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Sleep Disorders and Disordered Sleep

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Introduction

Observers who enjoy speculating about such statistics have offered various estimates as to how many times the stream of EEG paper generated in sleep research would reach around the world. The fact that a recording for a single night for one subject is often a quarter-mile in length stimulates a variety of metaphors to describe this almost endless flow made possible by the technological "breakthroughs" of the old dams which limited the size and scope of sleep studies. Hopefully, the thousands of miles of EEG wiggles and squiggles have produced information which can be useful to the clinician for the solution of problems he encounters in the everyday practice of medicine.

In this chapter, we will concentrate on the findings which are pertinent to sleep disorders. Under this category we will consider the so-called primary sleep disorders. These are conditions in which various abnormalities of sleep represent the cardinal and often only sign or symptom from which the patient suffers. We will discuss secondary sleep disorders in which chronic clinical problems are accompanied by specific or nonspecific sleep disturbances. Parasomnias, in which an activity normally associated with waking behavior appears during sleep, will be discussed. Sleep-modified disorders, in which the basic disorder worsens or occurs primarily in sleep, will be mentioned

briefly, and additional references will be suggested for the interested reader.

The clinical information and research data about sleep disorders and disordered sleep have been organized under the categories mentioned above for convenience. In most instances, the etiology and the pathophysiological mechanisms of these conditions are unknown or only suspected. This fact makes it impossible at this time to classify them by etiology or mechanisms as is typically done for diseases which are better understood. A group of investigators in the Association for the Psychophysiological Study of Sleep has been meeting periodically during the period of preparation of this chapter in an effort to develop a standardized classification of sleep disorders and disordered sleep which would provide a common point of reference for clinicians and researchers in the field. Hopefully, a standard will be developed with which the classification used in this chapter will be compatible.

The reader unfamiliar with the terminology employed by EEG sleep researchers should consult Chapter 8 in Volume 6 of this Handbook. Briefly, the classification of EEG sleep stages proposed by Dement and Kleitman, and used by most workers, consists of four sleep stages and the waking state: (1) wakefulness, or stage o, which is predominantly alpha activity; (2) stage 1, a mixed-voltage fast pattern without sleep spindles; (3) stage 2, K-complex or 12-16 cycles per second (cps) spindle activity against a low-voltage background; (4) stage 3, high-voltage, 1-2 cps activity (delta waves) during no

more than half of each scoring epoch; and (5) stage 4, delta activity during at least half of the scoring epoch. Conjugate, rapid eye movements (REMs), as monitored by the electrooculogram (EOG), and depressed electromyogram (EMG) activity, periodically accompany stage-1 sleep. This special form of stage-1 sleep is designated stage l-REM. Stage 1-REM, which has also been called paradoxical sleep, typically occurs four to six times per night in healthy adults, and subjects awakened from REM sleep usually report dreams much more frequently than when awakened from non-REM (NREM) sleep. Stages-3 and -4 sleep (slow-wave sleep) are commonly considered to be the deepest stages of sleep.

Primary Sleep Disorders

Under this category, as defined above, we have included insomnia, narcolepsy, chronic hypersomnia, the Kleine-Levin and Pickwickian syndromes, sleep paralysis, and frightening dreams.

Insomnia

This is probably one of the most common problems encountered by the physician in his day-to-day practice. Until recently, the term "insomnia" was often used loosely to describe any or all of the disorders discussed in this chapter. As research has progressed, it has become possible to distinguish a number of specific entities which were once lumped together under this general term. Many authors in the past have listed physical or organic factors as primary causes of some types of insomnia. We have been able to refine our classification so that many conditions can now be considered as sleep-modified disorders, or, as in the case of insomnia accompanying depression or schizophrenia, they can be listed as secondary sleep disturbances.

We view the disorders which we shall include under this heading as a very specific type of primary sleep disorder. Primary insomniacs suffer from a persistent inability to obtain adequate sleep but they exhibit no gross physical or psychological pathology. This restricted definition of insomnia is relatively new, and as a consequence there are limited data from polygraphic

studies of this condition where the more circumscribed definition has been utilized.

The incidence of insomnia has been assessed by both indirect and direct methods. There are many reports which provide indirect evidence about the prevalence of the disorder. The United States Department of Health, Education, and Welfare reported a 535 percent increase in retail sales of sedatives and tranquilizers between 1952 and 1963. In 1971, the consumer newsletter Moneysworth stated that $170 million is spent annually in the United States on sleeping pills.

More direct evidence is provided by Weiss et al., who obtained reports of sleep disturbances in 72 percent of 108 male veterans who were psychiatric outpatients, in 22 percent of 101 veterans being treated for medical complaints, and in 15 percent of 110 active Air Force personnel with no known medical or mental disturbance. They also found that sleep disturbances increased with increasing age. One should pay special attention to their finding of complaints in 15 percent of a supposedly healthy population.

In the past, the most commonly accepted etiology for most cases of insomnia was emotional disturbance. Such a conclusion was reached by a study of the case history and an examination of the psychodynamics. The

hypotheses developed by these approaches had implicated almost every type of psychopathological mechanism and led to a wide range of diagnostic formulations. Insomnia has been described as a habit and a psychoneurosis, a typical psychosomatic syndrome, or a type of reaction formation. Anxiety and fear, including fear of unconscious repressed desires, fear of homicidal or suicidal wishes, and fear of death, have all been implicated as primary causes.

Systematic studies of groups of insomniacs support the hypothesis that some are more disturbed psychologically than are noninsomniacs. Monroe examined the psychological, physiological, and sleep EEG characteristics of a number of poor and good sleepers. In a questionnaire, his subjects were asked about the length of time required to fall asleep, the number of nightly awakenings, and the degree of subjective difficulty in falling asleep. Although the poor sleepers self-categorized by the questionnaire were not suffering from severe sleep disturbances and did not consider themselves insomniacs, they were found to differ significantly from good sleepers because of greater pathology on nine of the thirteen clinical scales of the MMPI (Minnesota Multiphasic Personality Inventory). They also reported significantly more somatic and emotional symptoms on the Cornell Medical Index. In a similar study, Rechtschaffen was unable to detect any significant differences between good and poor sleepers on MMPI scores, although the poor sleepers had scores indicative of greater pathology on each of the scales. He suggested that a smaller sample size and smaller initial sleep differences between his good

and poor sleepers may have prevented the detection of statistically significant differences in the MMPI scores. Other workers have reported results similar to those of Monroe.

Monroe found that poor sleepers showed greater amounts of physiological activation than good sleepers. They exhibited greater numbers of body movements and peripheral vascular constrictions, and higher basal temperatures during sleep than the good sleepers. The poor sleepers also tended to have higher heart rates and pulse volumes. The poor sleepers appeared to be more activated—as reflected by levels of heart rate, peripheral vasoconstriction, and rectal temperature— than good sleepers, even before they retired. Rechtschaffen and Monroe concluded that the persistence of physiological activation during the sleep of poor sleepers may represent a failure of the rest-inducing mechanisms of sleep rather than a continuation of the presleep level.

Insomniacs have usually been classified according to the time during the sleep period when wakefulness is more troublesome. Some patients complain mainly of difficulty in falling asleep. Some complain of frequent and/or long awakenings after falling asleep. And others complain of early morning awakenings. Many clinicians are aware of patients who have of a combination of these complaints. However, if polygraphic data reported from the sleep EEG's of insomniacs can be considered more objective descriptors of the

qualitative and quantitative disturbances in the sleep of insomniacs, then it becomes clear that the classification mentioned above is too simplistic. Data from the limited number of polygraphic studies which have been performed indicate that there are many different types of insomnia and various combinations of disturbances. These studies have been reviewed elsewhere. As an example, we will briefly describe two studies performed in our laboratories. The first was a study of "hardcore" insomniacs. We found on the second and third laboratory recording nights that eight male and two female insomniacs between the ages of thirty and fifty-five exhibited significantly longer sleep latencies and longer latencies of arising (time from morning awakening to arising) than did the age- and sex-matched controls. Insomniacs also obtained less total sleep than controls, but the large variability in the insomniacs' total sleep times prevented this difference from attaining statistical significance. There was no difference between groups in the number of awakenings, primarily because some of the controls awoke quite frequently during the night. However, the ratio of total sleep time to time in bed, which summarized the relative sleep efficiency, was significantly smaller in the insomniacs. Many insomniacs and controls failed to obtain stage-4 sleep. Most of the subjects did obtain some stage 3, and the latency to the first appearance of this stage from sleep onset was significantly longer in the insomniacs. In the insomniacs, once stage l-REM sleep appeared it occurred at a faster pace than in the controls, with the average time between stage l-REM

intervals being consistently shorter. During the first four hours of sleep the cumulative minutes of stage l-REM was higher for the insomniacs. After the first four hours, however, the insomniacs began to wake up and no comparison was possible for the later hours of sleep. It is nevertheless clear that insomniacs establish and maintain a higher absolute amount of stage l-REM than controls as the night progresses.

In the second study, we examined the EEG sleep patterns of eleven male insomniacs, ages thirty-four to fifty-six, and their age- and sex-matched controls. Each subject's sleep was recorded for eight consecutive nights. We found that differences among subjects in the insomniac group were significantly greater than the differences among control subjects in the percentage of stage o and of stage 4. This suggested that our insomniac group may have contained several different subtypes of insomniacs. Furthermore, the insomniacs varied more from night-to-night than controls in total time in bed; total sleep time; ratio of total sleep time to time in bed; sleep latency; number of stage shifts; number of awakenings; percentages of stages l-REM, 2, and 4; latency to stage 4 from sleep onset; and the ratio of minutes of REM sleep to minutes of stage 4 sleep. These results led us to speculate that part of the insomniac's problem may be that he can never predict whether or not he will obtain a satisfactory night of sleep.

From our studies of insomniacs, we have noted several additional

factors which may contribute to the difficulties of adequately describing them. Some patients who complain of not sleeping at all have apparently normal sleep patterns in terms of the percentages of each sleep stage, but exhibit alpha activity superimposed on the delta waves. These patients are often quite resistant to pharmacological treatment. Other patients seem to exhibit greater amounts of theta and beta activity. Since these qualitative characteristics are not usually measured in the present sleep-stage scoring system they may have been overlooked in other studies.

In conclusion, insomnia has been redefined to refer to a persistent inability to obtain adequate sleep in individuals exhibiting no gross physical or psychological pathology. Judging from sales of hypnotic medications, insomnia is quite prevalent in the general population. Many early explanations of insomnia attributed it primarily to emotional disturbance, and more recent systematic studies support the conclusion that psychological factors may play a role. However, there is also evidence of a physiological basis for these patients' complaints. Their sleep is considerably disturbed, according to EEG criteria, both in terms of the kinds and amounts of sleep they obtain, the night-to-night variability of their sleep patterns, and the qualitative aspects of their EEG activity. From such studies it appears that there may be several subtypes of insomniacs. Although the study of insomnia, as we have defined it, has only just begun, it is obvious that these and future findings may have major implications for the identification of more rational

therapeutic procedures for this sleep disturbance.

