the second year of life.[1] Many of these infants will subsequently develop long-lasting, complicated, or severe sleep problems.[1-6]

Infant sleep problems are parentally defined and most often present as bedtime struggles (i.e. limit setting disorder) and/or frequent nighttime awakenings (i.e. sleep onset association disorder). Sleep problems in this age group (less than two years old) can have a major impact on the infant's health and have been associated with poor feeding and growth, dysregulated daytime behavior, decreased attachment/socialization, and slowed developmental progress.[1-2, 5-8] As is true of many pediatric problems, the consequences of infant sleep difficulties are not limited to the individual but usually affect family functioning as well. Specifically, infant sleep problems have been strongly associated with high levels of family stress and maternal depression in several research studies.[2, 9-11]

"The success of any extinction program depends on parental consistency."

Standard treatments for pediatric sleep problems are often behavioral in nature and require close follow-up with repeated health care visits.[1, 12] The goal of "sleep training" is to remove parental interventions during sleep times so that the infant can learn to self-soothe. This usually involves putting the infant to bed "drowsy but awake" and letting him/her "cry themselves to sleep". Several sleep training methods are described in the medical literature, many of which are widely recommended by pediatric providers. These include well established treatment methods, such as modified and unmodified extinction programs.[12-15] Other behavioral methods, such as positive bedtime routines and faded bedtime with response cost, are less established but appear promising.[12-13] This review will briefly discuss some of the common behavioral treatments for infant sleep problems, including the use of infant massage as an adjunct to sleep training. Lastly, the importance of early intervention and prevention for infant sleep problems will be discussed, along with some practical considerations faced by those in clinical practice.

Extinction Programs for Infant Sleep

Unmodified extinction programs involve putting the infant down for sleep at a designated bedtime, then ignoring the child until an appropriate rise time the next morning. Parents must limit their responses to infant crying, tantrums, and calls for help, and should interact with the infant only for illness, injury, or safety concerns. In many cases, infant behavior worsens in the first few nights of an extinction program, and prolonged crying and/or more frequent waking is often seen before infant sleep improves. This "extinction burst" can be dramatic, but usually resolves within three to five nights of treatment.[1]

The success of any extinction program depends on parental consistency. By responding to infant cries, parents can inadvertently reinforce inappropriate behaviors and make future attempts at treatment more difficult.[1, 12-15] Therefore, it is imperative that parents ignore all inappropriate infant behaviors regardless of frequency, intensity, or duration. Some parents find it difficult, if not impossible, to achieve this level of consistency due to various emotional or environmental factors. Parents who are unable to tolerate prolonged infant crying may find it easier to comply with a modified extinction program, such as extinction with parental presence or graduated extinction.

Modified extinction programs allow for an increased parental presence at bedtime and during infant wakings. These programs are similar to unmodified extinction, but may be more acceptable to parents who have concerns about the safety and/or emotional consequences of ignoring an infant who is out of sight.[1, 12-15] In extinction with parental presence, a parent stays in the infant's room but completely ignores the infant and his/her behavior. In contrast, graduated extinction programs allow for brief periods of interaction at specified intervals during times of infant distress. Parents may respond to infant crying with brief (less than 60 second) periods of verbal reassurance and/or physical comforting. The infant is ignored between checks, which occur at pre-determined intervals based on infant temperament and parental comfort (typically five to 20 minutes). These intervals are gradually increased as parents grow more comfortable with infant crying and/or infant sleep improves.

Of all the behavioral treatments for infant sleep problems, unmodified extinction, extinction with parental presence, and graduated extinction programs have been the most carefully studied.[12] Prior research supports the efficacy of these methods in the treatment of infant sleep problems, but no evidence suggests that one extinction program is more or less effective than the others. Therefore, the choice of an extinction program for infant sleep training must de-

pend largely on the needs of each individual infant and his/her parents.

Positive Routines/Faded Bedtime with Response Cost

Positive bedtime routines are designed to "cue" the infant for sleep by providing him/her with a predictable sequence of calm, enjoyable activities at bedtime. The infant's bedtime is delayed to encourage rapid sleep onset, and appropriate cues for sleep are paired with positive parent-child interactions. Once the infant's behavior is well established and he/she is falling asleep quickly, the bedtime is gradually advanced to the desired time.

Faded bedtime with response cost involves removing the infant from the crib for specified periods of time when sleep onset is delayed. This strategy is similar to positive bedtime routines. Both methods take advantage of the infant's decreased arousal at his/her natural sleep onset time to enforce appropriate bedtime behaviors, in contrast to extinction programs, which aim instead to decrease inappropriate bedtime behaviors (i.e. prolonged crying).

There is some evidence to suggest that positive bedtime routines and faded bedtime with response cost may be rapid and effective treatments for infant sleep problems.[12-15] Although these strategies have not been widely studied, they offer a promising alternative to families who are unable to tolerate any of the extinction methods of infant sleep training.

Infant Massage

The importance of parental consistency in the behavioral treatment of infant sleep problems has been discussed. However, many parents have difficulty adhering to these methods due to the perceived emotional and/or environmental consequences of letting their baby cry unattended. Even when successful, sleep training is work intensive for parents and health care providers alike. These difficulties have promoted an ongoing interest in alternative methods to treat infant sleep problems and improve parental adherence with behavioral treatments. Infant massage may be a safe, simple, and effective way to meet both of these goals.

Infant massage is commonly used in many areas of the world, especially Africa, India, and Asia. Its use has been steadily increasing in the West, and many hospitals now offer massage programs that apply specific techniques to infants and children. Research over the past 10-15 years has shown massage to be a beneficial adjunct to the medical treatment of many pediatric problems, including: prematurity, burns/trauma, mental health and behavioral issues, disordered and/or incompetent immune systems, respiratory illnesses, and chronic pain syndromes.[16-17] In infants, massage has been associated with improved alertness, temperament, consolability, and growth. Positive effects on learning, development, and sleep have also been reported.[17-18]

It has been postulated that the direct benefits of infant massage are due to a variety of behavioral and physiological factors. Physiologically, massage may decrease stress hormones such as cortisol, epinephrine, and norepinephrine, and increase relaxation hormones such as serotonin. Massage has been associated with increased vagal tone, which may increase alertness, improve growth, and promote a greater sense of well being.[17] Massage in adolescents and adults has also been associated with EEG findings that reflect a heightened sense of alertness, such as decreased alpha and beta wave amplitudes.[17, 19]

Infant massage may also benefit the person who gives the massage. Parents, other infant caregivers, and adult volunteers have all reported decreased anxiety and a heightened sense of well being after administering infant massage. In addition, previous research suggests that infant massage may significantly improve parent-child bonding and the quality of parent-child interactions.[17, 20]

Although the calming properties of massage are widely recognized, its effects on pediatric sleep have not been well studied. Existing research in this area is somewhat limited in scope and methodological design. However, recent studies have shown that massage in the newborn period may have a long-term effect on melatonin synthesis and the development of normal circadian rhythms.[21] Only a few studies have looked at massage as an intervention for pediatric sleep problems, all of which report shortened sleep onset latency, fewer nighttime awakenings, and improved daytime alertness/behavior following regular bedtime massage. Prior infant massage studies have typically measured infant sleep only by subjective measures, including parent report measures such as child behavior rating scales and sleep diaries.[21-23] Although some studies included brief periods of video monitoring to document sleep-wake patterns around the time of intervention, the effects of massage on infant sleep problems have yet to be measured with validated, objective measures of sleep (i.e. actigraphy, polysomnography).

Prevention and Parent Education

Research suggests that parent education and prevention are among the most cost-effective and efficient approaches to behavioral sleep problems in infancy.[12, 24-25] Parents who receive preventive education are able to support their infant's early sleep skills while avoiding the inadvertent reinforcement of negative night time behaviors. In addition, early education is an effective way to impact large populations of infants who may be at risk. The high prevalence and chronicity of infant sleep problems support the need for widespread, early preventive education in pediatric practice.

Practical Considerations for Clinical Practice

Most infants with sleep problems will respond to behavioral treatment. However, little research has been done to describe the efficacy of different sleep training methods relative to each other. Many of the existing studies involve at least two interventions, such as an extinction program paired with a consistent bedtime routine. It is therefore

impossible to choose a behavioral treatment for infant sleep problems based on empirical evidence alone. Instead, the choice of a behavioral program for infant sleep problems is based largely on the characteristics of each case.