Narcolepsy

Although the symptom complex had been described earlier, Gelineau was the originator of the term “narcolepsy” to refer to a condition consisting of recurring, uncontrollable episodes of brief sleep. This syndrome has been described with increasing refinement, and the criteria presented by Yoss and Daly form the basis for present diagnoses.

In narcolepsy the primary symptom of sleep attacks is often accompanied by one or more of three associated symptoms, i.e., cataplexy, sleep paralysis, and hypnogogic hallucinations. Yoss and Daly referred to this symptom complex as the “narcoleptic tetrad” and reported that 11 percent of approximately 300 narcoleptics examined at the Mayo Clinic presented the full set of symptoms.

Cataplexy, which occurred in 68 percent of Yoss and Daly’s patients, was first described by Loewenfeld in 1902.253 It is characterized by brief episodes of isolated or generalized muscular weakness, and the degree of disability may range from a subjective feeling of weakness, through loss of use of one or more extremities, to almost total paralysis. Emotion-provoking events and other strong stimulations are common precipitators of these attacks, and many patients develop peculiar stratagems for avoiding or

alleviating the effects of these situations.

Sleep paralysis is similar to cataplexy in that it involves loss of muscle tone. However, it is usually experienced as a full-blown paralysis of the entire body, and occurs solely during the transition between sleep and wakefulness, or vice versa. Yoss and Daly reported that 24 percent of their patients experienced this symptom. As will be discussed in a later section of this chapter, this symptom has been increasingly described as an isolated symptom in otherwise normal individuals. In either case, the individual usually remains quite conscious during the attack, which may last from several seconds to several minutes. A touch will usually terminate the attack, if it has not ended spontaneously.

Visual and auditory hypnogogic hallucinations often occur during sleep paralysis attacks in these patients. Yoss and Daly reported that 30 percent of the Mayo Clinic narcoleptics exhibited this symptom, while Roth and Bruhova observed an incidence of 19 percent in their sample of narcoleptics. The experience is often a frightening one, but many patients appear to be aware of the hallucinatory nature of it, which has prompted Roth and Bruhova to describe it as a pseudohallucination. In any case, these hallucinations are characteristically quite bizarre and kaleidoscopic in nature. Oswald has fully discussed the psychological and neurophysiological aspects of these events.

It has become common practice to differentiate between idiopathic narcolepsy and symptomatic narcolepsy. In the former the etiology of the disorder remains unknown, while in the latter there is a history of, or an association with, some organic disorder such as trauma, encephalitis, epilepsy, etc. As will be discussed below, data from polygraphic studies of narcoleptics suggest that there may be two forms of idiopathic narcolepsy-—independent narcolepsy, in which sleep attacks are the only symptom, and narcolepsy accompanied by one or more of the other symptoms in the narcoleptic tetrad.

Although no systematic studies have been made of the incidence of narcolepsy, Roth has estimated the incidence to be between 0.2 and 0.3 percent. At the Mayo Clinic, 241 cases were seen from 1950 through 1954, and in 1960 Yoss and Daly reported that approximately 100 new cases are seen there each year. The disorder appears to be equally distributed between the two sexes, and the typical age of onset is during the second or third decade. There is some evidence of a genetic basis for narcolepsy in the high incidence in certain families.

Diplopia is a common and early symptom of narcolepsy in many cases, and McCrary and Smith have described two narcoleptics with altered color vision. Gunne and Lidvall found narcoleptics to excrete greater amounts of noradrenaline in the urine than controls. These patients also exhibited

smaller daily fluctuations of noradrenaline levels. There were no abnormalities in urine levels of dopamine, adrenaline, or vanillyl-mandelic acid or in cerebrospinal fluid content of 5-hydroxyindolacetic acid. Administration of 100 mg. of L-dopa or 200 mg. of DL-dopa had no alerting effects on either patients or controls. These results should be somewhat cautiously interpreted, however, for the patients had been withdrawn from various medications, including amphetamine, just twenty-four hours prior to the beginning of the study. Sjaastad et al. reported increased estriol secretion in male narcoleptics, although some complicating factors did not allow them definitely to attribute this increase to the narcolepsy per se. And finally, Goodwin et al. have described a narcoleptic with an extremely high sensitivity to alcohol.

The nature of the narcoleptic's symptoms may often lead to the misdiagnoses of hypothyroidism, hypoglycemia, and epilepsy, and each of these disorders has at one time or another been assigned an etiological role in narcolepsy. However several lines of evidence suggest that these factors are not characteristic or critical in the etiology of the disorder. Yoss and Daly have commented that lower basal metabolism rates in these patients may seem to confirm the patient's complaint of being always tired. However, if care is taken to determine basal metabolism rates during times of relaxed alertness, normal values are usually obtained. Furthermore, administration of thyroid extract has not proved effective in increasing these patients'

alertness. Hypoglycemia may be diagnosed on the basis of the persistent drowsiness and periods of impaired consciousness. However, sleep attacks are often most common after meals, which would rule out hypoglycemia as a precipitator. Furthermore, some narcoleptics are actually hyperglycemic, while others exhibit no differences from controls in blood glucose values during various phases of nocturnal sleep.

The evidence concerning the relationship of narcolepsy to epilepsy is contradictory. Some investigators (see references 35, 72, 360, 395, and 414) have detected abnormal or epileptiform waveforms in the waking EEG's of narcoleptics. Others have found most patients to have essentially normal EEG's. In Dynes and Finley's study all but one of the seventeen patients with normal EEG's also suffered from cataplexy, while none of the five patients exhibiting EEG abnormalities suffered from this symptom. As a result, the authors proposed that patients with normal EEG's be considered idiopathic narcoleptics, and those showing EEG abnormalities as symptomatic. Daly and Yoss found only two grossly abnormal EEG's in a study of 100 patients during a true alert state. On the other hand, they noted that although true sleep was rare during the recordings, a majority of the patients exhibited patterns of drowsiness at some time during the recording, often from the very onset of the recording and for long periods. Daly and Yoss suggested that this persistent drowsiness may lead to the impression that the EEG shows generalized slowing. Furthermore, the EEG artifact produced by head

nodding during drowsiness may be misinterpreted as evidence of an akinetic seizure. Dement and Rechtschaffen and their associates have suggested that the periods of drowsiness (stage-i sleep) observed by Yoss and Daly may in fact have been REM sleep which was undetected because' eye movements were not monitored during the clinical EEG. However, Berti Ceroni et al. have confirmed that prolonged periods of stage-1 sleep without eye movements may characterize the daytime EEG's of these patients.

Psychological factors have quite naturally been assigned a role in the etiology of narcolepsy because of the apparent escapism involved in the symptoms and because of the apparent psychotic nature of the hypnogogic hallucinations. Sours has reviewed these propositions and particularly that concerning the relationship between narcolepsy and schizophrenia. More recently Mitchell et al. reported that all of twenty-two patients had undergone prolonged periods of sleep deprivation and disturbance, in association with major life transitions, prior to the recognition of their narcolepsy. Nevertheless, both Roth and Yoss and Daly, who have studied large numbers of these patients, have failed to detect any consistent evidence of psychopathology. As Yoss and Daly noted, the social and economic disruption in the narcoleptic's life due to his symptoms may well lead to emotional disturbance, but it remains to be shown that this disturbance is the basis of the disorder.

Although modern sleep-research techniques have been extensively applied to the study of narcolepsy since the early 1960s, their use has not yet supplied any clear-cut evidence concerning the etiology of this disorder. Use of them has, however, considerably refined the description of the various narcoleptic phenomena, and in this way will undoubtedly contribute to the ultimate explication of the etiology.

It is now rather commonly agreed that narcoleptics who experience sleep attacks and one or more of the auxiliary symptoms of the narcoleptic tetrad can be recognized on the basis of the sleep EEG. Whereas the normal individual, even when napping during the day, proceeds through various phases of NREM sleep before the first REM period occurs, narcoleptics with cataplexy and/or the other symptoms exhibit a very strong tendency to enter REM sleep directly from wakefulness during both daytime sleep attacks and nocturnal sleep (see references 30, 31, 89, 187, 312, 315-317, 355, 356, and 399). Although this sleep-onset REM period has not characterized every recording taken from every patient, it has occurred with sufficient frequency to suggest strongly that in this type of narcolepsy there is some neurophysiological or biochemical disturbance of the REM sleep system.

Furthermore, both direct and indirect evidence indicates that cataplexy, sleep paralysis, and hypnogogic hallucinations represent dissociated forms of REM sleep. It is well known that one of the unique and reliable characteristics

of normal REM sleep is the inhibition of muscle tone in some muscle groups, and of tibial nerve-calf muscle and tibial-plantar electrically induced reflexes. The relevance of this inhibition to cataplexy and sleep paralysis is obvious, as is the dreaming of REM sleep to hypnogogic hallucinations. In fact, it has been shown that, as in normal REM sleep, tonic EMG activity and H-reflexes are depressed during the narcoleptic's sleep-onset REM period, and that motor inhibition is more pronounced during the sleep-onset REM period than during these patients' later REM periods or during the REM sleep of normals. Polygraphic recordings (see references 31, 61, 88, 89, 184, 187, 189, 312, 313, 316, 317, 341, 355, 356, 399, and 402) during sleep-paralysis attacks and accompanying hypnogogic hallucinations have consistently revealed patterns of REM sleep. Although the early part of a cataplectic attack may be accompanied by waking EEG patterns, REM sleep may develop if the attack lasts long enough. Most patients who exhibit sleep attacks and other symptoms of the narcoleptic tetrad have nocturnal sleep which is characterized by numerous and long awakenings, decreased sleep time, and frequent body movements, and even though these patients typically exhibit sleep-onset REM periods, they obtain essentially normal amounts of REM sleep and normal numbers of REM periods. However, there have been occasional reports of increased REM time and numbers of REM periods. On the other hand, with only one exception, deep slow-wave sleep has been found to be rare or nonexistent in these patients.

Recordings of twenty-four-hour periods of patients with sleep attacks and auxiliary symptoms have revealed increased REM time, as compared to normals sleeping approximately eight hours, in many, but not all, patients. Passouant and his colleagues reported that the REM sleep attacks occur approximately every two hours during the day, suggesting a continuation during the daytime of the REM cycle of normal nocturnal sleep. These investigators also noted that the frequent daytime sleep attacks and interrupted night sleep of these patients produce a polyphasic twenty-four-hour sleep pattern, which contrasts with the monophasic pattern of normal adults but resembles the typical sleep pattern of infants.

In contrast to narcoleptics with auxiliary symptoms, narcoleptics who experience only sleep attacks very rarely exhibit sleep-onset REM periods (see references 30, 89, 187, 315, 316, 355, and 356). Instead, their attacks resemble normal NREM sleep periods. Furthermore, the nocturnal sleep of these patients appears to be essentially normal both quantitatively and qualitatively.

These observations originally suggested that only patients exhibiting auxiliary symptoms should be classified as narcoleptics, since the NREM sleep attacks of independent narcoleptics could not be distinguished from the NREM sleep periods of normals. However, it has been consistently observed that narcoleptics with auxiliary symptoms may at least occasionally exhibit

NREM sleep attacks and nocturnal sleep onset, that some of these patients never exhibit sleep-onset REM periods, and that NREM sleep frequently follows the sleep-onset REM period in an attack. Furthermore, imipramine, which is effective in alleviating the auxiliary symptoms of narcolepsy, but ineffective in relieving the sleep attacks, has been shown to suppress REM sleep in narcoleptics. On the other hand, amphetamine, phenmetrazine and methylphenidate, which are effective against sleep attacks but not against the auxiliary symptoms, have less drastic effects on REM sleep and also appear to decrease NREM sleep to a certain degree. These observations have led to more recent suggestions that there is a NREM sleep disturbance in many, if not all, narcoleptics, but that REM sleep disturbances are also important in narcoleptics with auxiliary symptoms.

Although the narcoleptic who exhibits sleep-onset REM periods displays an abnormal propensity to enter REM sleep, it has generally been argued that this does not reflect an excessive need to spend large amounts of time in REM sleep. This conclusion is based on observations that various degrees of REM-sleep deprivation in normal subjects, with the resulting, presumed build-up of a "need" for REM sleep, only rarely produce sleep-onset REM periods during the recovery period. Furthermore, the narcoleptic's typically normal amount of nocturnal REM sleep contrasts with the rebound of REM sleep during recovery from REM deprivation in normals.

As an alternative to this explanation, Rechtschaffen and Dement proposed that the REM disturbance reflects a failure of wakefulness and NREM sleep to inhibit the appearance of REM sleep. Passouant and his colleagues have made a similar suggestion. However, as Rechtschaffen and Dement have commented more recently, the admission of an important NREM-sleep disturbance would necessitate the postulation of a failure of wakefulness to inhibit NREM as well as REM sleep.

To summarize, narcolepsy and the narcoleptic tetrad of symptoms probably affect less than 1 percent of the population, but the bothersome and sometimes dangerous nature of the attacks makes them serious public-health problems. It is generally agreed that hypothyroidism, hypoglycemia, and epilepsy are not significant etiological factors. Although the narcoleptic may develop emotional disturbance as a result of the problems caused by the disorder, there is little empirical evidence that psychological factors play a major role in the etiology of this disorder. On the other hand, disturbances of both REM and NREM sleep would seem, in some as yet unknown fashion, to be basic to the disorder. There is substantial evidence suggesting that narcoleptics who experience only sleep attacks suffer primarily from a NREM sleep disturbance. In patients who also experience the other symptoms of the narcoleptic tetrad, both the REM and NREM systems appear to be disturbed, and cataplexy, sleep paralysis, and hypnogogic hallucinations probably represent dissociated forms of REM sleep. It has been suggested that the

narcoleptic's attacks reflect a failure of wakefulness to suppress REM and/or NREM sleep.

Chronic Hypersomnia

As its name implies, hypersomnia is characterized by excessive sleep. Although this disturbance may also characterize narcoleptics and patients suffering from the Pickwickian syndrome, and is a periodic manifestation in the Kleine-Levin syndrome, in chronic hypersomnia the excessive sleep is the primary chronic symptom. According to Roth there are two categories of chronic hypersomnia. In the first, there is good evidence that the excessive sleep or sleepiness is associated with or precipitated by some central-nervous-system (CNS) disorder such as skull trauma, brain tumor, encephalitis, or cerebrovascular accident, and for this reason Roth called it "symptomatic hypersomnia." Functional hypersomnia has no demonstrable organic basis. In patients with either disorder there is a notable increase in daily sleep time, and this increase may result from an excessively long nocturnal sleep period and/or frequent or long daytime sleep periods. Rechtshaffen and Roth noted that these patients rarely complain of disturbed nocturnal sleep, in contrast to narcoleptics. However, they often experience extreme difficulty in awakening and postdormital confusion, or "sleep drunkenness," once they do awaken. Daytime sleep attacks lack the compelling and irresistible nature of the narcoleptic's sleep attacks and may

last for several hours or days. In their latest report, Roth et al. concluded that there is a complete form of hypersomnia, consisting of postdormital confusion, very deep and prolonged sleep, diurnal hypersomnia, and rapid onset of nocturnal sleep. There is also an incomplete form, which consists only of postdormital confusion and deep and prolonged sleep.

Data on the incidence of this disorder are virtually nonexistent, both because of an as yet unclear distinction between *natural long sleepers* and hypersomniacs, and because of the relatively recent recognition of chronic hypersomnia as a distinct clinical entity. Roth et al. reported that 161 cases of hypersomnia, with and without sleep drunkenness, were seen in their clinic in Prague over the last twenty years, with 71 percent being classified as idiopathic cases. These investigators noted that incidence figures cannot be reliably based on numbers of self-selected clinic patients. They believe that many patients with hypersomnia do not seek medical help for their problem, and that the ratio of idiopathic to symptomatic cases may be higher in the general population since symptomatic cases are more likely to be seen in a clinic because of additional symptoms and more sudden changes in sleep patterns.

From the meager evidence concerning this disorder it appears that in idiopathic cases the age of onset may range from childhood through the third or fourth decade. In symptomatic cases, the age of onset would of course

depend on the age at which the CNS disorder occurred, but in one study of hypersomniacs with sleep drunkenness age of onset was generally later than in idiopathic cases. In both types the disorder usually continued throughout life, with only minor periodic increases or decreases in symptomatology. From the samples of patients studied there is a suggestion that hypersomnia occurs about equally in the two sexes. In idiopathic cases there is frequently a family history of the disorder.

In their study of these patients Rechtschaffen and Roth described the polygraphic nocturnal sleep patterns of a rather heterogeneous group of hypersomniacs. Ages ranged from twenty to fifty-three years, and some patients were essentially normal psychologically while others showed greater or lesser degrees of psychopathology; various constellations of the hypersomnia symptom complex were present. Although there was a relative decrease in symptoms during the laboratory sleep nights, Rechtschaffen and Roth felt confident in concluding that there were no deviations from normal patterning or percentages of sleep stages in these patients. None of the patients exhibited the sleep-onset REM periods characteristic of narcoleptics. Sleep averaged 8.8 hours in length, excluding one subject who typically slept over twenty hours in the laboratory. The sleep period beyond the normal seven or eight hours was a continuation of the typical alternation of sleep stages. Although the patients often complained of difficulty in awakening, there was no evidence of abnormal amounts of slow-wave sleep, in which

auditory awakening thresholds are elevated in normals. In two instances of postdormital confusion the EEG showed an alternation of wakefulness and stage-1 sleep.

In a second report Roth et al. described the daytime sleep patterns of hypersomniacs who experienced postdormital confusion and daytime hypersomnia. Sleep consisted primarily of alternations between stages-1 and -2 sleep, and was interrupted by frequent awakenings. Stages-3 and -4 sleep were rare, although this may have been due to the fact that most of the recordings were made in the early afternoon, when these stages are less prevalent in normals. REM sleep was also absent, but the authors noted that this may have resulted from the brevity of the recording period.

Among the most suggestive results in this series of studies was the fact that hypersomniacs exhibited faster heart and respiratory rates than “good sleepers,” “poor sleepers,” and “deep sleepers,” both before and during nocturnal sleep. There was some evidence that severity of hypersomnia might be related to the degree of elevation of these rates.

Although Rechtschaffen and Roth cautioned against speculating extensively on the basis of these findings until and unless they are replicated, these investigators have suggested that the heightened activation manifested by hypersomniacs may reflect activation of neural mechanisms controlling

heart and respiratory function as well as sleep, or release from centers which inhibit these functions. It may also be that the activation reflected by heart and respiratory rates produces an increased need for sleep in the hypersomniac. These are intriguing possibilities, but there remain many questions which must be answered before this disorder is fully understood. For example, Roth et al. have drawn attention to the fact that there seems to be more than a chance relationship between narcolepsy and the hypersomniac symptom of sleep drunkenness, even though hypersomnia and narcolepsy are typically clearly distinguishable from each other. On the other hand, the difference between the hypersomniac and the normal "long sleeper" described by Webb and Agnew is unclear, especially since postdormital confusion can occur in normals following excessive sleep.

Thus we have seen that there is a distinct clinical entity of chronic hypersomnia which may be symptomatic or functional. Rapid sleep onset, deep and prolonged nocturnal sleep, postdormital confusion, and diurnal hypersomnia characterize the complete form of this disorder, while deep and prolonged sleep and postdormital confusion characterize the incomplete form. The few studies exploring this disorder have failed to reveal any abnormalities in the sleep patterns of hypersomniacs, although these patients appear to exhibit higher heart and respiratory rates than normals and certain other types of individuals. Neither the mechanism of this disorder nor the manner in which hypersomniacs differ from natural long sleepers and other

patients who exhibit sleep attacks or excessive sleep has yet been elucidated.

The Kleine-Levin Syndrome

In 1942 Critchley and Hoffman called attention to the syndrome described by Kleine and Levin and characterized by periodic hypersomnia and morbid hunger. Critchley and Hoffman proposed that this syndrome be called the Kleine-Levin syndrome and described two additional cases. In 1962 Critchley reviewed the thirty-one cases reported up to that time, and emphasized several characteristics of the symptom picture. Among these were a preponderant or unique occurrence in males, a typical onset in adolescence, a spontaneous disappearance, compulsive eating rather than excessive appetite, and behavioral abnormalities. Critchley concluded that only twenty-six of the reported cases, including eleven described by him, could be considered genuine examples of this syndrome. Sours confirmed the rare incidence of the disorder. He reviewed the histories of 115 patients seen at Columbia Presbyterian Medical Center in New York for various complaints of excessive sleepiness from 1932 to 1961, and did not find a single case of Kleine-Levin syndrome. Since Critchley's review in 1962 a number of new cases have been described (see references 24, 29, 39, 98, 100, 105, 142, 150, 157, 190, 265, and 407), but in the process Critchley's original diagnostic criteria have been somewhat broadened and modified. For example, several female cases have been described. The case presented by Thacore et al. began

displaying symptoms at age eight and did not exhibit excessive eating, while Berti Ceroni's case evolved into narcolepsy. Such differences, as well as others to be discussed below, led Oswald and Thacore et al. to conclude that the existence of a distinct nosological entity characterized by periodic hypersomnia and excessive eating has yet to be proven, and that placement of a case in this category is largely a matter of preference. Pai had earlier concluded that the Kleine-Levin syndrome is not a definite clinical entity.