In order for infant sleep training to be successful, the pediatric provider must consider the best way to deliver information and provide support to parents. As with choosing a treatment method, the means of information delivery and parental support can vary widely and should be tailored to the needs of each family. Infant sleep training may therefore require a certain level of commitment from the provider as well as the infant's parents. Again, early prevention may be more time and cost effective than the treatment of established sleep problems, and many pediatric organizations recommend a routine sleep assessment during every well child visit.

Conclusion

Infant sleep problems are common and can impair individual and family functioning. Evidence supports the efficacy of unmodified and graduated extinction programs in the treatment of infant sleep problems. Other behavioral treatments, such as positive bedtime routine and faded bedtime with response cost, are less studied but promising alternatives to standard extinction programs. Infant massage may also be a helpful adjunct in the treatment of infant sleep problems. However, as is true in many pediatric behavioral disorders, early education and prevention may be the most efficient approach to the treatment of infant sleep problems.

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Sleep in Medically Compromised Children

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This article reviews the literature on pediatric sleep with a focus on children with chronic medical conditions. Children and adolescents with chronic medical conditions can display abnormal patterns of sleep, including frequent arousals, increased wake time, and reduction of stage 4 sleep. Poor sleep quality can contribute to problems with school attendance and performance, ability to concentrate, and neurocognitive function.[1] Additionally, sleep disturbances can be associated with more depressive symptoms and reduced social and emotional functioning.[2]

Sleep can be disturbed in medically compromised children for a number of reasons. Pain, whether from injury, from a chronic condition, or from hospital care procedures, can disrupt sleep. For hospitalized patients, light levels and noise volumes can be very different from typical sleeping conditions.[3] Procedures, diagnostic testing, and monitoring activities also frequently occur during nocturnal hours. In addition, medications can change both the onset and the architecture of sleep. Medications are typically administered to hospitalized patients for sleep promotion, anesthesia for procedures, depression, seizure, and anxiety. Additionally, certain commonly prescribed pharmacologic agents for chronic conditions can further alter sleeping patterns. Considerations for specific conditions are described below.

Asthma

Although asthma-related sleep disturbances have been reported in approximately 80% of adult patients with asthma, pediatric studies have been more limited. However, research indicates that one third of asthmatic children report at least one awakening per night.[1]

A number of nocturnal physiological changes could contribute to the exacerbation of asthma during sleep; e.g., a decrease in lung volume, increase in intrapulmonary blood volume, reduced muco-ciliary clearance, and nocturnal **gastroesophageal reflux (GER).**[1] Questionnaire-based studies have shown that asthmatic children rate themselves as significantly more tired in the morning compared with normal controls.[4]

Some nocturnal symptoms can be prevented by using sustained release or long-acting medications. Reduction of allergens in the sleeping environment (e.g., , use of hypoallergenic bedding materials and mattress and pillow covers, elimination of dust-mite collectors such as rugs and stuffed toys, addition of air-filtration systems) may be particularly helpful in children with reactive airway disease related to environmental allergies.

Burn injuries

Over half of patients recovering from burn injuries report sleep disturbances.[5] Pediatric burn victims can experience nocturnal disturbances such as arousals with nightmares, bedwetting, sleep-walking, or daytime abnormalities such as age-inappropriate need for naps. Factors that can negatively impact sleep in burn patients include pain, anxiety, depression, pruritus, medications, treatment setting, and upper airway obstruction.

A questionnaire-based study by Boeve et al. on burn victims indicated that while quantity of sleep did not change after burn injury, sleep quality diminished dramatically.[6] Polysomnography studies on sleep architecture in burn patients indicate changes such as increased stage 1 and stage 2 sleep, increased arousals, and decreased REM sleep and sleep in stages 3 and 4, also referred to as slow-wave sleep. This is especially troubling in pediatric patients, because peak **growth hormone (GH)** secretion occurs during the first period of slow wave sleep. There is a positive correlation between the reduction of GH release and the reduction of slow-wave sleep. Diminished GH secretion can have negative effects on wound healing, appetite and weight gain.[5]

Commonly prescribed medications to treat sleep disorders in burn victims include anti-depressants, hormone replacement therapy, and hypnotics such as benzodiazepines, non-benzodiazepines, or benzodiazepine receptor agonists, as well as non-prescription medications such as melatonin.[5] However, there are no medications approved by the Food and Drug Administration for use in childhood insomnia. Balancing treatment of pain and pharmacologic effects on sleep can also be difficult for patients on certain medications. Increasing pain medication dosage can cause negative side effects such as daytime drowsiness, while other medications, such as opiod analgesics, can be disruptive to sleep.[6]

Juvenile Rheumatoid Arthritis (JRA)

JRA, a condition characterized by episodic exacerbations and remissions, affects approximately 300,000 children in the United States.[7] Studies on adult patients with RA have indicated that up to 60% suffer sleep disturbances as a result of arthritis pain.[8] In pediatric populations, research has suggested that pain is positively correlated with sleep disturbances, and that children with this condition report greater sleep anxiety and more awakenings per hour and daytime sleepiness than normal controls.[2] Similar to burn victims, the timing and levels of GH secretion are a areas of concern for JRA patients, because these children tend to spend less time in slow-wave sleep.[7]

Benzodiazepines and barbiturates are commonly prescribed to treat insomnia. However, research indicates that sedative-hypnotics increase stage 2 sleep, but decrease sleep stages 1, 3, 4 and REM sleep. Certain studies have shown that arthritic patients who were prescribed sedative-hypnotics reported increased pain levels and greater disability at night than patients who were not sedated.[8] However, research on adult populations has indicated that low-dose amitryptilline or triazolam can improve sleep quality and factors such as pain and morning stiffness.[9]

For pediatric patients, there are a number of treatment options depending on the severity of the condition. Although ibuprofen and other non-steroidal anti-inflammatory agents are used as first line of managing JRA, ibu-

profen is known to delay deeper stages of sleep. Certain disease modifying anti-rheumatic drugs such as methotrexate and sulfasalazine, can irritate the gastrointestinal system, which in turn can disrupt sleep.[7]

Chronic pain

Chronic pain can encompass a number of medical conditions. Comorbid primary sleep disorders such as sleep apnea, restless legs syndrome, and periodic limb movement have been reported in patients affected by chronic pain. Fibromyalgia, which is characterized by widespread musculoskeletal pain and other somatic complaints, is one example of a chronic pain condition. Not only can it interfere with a patient's ability to function, but the illness can have negative effects on nocturnal sleep patterns. The relationship between fibromyalgia and alterations in sleep architecture has been explored in a number of studies which have concluded that these patients frequently display a characteristic EEG pattern, alpha-delta sleep, which is hypothesized to represent an intrusion of wakefulness rhythms into slow wave sleep. Researchers have suggested this is a measure of sleep fragmentation and that the amount of alpha intrusion corresponds to amount of psychological distress and pain caused by the condition.[8] Limited studies have shown that medications such as zolpidem can be effective in reducing sleep onset latency and increasing total sleep time in fibromyalgia patients. While **serotonin selective reuptake inhibitors (SSRIs)** are commonly used to treat patients with chronic pain conditions, these medications have been reported to cause insomnia in certain individuals.[8]

While there is a need for more research on the relationships between sleep and chronic pain, especially within pediatric populations, logistical difficulties complicate objective research. One of the most difficult obstacles to overcome in chronic pain patient recruitment is that researchers generally require participants to avoid taking CNS-active medications for two weeks prior to a polysomnographic sleep study. This can be a severe limitation for individuals treated for chronic pain conditions.

Strategies for addressing sleep problems

Practitioner awareness of primary and secondary sleep disorders can facilitate early screening and prevent symptoms such as mood changes and daytime sleepiness from being attributed to a child's underlying chronic condition.[10] Pain management can be an effective alternative to medication for facilitating sleep in children with chronic medical conditions. Relaxation techniques, such as hypnosis and biofeedback, can be an effective pain management strategy. Practitioners can also encourage strategies such as cognitive behavior therapy, maintenance of a regular sleep schedule, and parent education.

Conclusion

Children spend at least a third of their time sleeping, so disruptions in sleep duration and architecture can impair functioning and behavior. [9] The expense of objective sleep methodologies such as overnight polysomnography, and the difficulty of recruiting adequate numbers of participants, have contributed to the prevalence of research studies supported only by parental-report or subjective data for topics relating to sleep in medically compromised children. The limited objective studies on chronic medical conditions and their relation to juvenile sleep points toward the need for more research on pediatric populations using newer methodologies such as actigraphy (a portable, wristwatch-like device that measures and stores body movement data over days to weeks that may be used to estimate sleep-wake patterns). In addition, larger sample sizes in previously conducted research would better allow physicians and scientists to interpret results and understand the complexities of chronic conditions. Finally, more extensive research is needed on alternatives to pharmacologic treatments to mitigate sleep disruption. Relaxation, cognitive-behavioral intervention, exercise, and phototherapy all have the potential to be effective treatments for certain juvenile patient populations. The institution of sleep hygiene principles (e,g., , regular sleep-wake pattern, bedtime routine, avoidance of stimulants such as caffeine), and behavior modification techniques, including well-established insomnia strategies such as stimulus control and sleep restriction, also has the potential to alleviate sleep symptoms associated with certain conditions.

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Obstructive Sleep Apnea Syndrome: Clinical Features in Children vs. Adults

Thun-How Ong, MD

Obstructive sleep apnea conceptually does not seem to be a disease one is likely to find in children. Mention obstructive sleep apnea, and the image that springs to mind is that of Joe, the fat boy in Charles Dickens' *Pickwick Papers*, who falls asleep at every opportunity. Indeed, in 1889 the *British Medical Journal* listed snoring and restlessness at night as a cause of "backwardness and stupidity in children" (journals since then have had to adapt more politically correct terminology!)[1]

But the profile of a child suffering from **obstructive sleep apnea syndrome (OSAS)** may be more like that of a delinquent child from "Super-nanny" – hyperactive and out of control. In children, OSAS has an estimated prevalence of 1-3%[2]. Its pathogenesis, clinical presentation and treatment differ from the well-described adult disease, and the diagnosis may be easily missed if the practitioner is not familiar with this disease entity. If unrecognized and untreated, the child with OSAS may suffer from neurological, growth and cardiovascular sequelae. This article reviews the clinical features of pediatric OSA, the differences with adult OSA, and the treatment algorithms for pediatric OSAS.

"The gold standard of diagnosis remains an in-lab, monitored full polysomnography."

Epidemiology

In contrast to adults, OSAS occurs equally among males and females in the pediatric population, with a peak incidence between 2 and 6 years old (preschool population). The prevalence may be higher among African American individuals than among white individuals, and may also be increased in Asian populations. Other known risk factors for pediatric OSAS are listed in Table 1.

Table 1 Risk Factors for Pediatric OSAS

Adenotonsillar hypertrophy
Craniofacial malformations
Neuromuscular disease and reduced upper airway tone
Obesity
Family history of OSA
Prematurity
Down's syndrome
Achondroplasia
Mucopolysaccharoidosis
Spina bifida

Consequences of OSAS in Children

As in adults, the basic pathophysiology of OSAS arises from intermittent collapse of the airway when the child is sleeping. There may be desaturations or periods of hypoventilation associated with the periods of airway obstruction, as well as **electroencephalographic (EEG)** evidence of sleep disruption (arousals). In adults, the neurocognitive and cardiovascular sequelae are well-described: excessive daytime sleepiness, impaired neuropsychological functioning, hypertension, and increased cardiovascular and cerebrovascular morbidity and mortality.[3] In children, the clinical consequences of OSAS are less well-understood and often more subtle. At one end of the spectrum, some children suffering from severe OSAS may present with corpulmonale, pulmonary hypertension, and right heart failure; however, this level of disease is rarely seen.[4] OSAS in children has also been linked to glucose intolerance,[5] left ventricular hypertrophy[6] and higher diastolic blood pressures,[7] although systemic hypertension is much less commonly described than in adults. OSAS has also been linked to secondary enuresis in children, with resolution of the secondary enuresis in as many as 66-100% of children six months after adenotonsillectomy.[8] Frank daytime sleepiness is relatively rare in children with OSAS; rather, it is likely to manifest as more subtle cognitive and behavioural problems, including attentional problems, deficits in memory and executive functions, hyperactivity, impulsivity, poor frustration tolerance, aggression, and oppositional behavior.[9]

Clinical Features of OSAS in Children

The most consistent feature identified in most series of children with OSA is snoring, which is nearly universal among children with OSA. However, habitual (nightly) snoring is present in 6-12% of all children;[2,10] therefore, clearly not all snoring children have OSAS. Other features which may raise suspicion for OSAS are daytime mouth breathing, a history from parents that the child is a restless sleeper or sweats excessively at night, or has been observed to have breathing pauses in his or her sleep; however, observed apneic pauses are much less common in children compared to adults. Waking up with a dry mouth and/or morning headaches are also suggestive of OSAS, which should be elicited from patients and their parents. Note should be taken of any behavioral problems or learning difficulties, such as a history of **Attention Deficit/Hyperactivity Disorder (ADHD)**; these have been repeatedly associated with OSAS. A history of neurobehavioral problems is important in determining who needs treatment. Identification of possible risk factors such as a family history of OSAS, adenotonsillar hypertrophy, gastroesophageal reflux, and asthma or allergies is important. A detailed history of the child's sleeping patterns (time to bed and time actually asleep, history of nighttime wakening, wake time/ difficulty waking, number and timing of naps) should be taken to identify the presence of other confounding sleep issues such as insufficient sleep syndrome, sleep onset association disorder, or limit setting disorder.[11]

Table 2 Clinical Features of OSAS in Children

ADHD and behavioural problems
Daytime sleepiness
Observed apneas
Sweating
Snoring
Daytime mouth breathing
Failure to thrive
Restless sleep
Adenotonsillar hypertrophy
Learning problems

Comparison of OSAS in Children and Adults

Table 3 shows some of the common features of OSAS in children, compared to adults with OSAS. Two differences deserve to be highlighted: first, as noted above, excessive daytime sleepiness, which is nearly universal in adults, is not a common finding in children with OSAS (only about 30%). Second, children far more commonly present with neurocognitive consequences and clinical features similar to ADHD.

Physical Findings

No specific constellation of clinical features or physical findings reliably distinguish OSAS from primary snoring (snoring without ventilatory abnormalities). A **body mass index (BMI)** greater than 25 (indicating that the child is overweight) may suggest that the child is more predisposed to developing OSAS, but does not necessarily indicate that the disorder is present. More importantly, if the child is diagnosed with OSAS, a high BMI will indicate that weight loss measures may need to be implemented for successful treatment of the OSAS. While overweight and obesity are becoming more commonly associated with pediatric OSAS, similar to what is seen in adults, young children with OSA may also present with growth problems and failure to thrive; in the earlier descriptions of children with OSAS, failure to thrive was described as one of the features suggestive of OSAS.[12] Several studies have also shown that many children will experience a growth spurt after adenotonsillectomy for OSAS.[13]

A detailed assessment of the upper airway anatomy is important. Evidence of a deviated septum or enlarged turbinates should be looked for and documented. Nasality of speech may be assessed by having the child repeat a consonant phrase such as "funny bunny" or "99" both with and without the nose occluded; no change in the tone of speech suggests preexisting hyponasality, which in turn suggests adenoidal hyperplasia. Adenotonsillar hypertrophy is another important physical finding which, if present, may indicate a higher propensity for OSAS; again, the size of the tonsils is not predictive of the degree of OSAS. Even children without overt, obvious adenotonsillar hypertrophy may experience improvement in symptoms of OSAS after adenotonsillectomy. The presence of any significant overbite (distance between upper and lower teeth on biting), retrognathia, or micrognathia or other facio/skeletal abnormalities may also increase the likelihood of OSAS.[14] Finally, a systemic examination should be made, looking especially for cardiovascular complications of severe OSAS (loud pulmonary component of second heart sound, polycythemia,) and for any evidence of neuromuscular weakness that may contribute to sleep—disordered breathing.

Diagnosis

Unfortunately no clinical model has accurately predicted the presence or absence of OSAS, either in adults or in children. The gold standard of diagnosis remains an in-lab, monitored full **polysomnography (PSG).** The PSG lab needs to be specially attuned to the needs of these young patients, for instance, having the parents stay over with the child is essential to the success of the study, and the technicians will also need to be specially trained (and patient!) to deal with an apprehensive or curious child. The PSG involves the simultaneous monitoring of sleep stages (via EEG, EMG and chin EMG), respiration (movements and airflow), EKG, anterior tibial monitoring (for periodic limb movements), gas exchange (end-tidal or transcutaneous PCO2), and snoring. The PCO2 monitoring is important in children in whom hypoventilation and hypopneas may be more subtle than in adults.