With this controversy in mind, we will nevertheless review some of the major findings from the reported cases. One of the two primary characteristics of Kleine-Levin patients is what has been termed periodic hypersomnolence. Oswald has noted, however, that it has yet to be established that these patients in fact sleep excessively. For this to be done would require systematic monitoring of various physiological parameters, including brain waves, during the periods of so-called sleep. Although numerous investigators have reported EEG findings, the lack of precise descriptions of the patient's status (during or between exacerbations, asleep or awake) or of the examination situation (patient sitting or lying down, day or night recording, length of recording) makes it very difficult to derive a clear picture of the EEG characteristics of these patients. Furthermore, even the results which are clearly interpretable are contradictory. For example, Rosenkotter and Wende reported that sleep EEG activity during sleep attacks corresponded to that of natural sleep. Barontini and Zappoli found afternoon

sleep during an attack to be light and unstable, but concluded that there was "no evidence of significant abnormality of the cortical biorhythms . . ." Barontini and Zappoli's patient was a twenty-nine-year-old male and the recorded sleep period lasted from 4:30 to 8:00 p.m. We have reported that normal males between the ages of twenty-one and twenty-eight obtained 14 percent stage-4 sleep and 19 percent REM sleep during naps between 4 and 6 p.m. Barontini and Zappoli's patient obtained no stage-4 or REM sleep and only moderate amounts of stage-3 sleep. Thus, there did appear to be a significant lightening of this patient's sleep pattern during this hypersomnolent episode. On the other hand, other investigators failed to detect any spindles during "sleep" attacks. Since the presence of spindles is a criterion for the existence of EEG sleep, these data indicate that true sleep may not appropriately characterize the daytime state of the Kleine-Levin patient. Garland et al. reached a similar conclusion when they described their patient as withdrawn rather than somnolent during the exacerbation.

One recording made of the night sleep of a Kleine-Levin patient revealed that sleep was generally light and unstable, although stage-3 sleep was moderately present. Stage-4 sleep occurred several times but never for long intervals. Only two very short REM periods occurred during the seven-hour recording period. A similar recording made following the exacerbation revealed more normal amounts of deep sleep, but REM periods were still quite short. Markman confirmed this last result.

If these sleep-EEG data prove to be accurate when more subjects have been studied, it may well be argued that both the night and daytime sleep of Kleine-Levin patients is disturbed, especially in comparison to age-matched normals. From the sparse data available it would appear that these patients obtain significantly less REM and deep-stage-4 sleep at night. Their daytime sleep is either unusually light or not really sleep at all. Furthermore, even between attacks these patients seem to obtain abnormally low amounts of REM sleep at night. This last fact might indicate that this disorder is not truly periodic, as has been claimed, but that these patients suffer from persistent sleep abnormalities which are periodically exaggerated.

The second primary characteristic of this disorder is excessive eating. Although Critchley considered it to be a necessary component of the clinical syndrome, subsequent cases have not always exhibited this behavior. Critchley suggested that this characteristic consisted of compulsive eating rather than bulimia, but Gilbert has contested this view. Garland et al. have criticized Critchley's use of various terms for overeating and Pai noted that often there have been no quantitative data to support reports of overeating.

Among the other characteristics reported more or less frequently during excerbations in Kleine-Levin patients are sexual excitement or disinhibition; particular preference for sweets; irritability, especially when aroused from sleep; full or partial amnesia either during or following the

attack; and depression and insomnia following the attack. Weight gains during the attacks and euphoria following them have also been reported for some patients. There have been no consistent abnormalities discovered by radiological or laboratory studies.

Critchley found a psychiatric explanation of this disorder to be unsatisfactory, particularly since most of his patients appeared to be normal before the onset of symptoms. However Oswald noted that many of Critchley's cases showed apparent schizophreniform abnormalities during attacks. Pai concluded that the hypersomnolence and excessive eating characteristic of this disorder occur together coincidentally, and that both are hysterical in nature.

Levin proposed the first organic theory of the etiology of the syndrome bearing his name. He suggested that the symptoms result from excessive inhibition or exhaustion of frontal-lobe centers controlling these behaviors. Gallinek subsequently suggested that the frontal lobes and/or the hypothalamus are implicated on the basis of studies of lesions or tumors in these areas. Most authors (see references 24, 74, 98, 105, 140, 142, 157, 190, 311, and 351) have agreed that dysfunction of hypothalamic or diencephalic areas is involved, in view of the disturbances in sleeping, alimentary, and sometimes sexual behavior. Several investigators have proposed that this disorder is related to narcolepsy or to convulsive disorders.

Interactions between psychological and organic factors have received attention from some investigators. Thus Gilbert proposed that psychodynamically the Kleine-Levin exacerbation might represent an escape from a threatening environment by an individual who can sense its demands but who is unable to cope with them. According to Gilbert these psychological factors would determine the temporal occurrence of the syndrome, but an underlying diencephlic dysfunction would determine the specific manifestations of the syndrome. Earle suggested that this condition is a psychosomatic disorder which emerges when individuals with psychopathology in the oral sphere also experience some pathology on the organic level, and possibly at the level of the hypothalamus. Bonkalo has also proposed an interactive interpretation of the etiology of the Kleine-Levin syndrome and of other hypersomnia syndromes.

As we have seen, there is considerable debate about the exact nature of the characteristics defining the Kleine-Levin syndrome. There is suggestive evidence that patients suffering from this disorder may not in fact be truly asleep during their periodic attacks of daytime hypersomnolence; their nocturnal sleep patterns are abnormally light. In addition, two patients have shown persistent REM-sleep abnormalities following clinical improvement. Excessive eating has not been an entirely consistent finding in these patients, and there have been few quantitative descriptions of this symptom. A variety of abnormal behaviors, including sexual disinhibition, irritability, and

depression, have been reported to occur during or following the attacks. Most authors agree that some dysfunction at the diencephalic or hypothalamic level is the basis for this syndrome, although several have proposed exclusively psychological or combined psychological and organic explanations. At this point, the paucity of data concerning this disorder allows only speculation as to the etiology or localization of the dysfunction. The debate about the reality of the Kleine-Levin syndrome as a distinct clinical entity may contribute to the difficulty in more fully illuminating this rather interesting set of symptoms.

The Pickwickian Syndrome

Readers of Charles Dickens's *The Posthumous Papers of the Pickwick Club* will remember the description of the rotund lad, Joe, who could not manage to stay awake. Recalling this description in 1956, Burwell and his associates *coined the apt term "Pickwickian syndrome" to refer to a condition characterized by marked obesity, somnolence, twitching, cyanosis, periodic respiration, secondary polycythemia, right ventricular failure, hypoxia, and hypercapnea. The syndrome had previously been described under less spectacular names. Subsequent study of this condition has often failed to reveal all of the symptoms listed by Burwell et al., and obesity, hypersomnia and periodic respiration are now considered to be primary diagnostic criteria. Escande et al. have proposed that there are two subcategories of this syndrome,*

a "Burwell type," which is the most advanced form and is characterized by obesity, hypersomnolence, and alveolar hypoventilation and its concomitants, and a "Joe type," which consists only of obesity and hypersomnia.

Polygraphic studies have begun to provide some interesting information on the relationships between two of the primary symptoms of this disorder, hypersomnolence and periodic respiration. Drachman and Gumnit were the first to describe the cyclical changes in EEG and respiration patterns during the sleep of these patients, and their observations have been confirmed and elaborated by others. Very shortly after the Pickwickian patient enters sleep, apneic intervals lasting from five to sixty seconds begin to appear. During the periods of apnea typical sleep patterns occur, and the length of these intervals depends on the depth of sleep during which they occur, with deeper stages being characterized by longer, and possibly less frequent, periods of apnea. Just prior to the return of respiration there is an EEG arousal response consisting of alpha activity or a K-complex. The EEG may not necessarily show waking patterns, but only lightening of sleep. Concurrently the patient takes several deep breaths, and then the whole cycle begins again. During successive cycles the sleep stage during the apneic periods may progressively deepen. At the end of several cycles, the arousal terminating the apnea may be particularly intense and accompanied by a body movement. Eventually one of these more intense arousals becomes a more complete awakening, after which begins a new series of deepening

sleep episodes terminated by arousal.

This pattern of EEG and respiratory changes has been observed during both diurnal and nocturnal sleep in Pickwickian patients. As a result, it is not surprising that a cardinal feature of their sleep, whatever the time of day, is its discontinuity. Although these patients have been reported to obtain over ten hours of sleep per twenty-four hours, this represents the sum of many short sleep periods rather than one extended sleep period. The discontinuity is accompanied by further sleep abnormalities. In many cases REM and deep slow-wave sleep are absent or rare (see references 69, 147, 185, 211, 330, and 406). In other patients, REM-sleep periods may still be present but are somewhat shorter than normal. Some investigators have reported a lessening of the apneic disturbances during REM sleep, while others have found the disturbance to persist and interact with the respiratory irregularities normally characteristic of REM sleep.

Since the systematic study of Pickwickian patients is relatively new, there are, understandably, insufficient data to allow full agreement on the mechanisms and etiology of this disorder. As Escande and his colleagues have suggested, the parallel but virtually independent work performed by internists and electroencephalographers has also contributed to some of the debates about these matters. One widely discussed topic is the pulmonary function status of Pickwickian patients. Some investigators believe that

chronic hypercapnea and hypoxia, secondary to chronic alveolar hypoventilation, characterize the Pickwickian, possibly as a result of the increased work required to breathe in the extremely obese. Others maintain that in the "pure" Pickwickian waking pulmonary function is normal enough to allow adequate blood-gas exchange to occur. As noted earlier, Escande et al. have proposed that there may be two forms of the Pickwickian syndrome, one characterized by primary alveolar hypoventilation and the other not.

A second area of controversy is the nature of the apneic mechanism in these patients. Gastaut et al. found that 80 percent of one patient's apneic episodes were peripheral or obstructive in nature, while 15 percent were of central origin and 5 percent were of mixed type. Coccagna et al. also observed both central and obstructive types of apnea, but concluded that central mechanisms control the apnea, with the obstructive phenomena sometimes occurring as a result of hypotonia and thus prolonging the existent central apnea. Hishikawa et al. found that apnea was obstructive in nature in their two patients, but suggested that centrally determined apnea may eventually appear as a result of the development of a permanent hyposensitivity of the respiratory centers to $C0_2$ retention. This would occur following the rather chronic nocturnal hypercapnea accompanying the initial obstructive apnea.

Several authors have stressed the fact that the periodic respiration of Pickwickian patients is an exaggeration of respiratory changes occurring

during normal sleep. In normal individuals, the onset of sleep is characterized by decreased ventilation, increased $C0_2$ tension, and decreased arterial oxygen saturation, and the conclusion has been that respiratory centers are less sensitive to $C0_2$ during sleep. Bülow has reported that $C0_2$ sensitivity is lower during the deeper stages of sleep than during the lighter stages. Furthermore, some normal individuals may exhibit short apneic episodes during sleep. These observations have led to the suggestion that the nocturnal respiratory disturbances of the Pickwickian are a function of a coordinated disturbance of respiratory rhythm and sleep-waking regulation in the brain stem. However, the fact that disturbed nocturnal respiration may persist even after improvement of other clinical symptoms (hypersomnolence, pulmonary ventilation) following loss of weight, suggests that these patients retain a tendency to $C0_2$ hyposensitivity.

The postulation of an intimate relationship between disturbances in respiration and sleep-waking mechanisms naturally introduces the question of the etiology of the hypersomnolence in these patients. Jung and Kuhlo, as well as others, have suggested that chronic $C0_2$ hyposensitivity, with the resulting hypoventilation and hypercapnea, disposes the Pickwickian to diurnal sleep attacks in the absence of arousing stimuli. Another view is that diurnal sleepiness and sleep are the result of poor and disturbed nocturnal sleep. Still another view is that a primary disturbance of the sleep-waking mechanism, analogous to that of narcoleptics, produces the daytime sleep

attacks. It should be noted, however, that most investigators have clearly distinguished Pickwickians from narcoleptics, primarily on the basis of the facts that Pickwickians do not exhibit cataplexy, sleep paralysis, hypnogogic hallucinations, or the sleep-onset REM periods characteristic of many narcoleptic sleep attacks, while narcoleptics do not exhibit marked periodic respiration during sleep.

From this discussion it is clear that the Pickwickian syndrome, although relatively rare, has engendered lively interest on the part of sleep researchers. It has been confirmed that Pickwickians suffer from distinct disturbances in the maintenance and quality of sleep. These disturbances appear to be intimately related to these patients' respiratory disturbances, but the exact nature of this relationship, as well as the relationship of the sleep and respiratory disturbances to other clinical symptoms such as obesity, has yet to be fully determined.

Sleep Paralysis

Sleep paralysis, as described in the recent literature, occurs during the transition between the waking and sleeping states. The individual is aware of his surroundings but is unable to move voluntarily. Respiration is not usually impaired to a significant degree. In most cases the sufferer is unable to talk, although he may manage to moan and thus attract the attention of others.

Anxiety and hypnogogic hallucinations are frequent concomitants of the paralysis. In some cases the anxiety subsides as the individual becomes accustomed to the benign nature of the attacks, but in others the attacks are always accompanied by anxiety. The individual experiencing hypnogogic hallucinations is generally aware of the unreal nature of his perceptions. Most sleep paralysis attacks last a maximum of several minutes, but often the time sense of the sufferer is quite distorted. The frequency of attacks is highly variable both between and within individuals. In most instances any external stimulus, and particularly a touch, will terminate the attack, although in some cases a stronger stimulus is required. If the attack is not terminated by external means, it eventually ends spontaneously. In some cases the individual must get up and move around in order to prevent a series of attacks.

This disturbance has been most frequently described as one of the constituents of the narcolepsy syndrome. Thus 34.4 percent and 28 percent of two samples of narcoleptic patients displayed this symptom. There are also occasional reports of sleep paralysis accompanying psychosis. However, sleep paralysis as an isolated symptom has been described more and more frequently (see references 40, 67, 154, 247, 250, 363, 369-373, and 412). Although Rushton and Schneck had expressed the belief that isolated sleep paralysis is much more common than case reports would indicate, it remained for Goode to support this belief with a systematic incidence study.

He found that fifteen of 231 medical students, none of fifty-three nursing students, and two of seventy-five hospital inpatients reported isolated sleep paralysis. Subsequently Everett reported that 15.4 percent of fifty-two medical students claimed to have experienced sleep-paralysis attacks and none had experienced either narcoleptic sleep attacks or cataplexy. In Goode's study the age of onset of sleep-paralysis attacks ranged from eight to fifty years, and among Everett's medical students the onset age ranged from childhood to the college years in those individuals who responded to this question. Of Goode's subjects, three experienced both pre- and postdormital attacks, two experienced predormital attacks only, and twelve experienced postdormital attacks only. Several of Everett's subjects reported a greater likelihood of having attacks during naps than at night. Histories of parasomnias, such as sleep hallucinations, sleepwalking and sleep talking, were also reported by some of Goode's subjects.

There are contradictory data on the sex distribution of sleep paralysis. Approximately 80 percent of Goode's subjects who reported sleep paralysis were males. However, in his survey sample over two-thirds of the respondents were males, and this may have contributed to the unequal sex distribution among the sleep-paralysis sufferers. In a study of two families with isolated sleep paralysis Roth et al. found a conspicuous predominance of women with the disturbance. This study indicated that sleep paralysis is a genetically determined disturbance which is invariably transmitted by the

mother. Roth et al. concluded that dominant heredity bound to the X-chromosome is the method of transmission. Other authors have described cases with family histories of sleep paralysis.

Sleep paralysis is particularly difficult to study, both because of its variable frequency of occurrence, and because the stimulation involved in examining the patient during an attack usually terminates the paralysis. In addition, aside from the reports that individuals suffering from isolated sleep-paralysis attacks exhibit essentially normal waking EEGs, there are no systematic descriptions of the clinical characteristics of these individuals.

As is the case with many of the sleep disorders, etiological theories of sleep paralysis tend to stress either psychological or organic factors. Langworthy and Betz offered a psychological interpretation in which sleep paralysis is viewed as a neurotic defense against primary anxieties associated with realistic adjustments in interpersonal relationships. Others have suggested that the disorder is related to a state of confusion as to emotion and intention, fear of destructive impulses, or anxiety reflecting the individual's own specific conflicts. Schneck, who has written extensively on the topic, has modified his earlier assertion that sleep paralysis is an expression of homosexual conflict, and suggested more recently that general conflicts between passive and aggressive personality trends are involved.

The notion of dissociation or asynchrony between various aspects of the sleep mechanism has been invoked by some as a more organic explanation of this disorder. Other authors have considered sleep paralysis to be a variant of cataplexy. However, Chodoff and Goode have enumerated several differences between these two phenomena, suggesting that they are not identical disorders. Still others have proposed that sleep paralysis is a form of epilepsy. As Goode notes, however, EEG recordings made during sleep-paralysis episodes offer little support for this hypothecs

In 1953 Aird et al. advanced the hypothesis that either blockage of the reticular facilitatory system and the resultant predominance of the reticular inhibitory system, or primary stimulation of the inhibitory system, may be sufficient to produce sleep paralysis. Although it has not yet been determined whether isolated sleep-paralysis attacks are identical to narcoleptic sleep-paralysis attacks, recent polygraphic studies of narcoleptics have led to a revival of the dissociation hypothesis, in a more specific form, as the explanation of narcolepsy and of its concomitant symptoms. It has been amply demonstrated (see references 89, 187, 188, 341, and 355) that narcoleptics who exhibit sleep attacks and one or more of the other narcolepsy symptoms frequently experience REM periods at or soon after sleep onset. This contrasts with the normal pattern, in which the first REM period typically occurs approximately ninety minutes after sleep onset. Although earlier descriptions of EEG activity during sleep-paralysis attacks in

narcoleptics mentioned only patterns of drowsiness during the episode, more recent studies in which eye movements were monitored have indicated that the attacks are accompanied by REM sleep. Moreover, there is a loss of spinal reflexes during REM sleep in both normal subjects and narcoleptics, and early parts of the narcoleptic's sleep-onset REM period seem to be composed of lighter sleep than either the drowsy state, the later part of the sleep-onset REM period, or later REM periods. These data suggest that the mechanism of sleep paralysis in narcoleptics involves a dissociation of REM sleep. This dissociation refers to the occurrence of certain REM phenomena, such as muscular inhibition and dreamlike state, against a background of relative awareness. Roth et al. believe that independent sleep paralysis is also due to such a disturbance in the REM system. Whether or not this is the case must be explored in future work, along with a determination of whether there is an analogous explanation for postdormital sleep-paralysis attacks.

Frightening Dreams

Polygraphic investigations have provided evidence that there are two types of unpleasant nocturnal "dream" attacks, i.e., night terrors and dream anxiety attacks. The former, also called "pavor noctumus" in children and "incubus attacks" in adults, are characterized by a sudden scream and arousal. Intense anxiety, hypermotility, increased heart and respiration rates, confusion, unresponsiveness, hallucinations, choking sensations, and feelings

of impending doom accompany the arousal. The sufferer is usually unable to remember the attack the next morning. The dream anxiety attack is generally less intense than, and lacks the quality of panic associated with the night terror. It may, however, precipitate an arousal, and dream reports are typically more complete than after arousal from night terrors. Although these two types of nightmares are usually easily differentiated on the basis of sleep EEG data, Mack has pointed out that this may not be the case when only clinical reports are available.

These sleep attacks have been described in people of all ages and cultures, and are not confined to the mentally ill. The incidence of night terrors appears to be much lower than that of dream anxiety attacks. Fisher et al. cite a report by Kurth et al. according to which night terrors were described by 2.9 percent of 991 children between the ages of one and fourteen years. Hersen studied 352 inpatients who were primarily diagnosed as having psychotic disorders and found that 32 percent reported having frightening dreams leading to awakening at least once a month. Among college undergraduates the analogous figure was 5 percent. Whether the respondents in these two studies were reporting night terrors or anxiety attacks, or both, is not clear. After reviewing the literature on the incidence of unpleasant dreams in children, Mack concluded that such dreams predominate in preschool children and that the incidence decreases after six years of age.

Sleep EEG studies of the two types of dreams have shown that the night terror is a NREM, slow-wave sleep phenomenon, while the anxiety dream occurs during REM sleep. Most NREM sleep dreams occur during the first half of the night. During the first or second NREM period a K-complex or a burst of delta waves presages the onset of the attack. Alpha activity and investigative eye movements quickly follow, and are accompanied by sharp increases in heart and respiration rates, and by body movement and muscle contractions. With the end of the attack all measures gradually return to normal. Although Broughton reported that relative tachycardia characterized the slow-wave sleep of night-terror sufferers, Fisher et al. found heart and respiration rates to be normal, or even reduced, in the interval prior to the abrupt onset of the attack. They also noted that the length of the stage-4 interval preceding the attack and the quantity of delta activity during the interval were positively related to the intensity of the attack. Gastaut and Broughton were able to elicit only minimal dream content from subjects following arousal from NREM attacks, but several of Fisher's subjects provided lengthy reports. The content was of two types. The first consisted of a single vivid scene which appeared to occur at the same time as or just before the arousal scream. The second type was more elaborate and seemed to be related to the autonomic activity following the scream.

Autonomic activation may or may not occur before and during the arousal terminating a REM-sleep dream-anxiety attack. Fisher et al. studied

twenty such attacks in eleven subjects. They found that in twelve attacks which were characterized as producing mild to marked anxiety, there was no change from control levels of heart and respiratory rates. In five other attacks, less than maximal degrees of activation were present, and in the remaining three there were clear-cut increases in the heart and respiratory rates. Content elicited after REM attacks is much more elaborate than that elicited after NREM attacks, and one individual appears not to suffer from both types of attacks.

There are, of course, numerous psychological interpretations of these sleep attacks, but there have been relatively few systematic studies of the variables involved. One exception is the series of studies carried out by Hersen. In the first there was a significant relationship between conscious concern with death and frequency of nightmares in a college-student sample. In the second study similar results were obtained with psychotic inpatients. In addition, the degree of manifest anxiety and the number of other sleep disturbances were positively related to frequency of bad dreams, while ego strength was negatively related.