Normative values for PSG parameters in children and adolescents are still less clearly defined than in adults, and do show some important differences. In adults, for example, an apnea is defined by a cessation of airflow for 10 seconds or more; in children, an apnea or hypopnea is generally taken to be any breathing pause that is greater than 2 respiratory cycles. Obstructive hypopneas, which are the most common pattern of sleep-disordered breathing seen in children, are generally defined in adults as a decrease in airflow for at least 10 seconds associated with a 3-4% desaturation and/or an arousal (the definition of hypopnea is still not uniform, and specific criteria may vary according to the study or authority being quoted). In contrast to adults, however, obstructive events in children may be more subtle, are less likely to be accompanied by desaturations, and are less likely to have electroencephalographic evidence of arousals. Some children may not even manifest overt respiratory events, but will rather manifest upper airway resistance as escalating intrapleural pressures (detectable only via esophageal balloon manometry) accompanied by either desaturations or EEG arousals; this is known as upper airway resistance syndrome.[15] While the diagnosis of OSAS in adults generally requires an **apnea/hypopnea index (AHI)** greater than 5, most pediatric sleep specialists would consider an AHI of greater than 1 abnormal in children. However, this is a statistically derived value – the PSG determinants of morbidity or clinically significant cut-off points are still undefined, and the distinction between "child" and "adult" norms are blurred in adolescents with OSAS. In addition, there is mounting evidence that even "primary" snoring without PSG-identified ventilatory abnormalities may have significant morbidity in the pediatric population.

Treatment

The treatment of choice for pediatric OSAS in most cases is adenotonsillectomy; marked improvements in neurobehavioral functioning and quality of life[16] and nocturnal eneuresis[17] as well as improvements in AHI[18,19] have been documented. However, in many children, especially if they are obese, the AHI is likely to improve but not normalize completely. Hence, follow-up PSG is usually recommended at 6-8 weeks post adenotonsillectomy for children with sig-

nificant OSAS symptoms which do not resolve post-operatively, who have evidence of severe disease as manifested by significant sequelae (eg, failure to thrive, pulmonary hypertension), or who have additional risk factors (morbid obesity, Down syndrome). Children with severe OSAS and children younger than age 2 may be at higher risk for post-surgical complications, and should be monitored as in-patients with close pre-operative monitoring and post-operative evaluation; the risk of post-surgical complications (e.g., hemorrhage, pulmonary edema, marked desaturations or laryngospasm) in high-risk groups may be as high as 25%.[18]

For children who are not surgical candidates or for whom surgical intervention has been only partially successful, treatment with nasal **continuous positive airway pressure (CPAP)** should be considered. Although this treatment is far less commonly instituted in children compared to adults, even young children can be taught to use CPAP successfully. [20,21] As in adults, compliance is an issue and effective treatment will require the use of behavioral management strategies- a dedicated team effort will be needed to educate both parents and children. Children will need time and training to become accustomed to the mask even before titration can be carried out in the sleep laboratory; frequent evaluations are also needed to assess for changes in the required pressure &/or mask fit as the child grows. A child who requires CPAP treatment for OSAS is probably best assessed at a sleep center experienced in working with children.

Tracheostomy is another option, albeit one which is patently more invasive and generally reserved for very severe cases for which other treatment modalities have been unsuccessful; e.g., a child with cerebral palsy and severe OSAS secondary to neuromuscular problems or facial skeletal abnormalities, who is unable to use CPAP. Experience with other forms of treatment for OSAS is limited. Some centers have reported good success rates with oral appliances and with more complex surgeries such as rapid maxillary distraction or maxillomandibular advancement. Dental appliances have also been used in children; however, this requires rigorous monitoring and repeated adjustments in the device as the child grows.[22] Finally, adjuvant measures such as weight loss should be avidly encouraged in the overweight child, in whom obesity is likely to play a causative role in the OSAS. Referral to a nutritionist, and encouragement to pursue a more active lifestyle, should be encouraged.

The field of pediatric sleep medicine is evolving, leaving gaps in our understanding of the disease etiology and natural history of OSAS in children. Yet practitioners should be aware of this disease entity and screen for it; treatment of OSAS in children can prevent the development of devastating cardiopulmonary consequences and result in remarkable resolution of its neurocognitive and neurobehavioral sequelae.

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Table 3

Features of OSAS	Adult	Children
Age at presentation	Middle age, incidence increases with age	2-8 years
Sex	Male : female 2:1	Equal prevalence
Clinical features:	Snoring, observed apneas, daytime sleepiness	Behavior problems, neurocognitive deficits
Treatment	CPAP, oral appliances, surgery	Adenotonsillectomy, oral appliances, surgery, CPAP

CME Background Information

This CME activity is sponsored by Brown Medical School.

Target Audience: This enduring material is designed for physicians licensed in Rhode Island.

CME Objectives: At the conclusion of this course, participants should be able to:

*evaluate a child with ADD for sleep disorders
*evaluate a child with developmental disabilities for sleep disorders
*know behavioral and massage techniques for infant sleep problems
*identify clinical characteristics of obstructive sleep apnea in children
*identify potential sleep problems in medically compromised children

Needs Assessment: Many children suffer from sleep disorders, causing anguish to parents; this issue is designed to help physicians identify and treat sleep disorder in patients who present with a variety of diagnoses.

Accreditation Statement: Brown Medical School is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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Grant/Research Support: Sepracor, Cephalon, Eli Lilly, Johnson & Johnson
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The following authors have disclosed they have no significant commercial relationships:
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Acknowledgement: The material contained in this issue is a result of the editorial work by Judith Owens, MD, MPH, guest editor. The opinions expressed herein are those of the authors and do not necessarily reflect the views of the sponsors, publisher or the planning committee.

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Keep a copy for your files. Compare them with the correct answers, which will be made available upon request, and receipt of submission requirements.

Evaluation

Please evaluation the effectiveness of the CME activity on a scale of 1 to 5 (1 being poor, 5 being excellent) by circling your choice.

1. Overall quality of this CME activity	1	2	3	4	5
2. Content	1	2	3	4	5
3. Format	1	2	3	4	5
4. Faculty	1	2	3	4	5
5. Achievement of educational objectives					
*evaluate a child with ADD for sleep disorders	1	2	3	4	5
*evaluate a child with developmental disabilities for sleep disorders	1	2	3	4	5
*know behavioral and massage techniques for infant sleep problems	1	2	3	4	5
*identify clinical characteristics of obstructive sleep apnea in children	1	2	3	4	5
*identify potential sleep problems in medically compromised children	1	2	3	4	5

Please comment on the impact that this CME activity may have on your practice of medicine.

Additional comments and/or suggested topics for future CME activities.

Pediatric Sleep Disorders: CME questions. Please circle the correct answer.

1. Sleep problems in children with ADHD may be due to which of the following:
   a. Stimulant medication
   b. Co-morbid depression or anxiety
   c. Obstructive sleep apnea
   d. All of the above

2. Which of the following statements regarding the relationship between obstructive sleep apnea and ADHD is *not* true:
   a. OSA may present with neurobehavioral deficits similar to ADHD
   b. Treatment of OSA results in improvement of neurobehavioral symptoms
   c. 60% of children with ADHD have OSA
   d. Executive functions are particularly affected by OSA

3. Which of the following is not an appropriate management strategy for children with ADHD and sleep problems:
   a. Increasing the dose of psychostimulant medication
   b. Providing positive reinforcement for appropriate bedtime behavior
   c. Maintaining a regular bedtime and waketime
   d. Switching to a non-stimulant ADHD medication

4. All of the following statements about sleep in children with developmental disabilities are true EXCEPT:
   a. The severity of sleep disturbance is often linked to the severity of the neurodevelopmental symptoms.
   b. Sleep disturbances are more likely to become chronic in this population.
   c. Behavioral strategies usually effective in normal children are not applicable to children with developmental delays.
   d. Compared with typically developing children, more parental intervention may be required to address sleep problems.

5. Which of the following sleep problems has been identified as the most prominent amongst children with autism?
   a. circadian rhythm disturbance
   b. anxiety-related sleep problems
   c. nightmares
   d. behavioral sleep disorders

6. Evidence has been found to support each of the following statements EXCEPT:
   a. Melatonin supplements can be effective in improving the sleep of children with developmental disabilities, whose natural production of melatonin may be reduced.
   b. Functional assessment of sleep problems in children with developmental disabilities has shown that parents' behaviors have little impact on their children's nighttime patterns.
   c. Impaired child communication skills may impede the efficacy of parent interventions with children who have difficulty settling at bedtime.
   d. In children with intellectual disabilities, the level of disability has not been strongly linked with frequency of sleep disturbance.

7. Which one of the following statements is true?
   a. By 3 months of age, 70% of infants will sleep from midnight to 5:00 am.
   b. According to the literature, unmodified extinction is clearly more effective than graduated extinction in treating bedtime problems and night wakings in infants.
   c. Infant massage is common throughout Africa, Asia, and India.
   d. The use of positive bedtime routines has not been shown to be an effective behavioral management strategy for bedtime problems in infants.
   e. Sleep disorders (waking in the night, crying at bedtime) have no negative impact on infants' health and behavior.

8. What strategy is most effective in preventing sleep disorders in infants?
   a. Parental education regarding sleep training [correct]
   b. Unmodified extinction procedures
   c. Rocking an infant to sleep
   d. An extra feeding before bedtime
   e. Soothing music in the bedroom

9. Which of the following is not a classic feature of childhood OSAS?
   a. Snoring
   b. Secondary enuresis
   c. Excessive daytime sleepiness
   d. Attention-deficit Hyperactivity Disorder (ADHD)
   e. Adenotonsillar hypertrophy

10. Which of the following is an indication for initiation of CPAP for treatment of OSAS in children:
    a. Nocturnal Enuresis
    b. Snoring
    c. Obesity
    d. Adenotonsillar hypertrophy
    e. Persistence of behavioural problems and elevated apnea-hypopnea index post-adenotonsillectomy

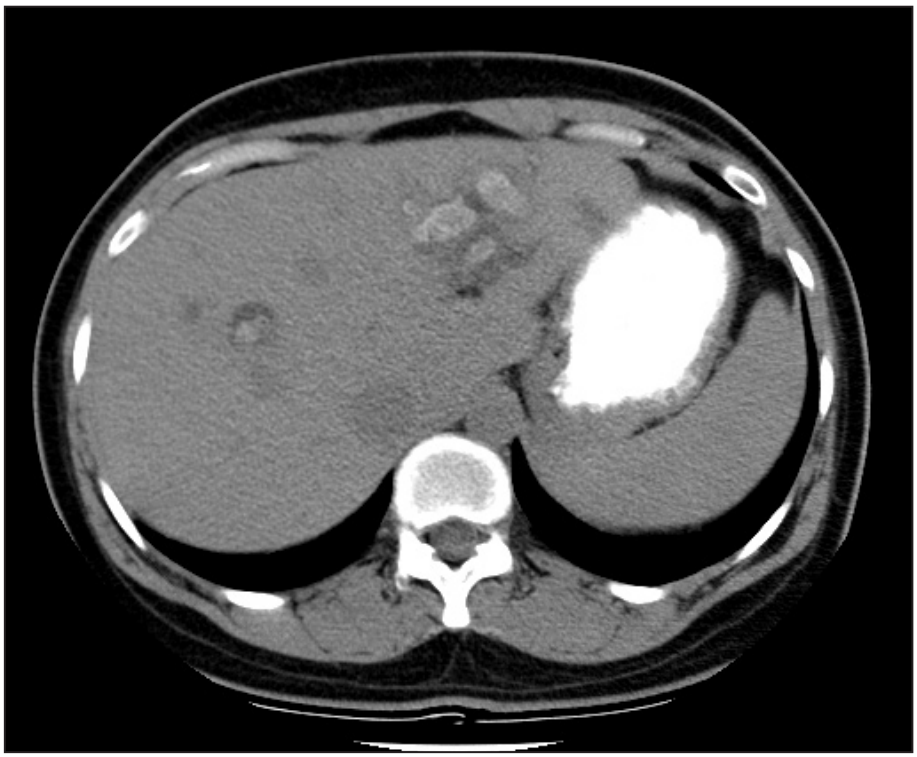
11. Sleep in children with chronic medical conditions may be disturbed for which of the following reasons
    a. Pain
    b. Medication effects
    c. Hospital environment
    d. Circadian-based alterations in disease state
    e. All of the above

12. Which of the following sleep alterations in pediatric burn patients does *not* negatively impact healing?
    a. Increased slow wave sleep
    b. Sleep disruption related to pain
    c. Sleep disruption related to pruritus
    d. Insomnia related to depression

Images in Medicine

Intrahepatic Calculi

Brian D. Midkiff, MD, MPH, Todd B. Baird, MD, and Brian L. Murphy, MD



This 29-year-old Caucasian woman presented with an acute episode of right upper quadrant pain and elevated liver function tests. A **computed tomography (CT)** examination of the abdomen demonstrated multiple calculi within irregularly dilated intrahepatic bile ducts. She was admitted for treatment with IV antibiotics and pain control.

Recurrent pyogenic cholangitis (RPC) typically presents with recurrent attacks of abdominal pain, fever, and jaundice. It is most prevalent in Southeast Asia, where it is the most common disease of the biliary tree requiring surgery, and was previously known as oriental cholangiohepatitis. However, it has been described with increasing frequency in the United States, particularly among Chinese immigrants, but also occasionally in the Caucasian population.

The exact cause of RPC remains unknown. *Escherichia coli* is the commonest infectious agent, but *Clonorchis sinensis* and *Ascaris Lumbricoides* may also be present. Histopathologic analysis of the liver reveals periductal abscesses, fibrosis of the ductal walls with focal areas of dilation and stenosis, and intraductal bile pigment calculi.

The natural course of the untreated disease is progressive destructive cholangiopathy with eventual liver failure. Treatment of acute exacerbations consists of antibiotics and pain control with surgery and interventional procedures reserved for selected cases in which local excision or drainage may be of benefit.

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UTILIZATION OF CONNECTICUT AND MASSACHUSETTS HOSPITALS BY RHODE ISLAND RESIDENTS, 1997 - 2003

KAREN A. WILLIAMS, MPH, AND JAY S. BUECHNER, PHD

Despite the generally easy access to inpatient care throughout the state, a proportion of Rhode Island residents receive inpatient care in hospitals in neighboring states, primarily Massachusetts and Connecticut. To obtain a complete picture of the health of Rhode Islanders, information on the health status of residents who are cared for out-of-state must be obtained and added to the information available from in-state health care providers. This is particularly important for inpatient discharges, since inpatients tend to be most severely impacted by illnesses and injuries.

A patient state-of-residence analysis conducted by the Healthcare Cost and Utilization Project indicates that discharges of Rhode Island residents from Rhode Island, Connecticut, and Massachusetts hospitals account for 99.5% of Rhode Islanders hospitalized in the 35 states included in the analysis in 2002.[1] Thus, data on residents hospitalized in Connecticut and Massachusetts hospitals, combined with data from Rhode Island hospitals, are sufficient to generate accurate estimates of population-based rates for monitoring disease and injury in the state's population. This report presents selected summary statistics on Rhode Island residents utilizing Connecticut and Massachusetts hospitals during the seven-year period 1997-2003, and examines the geographic patterns of Rhode Island residents seeking care out-of-state.

METHODS

Since October 1, 1989, acute-care hospitals in Rhode Island report to the Department of Health, Office of Health Statistics, a defined set of data items on each inpatient discharge, including information on patient demographics, clinical data, charges and expected pay source. Similarly, hospitals in Massachusetts and Connecticut report discharge data to the Division of Health Care Finance and Policy, Office of Health and Human Services and the Office of Health Care Access, respectively. The Connecticut Office of Health Care Access provided summary data on Rhode Island residents based on zip code of residence for discharges occurring 1997-2003. The Massachusetts Division of Health Care Finance and Policy provided patient-level data files for the same time period to the Rhode Island Department of Health, who extracted data on Rhode Island residents using zip code. For Massachusetts, the Rhode Island Department of Health was able to use Rhode Island patterns to estimate city/town of residence for discharges with zip codes that overlap town boundaries. Diagnoses and procedures are coded in the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), and were grouped as for published national data.[2] This analysis excludes discharges of newborn infants.

RESULTS

During 1997 – 2003, there were 4,207 and 38,724 non-newborn hospital discharges of Rhode Island residents from Connecticut and Massachusetts hospitals, respectively, an average of 601 discharges per year from Connecticut hospitals and 5,532 from Massachusetts hospitals. There were a total of 275 newborns discharged from Connecticut and 2,569 from Massachusetts. Annual utilization increased over the seven-year period from 536 to 632 discharges for Connecticut and 5,128 to 6,132 discharges for Massachusetts. Since the utilization of Rhode Island hospitals by Rhode Island residents also increased steadily over this time period, the annual percentage of discharges represented by Massachusetts and Connecticut hospitals remained almost constant, ranging from 4.6% to 5.0% for Massachusetts and remained constant at 0.5% for Connecticut.