Among sleep researchers there is agreement that these attacks are most probably psychological in origin. Broughton suggested that NREM night terrors are disorders of arousal, similar to enuresis and somnambulism, and that the sufferers are physiologically predisposed, possibly as exhibited by

their relative tachycardia during slow-wave sleep and their hyperactive heart rate during the arousal response, to experience night terrors during otherwise normal slow-wave sleep arousals. The exact precipitator of the attacks on any particular night may be the expression of repressed conflicts by mental activity released when protective barriers are lowered during the deepest stages of sleep. Or it may be that the attacks arise out of a "psychological void" and that the subjective experience of terror on arousal derives mainly from the perception of the accompanying physiological changes. In another formulation, Broughton elaborated on the first explanation and proposed that unresolved conflicts alter the arousal mechanism of the night-terror sufferer, producing a psychosomatic arousal disorder.

Fisher et al. believe that more immediate psychological factors precipitate both REM and NREM attacks. Specifically, increasing ego regression accompanying the progressive deepening of stage-4 sleep is suggested as the precipitator of NREM terrors, although the fact that attacks can be produced by sounding a buzzer during stage-4 deep suggests that external stimulation may also play a precipitating role. On the other hand, the REM dream is hypothesized to have a modulating influence on anxiety, and by reducing or eliminating the physiological concomitants of anxiety it serves to guard REM sleep. This would explain the desomatization of the anxiety accompanying a majority of the REM attacks these investigators have

described. When the desomatization mechanism breaks down, however, autonomic activation is seen to accompany the anxiety dream. It is the view of Fisher and his colleagues that the stage-4 nightmare represents a failure of the ego to control anxiety, and, rather than being a dream, it is a relatively rare pathological formation of NREM sleep. By contrast, the REM anxiety dream is a normal phenomenon throughout life and deals with controlled anxiety.

Secondary Sleep Disorders

Schizophrenia

Throughout the history of modern medicine, clinicians and researchers have been intrigued by the possibility of a relationship between sleep disturbances and psychopathology. The apparent similarity between dreams and hallucinations has led a number of authorities to speculate upon the etiological role of disturbances in the dreaming process in the development of schizophrenia.

The discovery of REM sleep and initial reports that REM deprivation in normal subjects resulted in various psychological disturbances seemed to provide tentative support for this speculation. Although later studies have raised questions about the consistency and severity of these psychological effects, the earlier studies and the theories accompanying them served as compelling stimuli for polygraphic examination of the sleep of schizophrenics.

One hypothesis which attracted investigators was that the hallucinations and delusions of the schizophrenic represent eruptions of REM "pressure" into the waking state. As Vogel discusses, this notion, which is essentially hydraulic in nature, implies that some condition such as chronic REM deprivation exists in schizophrenics prior to the psychotic episode. In addition Vogel and Traub pointed out that it has never been clear whether the

intrusion of REM sleep into wakefulness represents a continuation of the build-up of REM pressure or a discharge of that pressure, and thus predictions of how REM should behave during the course of the disease are often confusing and contradictory.

In any case, persistent efforts to find evidence of REM phenomena during wakefulness and of REM abnormalities during sleep in schizophrenics have produced far from conclusive results. In examining five actively ill patients, newly admitted to the hospital, Rechtschaffen et al. were unable to detect any consistent patterns of EEG, EOG, and EMG activity which indicated the presence of REM sleep during wakefulness. Chronic adult schizophrenics and children exhibiting schizophrenia or autism have shown no severe abnormalities of REM sleep, although adults at or near remission have been found to exhibit increased amounts of REM, decreased latencies to REM onset, and incomplete EMG suppression during REM sleep. “Actively ill” or acute patients have not shown significant changes in REM time, although changes in REM latencies have been observed in some. Feinberg et al. did observe lower REM times in short-term as compared to long-term patients. In addition, hallucinating patients have exhibited greater eye-movement densities than nonhallucinating patients. Feinberg and his colleagues have consistently failed to find any REM abnormalities in several remitted patients.

The general conclusion would seem to be that schizophrenics do not

exhibit striking changes in REM sleep or evidence of REM phenomena during wakefulness. The occasional changes observed, however, may to some extent reflect drug effects, for in these studies varying degrees of control have been exercised over the drug status or length of time since drug withdrawal. In addition, the exact type and point of evolution of the patient's disease may be a significant factor. For example, Struve and Becka found that "B-mitten" EEG discharges occur in a significantly greater proportion of reactive schizophrenics than process schizophrenics. Furthermore, Snyder and Kupfer et al. observed several patients longitudinally through the course of an acute psychotic episode and described distinct changes in various sleep parameters, including those of REM sleep, associated with both the waxing and waning phases of the episode.

Although the evidence of changes in the conventional measures of REM sleep of schizophrenics is at best inconclusive, there is suggestive evidence that the schizophrenic's response to experimental manipulation of REM sleep depends on the phase of the disease, and this may indicate that the underlying neurophysiological and biochemical mechanisms of the REM state operate differently in these patients. For example, actively ill patients exhibit little or no compensatory increase in REM sleep following several nights of REM deprivation, but remitted patients exhibit normal or even exaggerated REM rebounds following such procedures. Zarcone and Dement have updated the REM-intrusion hypothesis of schizophrenic symptoms by suggesting that

it is the behavior of pontine-geniculate-occipital (PGO) spikes which accounts for these differential effects of REM deprivation, and possibly for the psychotic symptoms. In animals, these PGO spikes are normally confined to REM-sleep periods, and it is suspected that deprivation and rebound of these spikes, rather than of other aspects of REM sleep, produce the REM rebounds following REM-sleep deprivation. When animals are administered p-chlorophenylalanine, an inhibitor of serotonin synthesis, the PGO spikes can be dissociated from REM sleep and may be discharged during the waking state. With this waking discharge of PGO spikes the animals may exhibit what appear to be hallucinations accompanying the PGO spike bursts, restlessness, insomnia, and decreases in REM time. Zarcone and Dement have noted that the last three symptoms are very similar to those described by Snyder and Kupfer et al. for patients at the onset of an acute psychotic episode. Furthermore, REM deprivation in animals exhibiting PGO spikes during the waking state does not result in a compensatory rebound of REM. Zarcone and Dement have speculated that REM deprivation is ineffective because the PGO spikes are no longer confined to the REM periods. Since extended REM deprivation is not sufficient to produce a dissociation of the PGO spikes and other REM phenomena, they suggested that some abnormality of the neurochemical regulators of PGO spikes, which appear to include serotonin, must account for this dissociation of PGO spikes. Zarcone and Dement believe that such an abnormality of PGO function could determine many of the

symptoms of the schizophrenic psychosis. It must be understood, however, that the existence of PGO spikes, or functionally equivalent events, in humans has yet to be demonstrated.

The early emphasis on the REM-sleep characteristics of schizophrenics resulted in a comparative neglect of the other aspects of EEG sleep. However, deficits in the stage-4 sleep of schizophrenics are well-documented, and appear to be much more prevalent than abnormalities of REM sleep. Although some authors have hesitated to attribute any specific importance to these deficits since similar types of disturbance are observed in various other disease or natural conditions, Feinberg noted that the same could be said of the sporadically observed REM-sleep abnormalities. Furthermore, since sleep deprivation is ineffective in producing increased levels of stage-4 sleep in schizophrenics, there is evidence equivalent to that for REM sleep that basic disturbances of the sleep mechanisms themselves are important characteristics of schizophrenia.

In conclusion, although sleep researchers have found a REM-intrusion hypothesis to be particularly attractive as an explanation of the schizophrenic's psychotic symptoms, there is little consistent evidence that the more traditional measures of REM sleep are significantly changed in many schizophrenics. However, more attention to the specific types of schizophrenics, to the changes occurring during the evolutionary course of

the disease, and to the phasic events of REM sleep, may reveal specific disturbances in the basic mechanism of REM sleep. This is particularly suggested by the failure of acute schizophrenics to exhibit a compensatory REM rebound following REM-sleep deprivation. On the other hand, schizophrenics also appear to suffer from important disturbances of slow-wave sleep. It seems certain that these sleep disturbances will be found to be intimately linked to biochemical abnormalities associated with schizophrenia.

Depression

Sleep disturbance is one of the more common and important features of the depressive illnesses, and it has long been thought that certain types of sleep disturbance discriminate reliably among the various subtypes of depression. Thus, delayed sleep onset has been thought to characterize reactive depression, while early awakening supposedly occurs more in endogenous depression.

The objective description of the polygraphic sleep patterns of depressed patients was initiated by Diaz-Guerrero et al. in 1946, before the discovery of REM sleep. These pioneers observed that in comparison to normals, manic-depressive patients in the depressive phase of their illness exhibited difficulty falling asleep, early and frequent awakenings, greater proportions of light sleep, and greater numbers of shifts from one sleep stage to another.

Since this early study, much information has accumulated on the EEG sleep patterns of depressed patients, and many more refined descriptions have appeared. Although certain characteristics of EEG sleep have been consistently noted in these studies, other characteristics are still disputed. It has generally been observed (see references 93, 158, 160, 179-181, 254, 272, 273, 308, 385, 386, and 446) that depressed patients take longer to fall asleep, obtain less sleep, awaken more often, and awaken earlier than normals. In a vast majority of cases slow-wave or stage-4 sleep is moderately to markedly suppressed. Increased frequencies of stage shifts have also been noted occasionally.

These consistent observations can be contrasted with the results pertaining to REM sleep (see references 158, 160, 174, 175, 177-181, 254, 272, 273, 308, and 385-387). Many investigators have reported decreases in REM-sleep time in depressed patients, but several have also commented upon the high variability among patients with respect to REM time. Others have described normal or elevated REM times. Latency to REM onset has generally been found to be shorter than average, and sleep-onset REM periods have been observed in some cases. Measures of the density of eye movements during REM, when made, have usually been high.

Clinical improvement, whether occurring spontaneously or with the aid of pharmacological or electroconvulsive therapy, is generally accompanied by

a normalization of the disturbed sleep parameters. However, slow-wave sleep may not return to normal levels even with clinical improvement (see references 158, 160, 180, 181, 272, and 274).

Vogel et al. found that experimental REM deprivation in these patients has varying effects. Some patients show evidence of REM "pressure" (decreased latency to REM onset, increased number of awakenings required to effect the deprivation) during deprivation and exhibit REM rebounds following the deprivation period. The REM sleep of others seems to be unaffected by the procedure. When deprivation is accompanied by the buildup of REM pressure there is a concomitant improvement in the clinical picture. A similar improvement accompanies the REM deprivation associated with administration of monoamine oxidase inhibitors.