During the most recent three-year period, 2001-2003, Rhode Island hospitals were net exporters of inpatient care to residents of both Massachusetts and Connecticut. There was an annual average of 6,864 discharges of Massachusetts residents from Rhode Island hospitals compared to an average of 5,897 discharges of Rhode Island residents from Massachusetts hospitals; these volumes translate into a net positive ratio of 1.17 patients coming from Massachusetts for each patient going there. Similarly, there was an annual average of 1,936 discharges of Connecticut residents from Rhode Island hospitals compared to an average of only 635 discharges of Rhode Island residents from Connecticut hospitals, for a net positive ratio of 3.05 during this three-year period.

Rhode Island residents age 45-64 years were the most likely to be treated out-of-state in both Massachusetts and Connecticut. (Figure 1) Those age 0-14 years were the least likely to seek care in Connecticut whereas those over 65 years were the least likely to seek care in Massachusetts.

The most common reasons for hospitalization differed slightly between Connecticut and Massachusetts hospitals. (Table 1) Heart disease was the most common reason for both, with 1,297 discharges of Rhode Island residents from Connecticut and 5,486 of discharges from Massachusetts. Deliveries (241 discharges), psychoses (177 discharges) and malignant neoplasms (168 discharges) were the next leading reasons for admission for Connecticut. Malignant neoplasms (3,494 discharges), deliveries (2,546 discharges) and pneumonia (1,092 discharges) ranked second, third, and fourth for Massachusetts.

Rhode Island towns bordering Connecticut and Massachusetts had the highest percent of residents seeking care out-of-state. (Figure 2) Almost three-fourths of hospitalizations of Tiverton and Little Compton residents occurred out-of-state, primar-

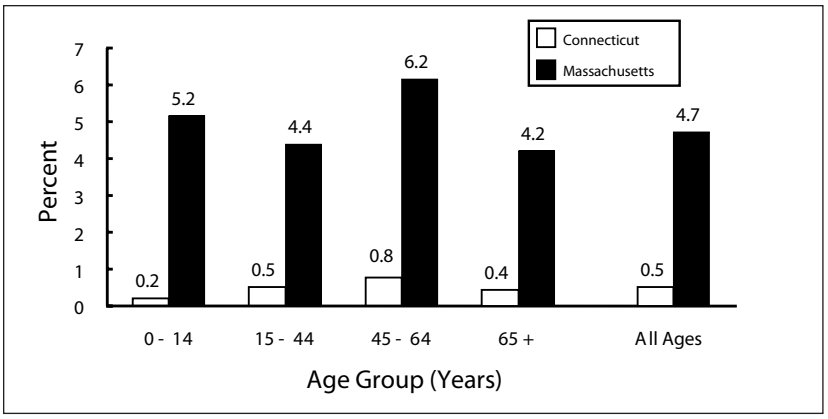

Figure 1. Inpatient Discharges of Rhode Island Residents From Connecticut and Massachusetts Hospitals, by Age Group and State of Hospitalization, 1997 – 2003

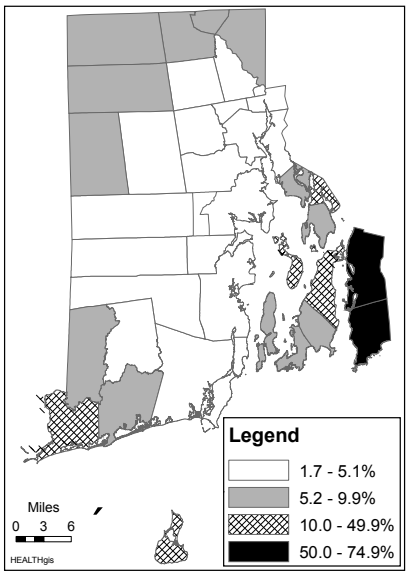

Figure 2. Inpatient Discharges of Rhode Island Residents From Connecticut and Massachusetts Hospitals, by Town of Residence, 1997 - 2003

Table 1.
Most Common Diagnosis (First-Listed), by State of Hospitalization, Rhode Island Residents, 1997 – 2003

Rank	Connecticut	Massachusetts	Total
1	Heart disease (1,297)	Heart disease (5,486)	Heart disease (6,783)
2	Deliveries (241)	Malignant neoplasms (3,494)	Malignant neoplasms (3,662)
3	Psychoses (177)	Deliveries (2,546)	Deliveries (2,787)
4	Malignant neoplasms (168)	Pneumonia (1,092)	Fractures, all sites (1,215)
5	Intervertebral disc disorders (164)	Fractures, all sites (1,065)	Pneumonia (1,140)
6	Fractures, all sites (150)	Osteoarthrosis and allied disorders (959)	Cerebrovascular disease (1,074)
7	Cerebrovascular disease (149)	Cerebrovascular disease (925)	Osteoarthrosis and allied disorders (1,024)
8	Osteoarthrosis and allied disorders (65)	Chronic bronchitis (678)	Psychoses (714)
9	Pneumonia (48)	Benign neoplasms (623)	Chronic bronchitis (705)
10	Benign neoplasms (48)	Psychoses (537)	Benign neoplasms (671)

ily to Massachusetts hospitals (74.9% and 69.5%, respectively). Portsmouth (25.4%) and Warren (10.7%) were the only other towns whose residents received at least 10% of their care in Massachusetts. Westerly (8.8%), New Shoreham (5.6%), Foster (4.4%), Charlestown (4.2%) and Hopkinton (3.9%) were the towns with the highest percent of residents seeking out-of-state inpatient care in Connecticut. The towns with the lowest proportion of residents seeking care out-of-state were West Warwick (1.7%), Providence (2.0%) and Johnston (2.0%).

The largest numbers of discharges of Rhode Island residents were from Massachusetts hospitals in Fall River and Boston. Southcoast Health System – Charlton and St. Anne's Hospital in Fall River had the highest numbers of discharges with 9,102 and 5,802, respectively. Brigham and Women's Hospital (3,731) and Massachusetts General Hospital (3,157), both in Boston, had the next largest numbers. These four hospitals comprise 56.2% of the discharges from Massachusetts hospitals. The top four Connecticut hospitals account for 80.6% of Rhode Island residents hospitalized in Connecticut. Yale-New Haven Hospital, located in New Haven, had 1,326 discharges, followed by Lawrence and Memorial Hospital in New London (997), William W. Backus Hospital in Norwich (680) and Day Kimball Hospital in Putnam (388).

Discussion

Because more than 5% of hospitalizations of Rhode Island residents occur out-of-state, it is important to include residents seeking care out-of-state when describing and monitoring the healthcare utilization and disease patterns of Rhode Islanders. The hospitals in Massachusetts and Connecticut with the greatest number of discharges of Rhode Island residents include a mix of hospitals that are located close to the Rhode Island border and hospitals located in more distant urban centers, such as Boston and New Haven. This geographic distribution suggests that the utilization is driven by a combination of geographic proximity and demand for specialty care. Further analysis examining the specific diagnoses and procedures of out-of-state discharges is needed to determine

whether the demand for specialty care results from a lack of particular types of specialty care in Rhode Island, from a perception of better care out-of-state, or from established referral practices.

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ERRATA

December 2005: "Preliminary Results from the Rhode Island Violent Death Reporting System" -- Table 1 on page 444 was printed without column headings. The complete table appears below.

Table 1.
Violent deaths per 100,000 population, by manner of death, race/ethnicity, and sex, Rhode Island (2004) and United States (2002)

Manner of Death	White		Black		Hispanic	
	Male	Female	Male	Female	Male	Female
	Rhode Island					
Homicide	2.9	0.7	11.5	3.8	19.8	1.8
Suicide	14.9	2.6	7.6	3.8	7.2	0
Undetermined intent	14.4	7.1	22.9	7.7	10.8	3.6
All violent deaths	**32.1**	**10.4**	**42.0**	**15.4**	**37.7**	**5.3**
	United States					
Homicide	3.9	1.9	40.1	7.2	13.6	2.7
Suicide	21.9	5.3	9.3	1.6	8.3	1.6
Undetermined intent	2.3	1.3	2.9	1.2	1.2	0.4
All violent deaths	**28.1**	**8.5**	**62.3**	**9.9**	**23.1**	**4.7**

January 2006: "Tertiary Cardiac Care Services in Rhode Island" – On page 41 the date when Landmark Medical Center was designated for coronary angioplasty and CABG programs was stated incorrectly. The correct date is March 2005.