One of the most striking characteristics of the patients in these studies, and probably one of the determinants of the inconsistent results with respect to REM sleep, is the high degree of variability among patients, even within the same study. Hawkins and Mendels have repeatedly emphasized this point, and have suggested that differences in severity of illness may determine much of this variability. Although these investigators were unable to detect any statistically significant differences between patients rated as severely depressed and those rated mildly to moderately depressed, there was a tendency for the severely depressed patients to exhibit greater sleep

disturbance. Furthermore, patients over fifty years of age tended to have more disturbed sleep than younger patients.

It appears that an even more important contributor to the variability in the EEG sleep patterns of depressed patients are differences in the diagnostic subtypes of the patients. Although there has been no consistent evidence that endogenous depressives are characterized by early awakening while reactive depressives have difficulty falling asleep, Mendels and Hawkins found that psychotic depressives show significantly greater sleep disturbance than neurotic depressives. In addition, Hartmann found that manic depressives exhibit sleep abnormalities somewhat different from those reported for groups of mixed psychotic depressives. He also observed that sleep disturbances during the depressed phase are different from those in the manic phase. However, Mendels and Hawkins have reported that the sleep patterns of one hypomanic patient were generally similar to those of patients with psychotic depressive illness. Finally, Detre et al. have recently described distinct differences in reported sleep patterns between bipolar and unipolar depressives, as well as evidence of hypersomnia in many patients, and particularly in bipolar depressives.

As with interpretations of the sleep disturbances characteristic of schizophrenia, some researchers have sought to relate the depressive's clinical symptoms to abnormalities in REM sleep. On the basis of his data

Snyder concluded that psychotic depression is accompanied and perhaps exacerbated, by the effects of REM deprivation (REM pressure). The fragmented and short sleep of these patients would gradually produce this deprivation, and therefore the degree of REM pressure should reflect the duration of earlier unrelieved sleep disturbance. Hartmann also believes that REM pressure is an important aspect of depression, but he suggests that it may be intrinsic to depression rather than the result of earlier deprivation. Furthermore, according to Hartmann this REM pressure is associated with low levels of available functional norepinephrine. On the other hand, in discussing their study of experimental REM deprivation in depressives Vogel et al. suggested that REM pressure produces an accumulation of catecholamines which alleviates depression.

Other researchers have taken a more global view of the depressive's sleep disturbances. Mendels and Hawkins have interpreted the short, light and fragmented sleep patterns and the reductions in REM and stage-4 sleep as indicating increased activity of CNS arousal mechanisms. Presumably the heightened arousal characteristic of depression would tend to prevent these two sleep stages from occurring. More recently Whybrow and Mendels reviewed neurophysiological, electromyographical, waking and sleep EEG, and chemotherapeutic evidence suggesting that in depression, and possibly mania, there is a state of CNS hyperexcitability.

Iskander and Kaelbling concluded that changes in delta or stage-4 sleep are probably of greater significance in the etiology of depression than changes in REM sleep. In their opinion, the deficits in REM sleep are secondary to the deficits in slow-wave sleep since REM sleep typically occurs only after a "primer" period of delta sleep. Therefore if slow-wave sleep failed to occur, or occurred only minimally, there would be less likelihood that REM sleep would occur. Iskander and Kaelbling also suggested that the residual disturbance of delta-sleep patterns exhibited by clinically improved depressives lends further support to their conclusion.

In summary, arousal disturbances of EEG sleep (short sleep time, long sleep latency, high number of awakenings, etc.) have consistently been found to characterize depressed patients. The reduction or absence of delta sleep is also a reliable characteristic. Many patients obtain less REM sleep, but this has been less consistently observed than the above disturbances. Depressed patients appear to be rather variable in their EEG sleep patterns. Differences in severity of illness, age, and diagnostic subtype may contribute to this variability. Attempts have been made to implicate both REM- and NREM-sleep disturbances in the etiology and maintenance of depression, but, as with many clinical disorders, there is as yet no completely satisfactory explanation of this relationship.

Alcohol and Chronic Alcoholism

The effect of alcohol on human sleep patterns has received attention from researchers for several reasons. First, alcohol, caffeine and nicotine are probably the most widely used drugs in the general population, and, for this reason, all are potential contaminators of polygraphic sleep studies. Second, it is suspected that alcohol may play some role in either the precipitation or the maintenance of some types of sleep disturbance. Finally, sleep disturbance has long been observed to be one of the symptoms of various phases of the chronic alcoholic's disease process.

Administration of one g./kg. of body weight of 95 percent ethonol to normal subjects on one night resulted in a significant decrease in REM sleep. Continued administration of identical amounts of alcohol either immediately before retiring, or four hours before retiring, for several consecutive nights, had a similar effect on REM sleep during the first one or two nights. However on subsequent nights of alcohol administration, REM returned to normal levels or above. On early recovery nights, REM remained at high levels or even increased more, but it returned to control levels by the third or fourth recovery night. When alcohol was given immediately before retiring stage-2 sleep varied inversely with REM sleep, while stages 3 and 4 tended to fluctuate around control levels. There were no consistent changes in the time awake, the number of stage shifts, body movements, or latency of the first REM period. When alcohol was consumed four hours before retiring the changes in REM and NREM sleep were less consistent. In a longterm study of

one normal subject drinking somewhat lower doses of alcohol, there was evidence of a dose-response effect in the suppression of REM, as well as an indication that increasing the dose during subsequent nights resulted in a continued suppression of REM below control levels.

From these studies of normal individuals it would appear that alcohol has an initial suppressing effect on REM sleep, that this effect decreases with continued constant doses of alcohol, that increasing doses of alcohol may sustain the effect, and that following several consecutive nightly doses of alcohol there may be a rebound of REM sleep on nonalcohol nights. Although the data are still meager, it appears that NREM sleep and certain variables reflecting wakefulness are unchanged by acute alcohol consumption.

There are no data specifically related to the use of alcohol by insomniacs. Nevertheless, it is well known by clinicians that some insomniacs use alcohol at bedtime as a hypnotic. The fact that alcohol has a stimulating effect at low doses, and must be taken in large amounts for depressant effects to appear undoubtedly results in the insomniac's having to ingest rather large quantities to obtain the desired effect. Moreover, the demonstrated sleep-disturbing effects of alcohol may well prompt the patient to discontinue his self-treatment. Withdrawal effects on sleep patterns may then lead him to resume his use of alcohol, or perhaps some other hypnotic. In this manner he may become trapped in a vicious circle of alcohol consumption and

withdrawal, both of which are accompanied by the sleep disturbance he is trying to prevent.

The nature of the sleep disturbances in the alcoholic psychoses is somewhat clearer. It appears that both delta sleep and REM sleep are disturbed throughout the various stages of this disorder. During inebriation in chronic alcoholics REM sleep is moderately to severely suppressed, at least initially. Continued suppression of REM may depend on increasing dosages of alcohol. However, there are nights on which "REM escape" or abnormally high amounts of REM may occur. There is some disagreement about the exact nature of the delta-sleep disturbance during this phase. In two patients undergoing chronic alcoholization, Gross and Goodenough observed an initial increase in delta sleep, followed by a decrease to normal or subnormal levels. On the other hand, Johnson et al. found thirteen of fourteen patients undergoing acute alcoholization to be completely without stage-4 sleep and eight were without stage-3 sleep. They also noted that, compared to withdrawal nights, there were a greater number of stage shifts and awakenings, greater amounts of wakefulness, and fewer K-complexes during this phase. Although Gross and Goodenough described disturbances in spindle activity during acute intoxication, Johnson et al. failed to find such changes in their patients. In a non-EEG study Mello and Mendelson observed that chronic inebriation resulted in an increased amount of daily sleep, although sleep became more fragmented.

During the chronic alcoholic's withdrawal from alcohol ingestion, there are consistent reports of increased REM sleep on initial recovery nights, with a gradual return to normal levels on later recovery nights. Johnson et al. have also described decreased REM-onset times and increased numbers of REM periods in these patients. They found that the increased REM time reflected shorter intervals between REM periods rather than longer REM periods. In addition, the patients appeared to have difficulty maintaining REM sleep, as evidenced by the noticeable fragmentation of this sleep stage. There appears to be a strong relationship between this increased REM sleep during alcohol withdrawal and both the delirium and the hallucinations which are frequent signs of withdrawal. Greenberg and Pearlman found that patients who exhibited delirium had more nights with increased REM sleep and showed greater increases in REM than patients who did not exhibit this symptom. Gross and Goodenough observed that one patient began experiencing hallucinations on the first day of withdrawal and following a night without REM or stage-4 sleep. Another withdrawing patient with 100 percent REM sleep also exhibited hallucinations, while a third with 44 percent REM sleep did not. These authors interpreted this as evidence that the rebound of REM above a certain threshold following alcohol-induced REM suppression is the basis for the hallucinations. Gross and Goodenough believe that REM rebound is also related to seizures during withdrawal.

It has also been reported that stage 4 is absent during the withdrawal

phase. Gross and Goodenough have suggested that the complaints of sleep disturbance in these patients are related to this decrease in stage 4, and that "sudden and massive" return of stage 4 is signaled by the terminal sleep often observed in the recovering patient. Rut Johnson et al. have suggested that lack of stage 4 is a characteristic of chronic alcoholics in general, and that the return of stage 4 is not a necessary condition for clinical improvement.

Insomnia is commonly accepted as one of the clinical symptoms of withdrawal. Many of the patients described by Gross and Goodenough were sleepless on some nights during recovery, and these authors suggested that complete insomnia is related to a more advanced state of withdrawal. Johnson et al. reported a significant improvement in various measures of restless and disturbed sleep during the withdrawal phase, as compared to the alcoholization period, but noted that their patients still appeared disturbed by normal standards. Mello and Mendelson found that fragmented sleep was a frequent, but not invariable, concomitant of withdrawal. In addition, abrupt withdrawal was not necessarily accompanied by insomnia.

In summary, alcoholization in chronic alcoholics is accompanied by significant changes in REM sleep and delta sleep, as well as by fragmented or disturbed sleep. Total sleep time per day may increase, however. During withdrawal there is a rebound of REM sleep, which may be related to the appearance of both hallucinations and seizures. Delta sleep remains

depressed in many cases, although a rebound of this type of sleep may accompany the terminal sleep observed in some patients. Insomnia or other complaints of sleep disturbance may occur, but they are not invariable symptoms of withdrawal. Although there is an improvement in the quality of sleep during withdrawal, these patients continue to exhibit noticeable sleep disturbances as compared to normals.

Chronic Renal Insufficiency, Hemodialysis, and Renal Transplantation

Clinical reports have indicated that the uremic syndrome, in addition to its characteristics of lethargy, depression, restlessness, and muscular twitching, is frequently characterized by a paradoxical state of daytime drowsiness and nighttime insomnia. This disturbance has been reported to persist when the patients are maintained on hemodialysis, although Shea et al. noted that the dialysis procedure may have some immediately beneficial effects on sleep. One report indicated that dialyzed patients suffer predominantly from difficulty in falling asleep, and several investigators found these patients to be particularly refractory to pharmacological treatment of the sleep disturbances.