PUBLIC HEALTH BRIEFING
RHODE ISLAND DEPARTMENT OF HEALTH
DAVID GIFFORD, MD, MPH, DIRECTOR OF HEALTH
EDITED BY JOHN P. FULTON

OLIVE OIL IN THE TREATMENT OF HYPERCHOLESTEROLEMIA

KATHLEEN CULLINEN, RD, PHD

Olive oil makes up 29% of the daily caloric intake of the Mediterranean diet That diet, associated with a low incidence of coronary heart disease and long life expectancy, is also characterized by a high to moderate consumption of fruit and vegetables, cereal products, fish and legumes, in combination with little meat and wine with meals.[1] A "functional food," olive oil is known for its high levels of monounsaturated fatty acids and is a good source of phytochemicals including polyphenolic compounds, squalene and alpha-tocopherol.[2] This paper will highlight the positive effects of olive oil on hypercholesterolemia, other risk factors for coronary heart disease, and other chronic diseases.

EFFECTS OF OLIVE OIL ON LIPIDS, LIPOPROTEINS AND LDL OXIDATION

Studies have indicated that the substitution of olive oil for saturated fat reduces plasma **low-density lipoprotein (LDL)** cholesterol without decreasing the concentration of **high-density lipoprotein (HDL)** cholesterol.[3] Olive oil contains oleate, the main monounsaturated fatty acid in plasma and tissues. Oleic acid directly interferes with the inflammatory response in early atherogenesis by inhibiting endothelial expression of adhesion molecules for circulating monocytes. A decreased expression of endothelial leukocyte adhesion molecules and other pro-inflammatory proteins accompanies incorporation of oleic acid into total cell lipids.[4] High in oleic acid and low in saturated and omega-6 fatty acids, olive oil does not compete with the incorporation of omega-3 fatty acids into the red cell membrane phospholipids, an additional benefit to the functions of omega-3 fatty acids.[5] When the goal is to reduce a patient's plasma LDL-cholesterol concentration, consumption of olive oil (i.e., oleate) is preferable to that of the plant oils that are rich in omega-6 fatty acids (e.g., corn, sunflower seed, and safflower oils) that contain large amounts of linoleate, because oleate will render circulating lipoproteins less sensitive to oxidation and inhibit the development of atherosclerosis.[6]

OLIVE OIL AND CELLULAR OXIDATIVE STRESS

Antioxidants in olive oil are able to scavenge free radicals and afford an adequate protection against cellular oxidation. The major phenolic compounds identified and quantified in olive oil belong to three different classes: simple phenols (hydroxytyrosol, tryrosol); secoiridoids (oleuropein, the aglycone of ligstroside, and their respective decarboxylated dialdehyde derivatives); and the lignans [(+)-1-acetoxypinoresinol and pinoresinol]. All three classes have potent antioxidant properties. High consumption of extra-virgin olive oils, which are rich in these phenolic antioxidants, protect against coronary heart disease, certain types of cancers and aging, by inhibiting oxidative stress.[7] Alpha-tocopherol significantly lowers plasma C-reactive protein, a risk factor for cardiovascular events, and minimizes other aspects of the acute phase response and inflammatory damage in atherosclerosis.[8]

OTHER HEALTH BENEFITS OF OLIVE OIL

Olive oil has been proven to contribute to improved control of hypertriglyceridemia accompanying diabetes. Olive oil can be beneficial in inflammatory and autoimmune diseases, such as rheumatoid arthritis, because it might modify inflammatory cytokine production. Olive oil enhances gallbladder emptying, reducing cholelithiasis risk, and decreases the pancreatic exocrine secretion and gastric secretory function in response to food intake. Finally, a diet rich in olive oil is associated with a high percentage of gastric ulcer healing and affords a higher resistance against non-steroidal anti-inflammatory drug-induced gastric ulcerogenesis.[9,10]

SUMMARY

Olive oil consumption increases HDL-cholesterol levels, while decreasing LDL-cholesterol levels, LDL susceptibility to oxidation and lipid peroxidation. The reduction of cellular oxidative stress, thrombogenicity and the formation of atheroma plaque can explain the preventive effects of olive oil on atherosclerosis development.[11] In addition to reducing risk factors for coronary heart disease, olive oil might also help prevent certain types of cancers, and beneficially modify immune and inflammatory responses.

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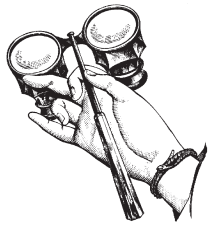


Letters To The Editor

To the editor:

I read with interest the article, "A Collaborative Management Model for Mental Health Care at the Rhode Island Free Clinic" (August 2005). The collaborative management model described is very similar to the one we have been using at Crossroads RI informally since 1995 and formally as part of a National Health Disparities Collaborative (http://www.healthdisparities.net/) since 2003.

Crossroads RI (formerly Travelers Aid, http://www.crossroadsri.org/) is one of two organizations in RI receiving federal aid to treat the homeless. Crossroads, however, is the only site dedicated exclusively to the needs of the homeless. Between our mobile medical van and our fixed downtown Providence site we see approximately 1350 patients per year for more than 6330 total patient visits.

Although our target population is different, our patients share many similarities with those of the Rhode Island Free Clinic: a high rate of uninsured, multiple barriers to obtaining adequate mental health care and high rates of mental health disorders. The key differences in our respective populations are homelessness (which brings a well-documented list of associated problems) and, notably, high rates of substance-use disorders. We found that in a survey of 52 consecutive homeless patients, 81% had a major mental illness and 69% had a substance-use disorder. Over 50% had co-occurring major mental illness and a substance-use disorder.

Since 1995, when our primary care clinic was established, I have worked side-by-side with volunteer psychiatrists. We share charts and keep a unified problem list. Because Crossroads is a social services agency, we collaborate with social service staff in our facility (logistical constraints kept us from sharing charts in the past). In early 2003 we instituted use of the PHQ-9 depression questionnaire at every patient visit. Building on this experience, we joined the National Health Disparities Collaborative in May of 2003. The Health Disparities Collaborative brings together the Bureau of Primary Health Care, The Institute for Healthcare Improvement and the National Association of Community Health Centers, Inc. and more than half a dozen other organizations which offer leadership and support. The Health Disparities Collaborative utilizes the Chronic Care Model (http://www.improvingchroniccare.org/change/model/components.html) and includes targeted outcome measures. By joining the Health Disparities Collaborative we formalized our collaborative effort and expanded our on-site mental health services. This multi-disciplinary approach includes a primary care physician and nurse practitioner, three volunteer psychiatrists, individual and group therapy sessions with social work therapists and mental health counselors specializing in co-occurring disorders, and complete chart sharing.

Crossroads has enjoyed a great deal of success in utilizing the Health Disparities Collaborative model. In the first year of the Collaborative, we outperformed our benchmarks in four of five goals set (the fifth goal, staying on medication for greater than six months, was difficult to achieve due to the transient nature of our population). As suggested in the Rhode Island Free Clinic article, our experience has also shown that success in treating uninsured, marginalized populations will improve utilizing a multi-disciplinary, collaborative management model to address mental health and substance use disorders, which, in addition, reduces traditional barriers to mental health care. We continue to believe that integrating mental and behavioral health into primary care and utilizing the Health Disparities Collaborative model allow us all to be most effective at caring for the homeless and excluded.

Ivan S. Wolfson, MD
Medical Director
Crossroads, RI
Clinical Assistant Professor of Family Medicine
Brown Medical School

A Physician's Lexicon

A Skeletal Etymology, Part I

Stanley M. Aronson, MD

Whoever uttered the phrase, "dry as bones," must surely have been a desperate first-year medical student burdened by the study of a Byzantine aspect of anatomy called osteology. For hundreds of years medical students worldwide have invested endless numbers of hours struggling to memorize the names of the many bones comprising the human skeleton, their ridges, bumps and depressions, and the origins and insertions of countless muscles, ligaments and tendons. And not a few of them wondered when, and whether, this mountain of dessicated information would ever be critical or even marginally useful in their daily practice of medicine. But nonetheless they learned these names for a variety of unreasonable reasons.

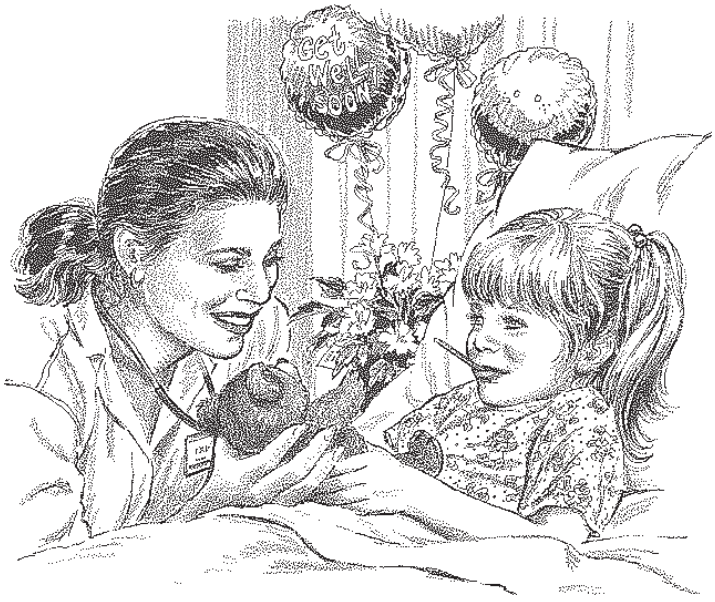
They remember many of the names that they had once committed to memory; but they are wondering when this information will prove to be useful. Most of the names, they surmised, were of Latin or Greek origin. For example, the human arm, they recall, is composed of three major bones, two others contributing to the structure of the shoulder, and then a pile of bones in the wrist and fingers.

The name, humerus, is derived from the Latin, *umerus* [the letter 'h' came later] which in turn was from the Greek, *omos*, meaning shoulder. The radius is from a Latin word meaning spoke of a wheel or pole or beam. And ulna is also derived from a Latin word meaning elbow. Derived from the same Latin root is the English word, ell, a primitive measure of length equaling about 45 inches.

The wrist [the carpus, from a Greek word meaning to rotate] consists of eight bones. More than one 16th Century anatomist wondered why these small bones required complex Greco-Roman names rather than simple numerals such as I to VIII. In any case, the carpal bones consist of the trapezium [from the Greek originally meaning a small table but later signifying any four-sized figure with non-parallel sides; the trapezoid, meaning much like a trapezium; the scaphoid, from the Greek meaning shaped like a ship, and hence cognate with words such as bathyscaphe and scaphocephalous [another name for this bone is the navicular, Latin for little ship; the lunate, from the Latin meaning crescent or moon shaped and hence such related words as lunar and lunacy; the hamate, from the Latin meaning a small hook; the capitate, from the Greek meaning rounded or head-shaped; the pisiform, from the Latin meaning pea-shaped; and finally, the triquetral, from the Greek meaning three-cornered; this little structure is also called the cuneiform bone, from the Latin meaning wedge-shaped. The word also defines the alphabetic writings of the Babylonians.

The phalanges are derived from the Latin word, *phalanx*, meaning infantry formation in close order and from an earlier Greek word meaning logs or battle arrays. Anatomists viewed the knuckles as resembling a close-order infantry squad and hence the choice of the word. The prefix, meta- , of the word metacarpal, is from the Greek meaning higher or altered.

The scapula, a component of the shoulder joint, stems from a Latin word which in turn is derived from an earlier Greek term meaning shovel. It is likely that early anatomists viewed the scapular flange as shovel-like. The clavicle is from the Latin, *clavicula*, meaning little key [and from the Latin, clavis]; cognate words include clavier, clavichord, autoclave, conclave and subclavian.



Information for Contributors,

Medicine & Health/Rhode Island

Medicine & Health/Rhode Island is a peer-reviewed publication, listed in the *Index Medicus*. We welcome submissions in the following categories.

Contributions
Contributions report on an issue of interest to clinicians in Rhode Island: new research, treatment options, collaborative interventions, review of controversies. Maximum length: 2500 words. Maximum number of references: 15. Tables, charts and figures should be camera-ready. Photographs should be black and white. Slides are not accepted.

Creative Clinician
Clinicians are invited to describe cases that defy textbook analysis. Maximum length: 1200 words. Maximum number of references: 6. Photographs, charts and figures may accompany the case.

Point of View
Readers share their perspective on any issue facing clinicians (e.g., ethics, health care policy, relationships with patients). Maximum length: 1200 words.

Advances in Pharmacology
Authors discuss new treatments. Maximum length: 1200 words.

Advances in Laboratory Medicine
Authors discuss a new laboratory technique. Maximum length: 1200 words.

Medical Myths
Authors present an iconoclastic, research-based analysis of long-held tenets. Maximum length: 1200 words.

For the above articles: Please submit 4 hard copies and an electronic version (Microsoft Word or Text) with the author's name, mailing address, phone, fax, e-mail address, and clinical and/or academic positions to the managing editor, Joan Retsinas, PhD, 344 Taber Avenue, Providence, RI 02906. phone: (401) 272-0422; fax: (401) 272-4946; e-mail: retsinas@verizon.net

Images in Medicine
We encourage submissions from all medical disciplines. Image(s) should capture the essence of how a diagnosis is established, and include a brief discussion of the disease process. Maximum length: 250 words. The submission should include one reference. Please submit the manuscript and one or two cropped black and white 5 by 7 inch prints with the author's name, degree, institution and e-mail address to: John Pezzullo, MD, Department of Radiology, Rhode Island Hospital, 593 Eddy St., Providence, RI 02903. Please send an electronic version of the text to: JPezzullo@lifespan.org.

THE RHODE ISLAND MEDICAL JOURNAL
The Official Organ of the Rhode Island Medical Society
Issued Monthly under the direction of the Publications Committee
VOLUME 1
NUMBER 1
PROVIDENCE, R.I., JANUARY, 1917
PER YEAR $2.00
SINGLE COPY, 25 CENTS

Ninety Years Ago, March 1916

One Editorial, "The Cause of Drug Addiction," criticized an article by McIves and Price (*JAMA* February 12, 1916). The duo analyzed 147 cases and drew "unwarranted conclusions." The majority of women in the *JAMA* study sample were prostitutes; and the men were thieves, crooks, "dwellers in, or frequenters of, the 'tenderloin.'" The authors blamed physicians for "professional medication," and suggested: "They are all notorious liars."

A second Editorial, "Aid for the District Nursing Association," supported the City of Providence in its quest for legislative authority to give money to the District Nursing Association.

A third Editorial, "Baby Week," suggested that Providence emulate Boston, with a campaign for "Plumper Prettier Providence Progeny," as a response to Boston's Child Welfare conference slogan: "Bigger, Better Boston Babies."

A fourth Editorial, "A Good Suggestion," supported the State Board of Pharmacy's recommendation for a law forbidding the manufacture and sale of patent medicines with opium.

Fifty Years Ago, March 1956

Charles C. Higgins, past president, American Urological Association, and head of the Department of Urology, Cleveland Institute, contributed "Undescended Testis," initially presented at the 144th annual meeting of the Rhode Island Medical Society.

Manuel M. Pearson, MD, Assistant Professor of Psychiatry, University of Pennsylvania School of Medicine, contributed "Miracle Drugs and Electroshock – What They Can and Cannot Do," initially presented at a meeting of the Rhode Island Society for Mental Hygiene.

John H. Garlock, Senior Surgeon, Mt Sinai, contributed "Surgical Treatment of Ulcerative Colitis," initially presented at the interim meeting of the Rhode Island Medical Society

An Editorial, "Why We Don't Like It," criticized 1) patent medicine's claims for medical endorsements, and 2) *US News and World Report's* poll of cardiologists on President Eisenhower's fitness for another term.

Twenty-Five Years Ago, March 1981

Gary Witman, MD, and Robert Davis, MD, in "A Lupus Erythematosus Syndrome Induced by Clonidine Hydrochloride," described this "rare complication" of clonidine therapy.

D.S.Liang, MD, and J. Ballou, RN, contributed "Long Term Catheter Care with Infected Urine." "Since type of management does not affect results," the authors recommended "closed system as simplest method."

Rhode Island Department of Health
David Gifford, MD, MPH,
Director of Health

Vital Statistics

Edited by Roberta A. Chevoya, State Registrar

Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data from the Division of Vital Records

Underlying Cause of Death	Reporting Period			
	March 2005	12 Months Ending with March 2005		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	257	3,018	282.1	4,625.5
Malignant Neoplasms	205	2,467	230.6	6,592.0
Cerebrovascular Diseases	48	497	46.5	840.0
Injuries (Accident/Suicide/Homicide)	29	413	38.6	6,480.5
COPD	65	514	48.0	592.5

Vital Events	Reporting Period		
	September 2005	12 Months Ending with September 2005	
	Number	Number	Rates
Live Births	1168	13,403	12.5*
Deaths	740	10,253	9.6*
Infant Deaths	(7)	(94)	7.0#
Neonatal deaths	(6)	(81)	6.0#
Marriages	973	7,644	7.1*
Divorces	266	3,265	3.1*
Induced Terminations	424	5,310	396.2#
Spontaneous Fetal Deaths	92	1,050	78.2#
Under 20 weeks gestation	(86)	(974)	72.7#
20+ weeks gestation	(6)	(76)	5.7#

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,069,725

(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population # Rates per 1,000 live births