Only two polygraphic studies of uremic patients have been reported. In 1970 Passouant et al. described the sleep patterns of eighteen patients, some of whom were undergoing regular dialysis and some of whom were treated

principally by dietary means. They studied five patients both before and after dialysis. Although this report is rather unclear as to the observations contributing to the data presented, the authors concluded that in the uremic syndrome sleep is characterized by decreased sleep time; increased awake time, primarily in the middle of the night; decreased slow-wave sleep; irregularity of sleep cycles; and frequent body movements. The sleep of patients regularly maintained on dialysis was not significantly disturbed, although there were some differences in sleep patterns before and after dialysis. Before dialysis, the alternations between NREM and REM were normal, but there were frequent awakenings and reductions in slow-wave and REM sleep. After dialysis, the number of awakenings decreased and slow-wave and REM sleep increased. In the patients who were dialyzed only when other means of management were temporarily ineffective, sleep problems were constant during periods of stabilization, i.e., there were frequent awakenings and decreases in slow-wave and REM sleep. The number of sleep cycles was normal and the lengths of the cycles were regular. During exacerbations the existing sleep problems were magnified, sleep cycling became very irregular, and the number of body movements increased. Dialyzing these patients, either peritoneally or by artificial kidney, resulted in increases in slow-wave and REM sleep and stabilization of REM sleep. The number of body movements remained high until several dialyses had been performed. In three patients who underwent peritoneal dialysis REM sleep

appeared within ten minutes after sleep onset. Correlations among sleep and other physiological variables indicated that an increase in blood urea nitrogen was significantly correlated with decreases in slow-wave and REM sleep and increases in the number of awakenings.

In a recent study, we have systematically examined the EEG sleep patterns of ten uremic patients on the night immediately preceding and the night following regular hemodialysis sessions, and have compared these patterns to those of age- and sex-matched healthy controls. In comparison to the controls, before dialysis the patients exhibited significantly shorter total sleep times, increased numbers and lengths of awakenings and percentages of awake time, decreased time from sleep onset to the first awakening, decreased ratios of total sleep time to time in bed (sleep efficiency), decreased percentages of REM and stage-2 sleep, and increased percentages of stage-3 sleep. In comparison to controls, patients after dialysis exhibited significantly lower sleep efficiency, greater percentages of awake time, longer awakenings, and lower percentages of stage-2 sleep. Direct comparisons of the patients before and after dialysis revealed no significant differences in the quantitative measures of sleep, although the fewer number of significant differences from control values in the patients after dialysis suggested that some improvement in sleep patterns had occurred as a result of the dialysis. This was further evidenced when we examined the sequence in which the various sleep stages first appeared during the first cycle. In the controls, this

sequence (stage 1, 2, 3, 4, REM, o) was identical to that usually observed in healthy subjects. Before dialysis, the sequence (1, 2, 3, 0, 4, REM) was interrupted by the early appearance of the first awakening. After dialysis, the sequence (1, 2, 4, 3, REM, o) approached that of the controls, indicating that dialysis resulted in a more normal sleep organization during the first sleep cycle.

In a second study we examined the sleep patterns of nine uremic patients who had received kidney transplants from three months to four years before the study. Compared to age- and sex-matched controls, these patients exhibited significantly greater percentages of awake time and lengths of awakenings, greater numbers of REM periods, shorter latencies to REM sleep, and lower percentages of stage-4 sleep. The sequence of stages during the first sleep cycle was perfectly normal.

In addition to these findings, we noted that both dialysis and transplant patients showed certain qualitative changes in their sleep EEGs. Some patients exhibited an intermingling of alpha activity with delta activity. Decreased numbers, durations, and quality of spindles were common. The K-complexes were poorly formed and had unusually low voltages. Some patients showed an increase in theta activity. Abnormally low-voltage delta activity was characteristic of many patients, both young and old. Dialysis and kidney transplantation appeared to have no significant effect on these EEG

changes.

Although both dialysis and renal transplantation appear to produce some improvement in uremic patients' sleep patterns, there is never a complete normalization of sleep following these procedures. This fact suggests that chronic renal insufficiency may produce irreversible, fundamental changes in the CNS. These changes are undeniably seen at the functional level, and may even exist at the cellular level.

Pregnancy and Postpartum Emotional Disturbance

Disturbances in the sleep system have long been considered important symptoms of postpartum emotional disturbances (see references 78, 137, 171, 201, 202, 206, 258, 367, and 432). Although there have been no systematic polygraphic studies of these concomitant sleep disturbances, indirect evidence from studies of other psychiatric disorders, such as depression and schizophrenia, and from studies of certain hormonal disorders would suggest that disturbed EEG sleep patterns might be an important concomitant of the postpartum emotional disturbances. More recent studies of sleep patterns during normal pregnancy and the postpartum period have provided further evidence of this. During the early stage of normal pregnancy there is a noticeable increase in time spent asleep. Sleep time normalizes during the second trimester, decreases to below normal

during the third, and remains low for some time following delivery. During the second trimester several additional changes begin to appear, i.e., awakenings become more frequent and the number of REM periods may temporarily increase. Of even greater significance, however, is the fact that stage-4 sleep begins to decline during this period. Although decreased levels of stage 4 are the most striking characteristic of groups of pregnant women in their last trimester of pregnancy, individual women may exhibit various degrees of variability in this pattern. In some women REM sleep may decline slightly during the second trimester, only to increase sharply during the third and begin to decrease as delivery approaches. In others, the decline in REM sleep may persist through the last trimester. During the last trimester there are also increased sleep latencies, increased amounts of awake time and numbers of awakenings, and increased percentages of stage-2 sleep.

Petre-Quadens et al. observed that sleep patterns during the two weeks following delivery were similar to those of late pregnancy in their subjects (high REM, decreased or absent stage 4), and that by the third postpartum week REM and stage-4 sleep had begun to move toward normal levels. In our studies we looked closely at the two or three nights immediately following delivery. On the first night there was a sharp increase in awake time and a sharp decrease in REM sleep. Stage-4 sleep was slightly increased above late prepartum levels. During the second and third postdelivery nights these parameters showed gradual movement toward normal levels. Nevertheless,

the immediate postpartum period as a whole was still significantly disturbed in several respects. Compared to nonpregnant control subjects the new mothers exhibited longer sleep latencies, greater amounts of awake time and numbers of awakenings, decreased REM time, and decreased stage-2 sleep. Even with the return of the menses, sleep patterns had still not completely normalized in the new mothers. Although sleep latency had become more normal, there were still significantly high amounts of wakefulness and numbers of awakenings. REM sleep had essentially reached normal levels, but stage-2 sleep was somewhat depressed. The amount of stage-4 sleep was often greater than in nonpregnant controls.

These data from normal women would seem to indicate that rather profound alterations in sleep patterns are natural concomitants of the pregnancy and postpartum periods. Although sleep patterns generally normalize during the first several postpartum weeks, at the onset of the first menses following delivery there is still sufficient disturbance to suggest that this event does not represent the full attainment of the prepregnant state. The striking changes in total sleep time, and particularly in stage-4 sleep, during late pregnancy seem to be especially important since significant decreases in stage-4 sleep are concomitants of various types of psychopathology (see references 62, 93, 160, 179, 386, and 446). We may speculate that a mother's failure to recover this type of sleep following delivery is a prodromal sign of, or perhaps even an etiological factor in, postpartum emotional disturbance.

This must remain a speculation, however, until more direct studies of postpartum emotional disturbances can be undertaken.

Perusal of any medical textbook and clinical experience will uncover numerous other conditions which produce or are accompanied by disordered sleep. Various CNS disorders, including infections and other toxic states, and certain nutritional and endocrine disorders, are known to be accompanied by changes in EEG sleep patterns. Many more remain to be examined by sleep researchers. From this review it should be clear that although the information produced by sleep research has raised more questions than it has answered, the sleep EEG provides a unique tool for the exploration of the neurophysiological bases of many medical and psychiatric conditions.

Parasomnias

Sleepwalking

In sleepwalking, the individual sits up in bed, arises, and begins to move around in an uncoordinated manner. His eyes are open but his appearance is rather blank and dazed. Most often his movements are stereotyped and purposeless, but occasionally more complex behaviors, such as dressing or going to the bathroom, may be exhibited. The sleepwalker may mumble or emit other sounds, but rarely does he converse if spoken to. Eventually he returns to bed or is easily led there. It is very difficult to awaken the sleepwalker during his wanderings, and if he is awakened he is quite confused and disoriented. He is usually amnesic for the episode when either awakened during it or questioned about it the next morning.

The reported incidence of sleepwalking varies with the age and clinical condition of the groups sampled, and with their past or current history. From 1-33 percent of various groups have reported current histories of sleepwalking (see references 11, 138, 309, 362, and 380), while from 3-34 percent of groups sampled have described a past history of this disturbance (see references 79, 138, 299, 319, and 404). It is commonly stated that sleepwalking occurs more often in males. However, several studies failed to reveal any significant male predominance, and one case was remarkable for the number of female relatives of the patient who were also sleepwalkers. As

with this patient, many sleepwalkers show a positive family history for the disturbance *(s*ee references 10, 21, 79, 219, 321, and 365).

Sleepwalking typically first appears in childhood or adolescence (see references 11, 138, 219, 325, and 391), and in many cases disappears by the third decade. However, if the disturbance persists into adulthood it often first appeared at puberty. Among the various concomitants of sleepwalking in many patients are EEG evidence of epilepsy and other EEG abnormalities, CNS infection or trauma, genitourinary complaints, and more or less severe forms of psychopathology (see references 5, 10, 11, 115, 192, 196, 198, 212, 219, 252, 299, 309, 319-321, 365, 391, 400, 405, and 421).

Several other types of sleep disturbance are frequently observed in sleepwalkers. Pierce and Lipcon found that three times as many enuretic naval recruits reported a past history of sleepwalking as did nonenuretic recruits. In a second study these authors found that 47 percent of sleepwalkers reported concurrent nocturnal enuresis, whereas controls did not. Others also noted the parallel occurrence of these two phenomena. Sleeptalking occurs in some sleepwalkers, as do nightmares and night terrors (see references 101, 198, 212, 217, 219, and 320).

Sleep-EEG studies of sleepwalking have revealed that the episodes occur during slow-wave sleep (see references 53, 144, 198, 200, 216, and

217), although Gastaut and Broughton have reported one episode which occurred during the transition from stage-2 to REM sleep.

Gastaut and Broughton described episodes whose onset consisted of intense awakening EEG reactions concomitant with or shortly preceding signs of movement. Flattening of the EEG records and then continuous ample nonreactive alpha activity followed, with the latter giving way to stage-2 or occasionally REM sleep at the end of the episode.

Jacobson et al. described the episode as starting with the sudden appearance of increased EMG discharge and 1-3 cps high-voltage EEG activity. After ten to thirty seconds of this EEG pattern, lower-amplitude delta waves appeared, producing a pattern resembling slow-wave sleep. If the incidents were brief (twenty to forty seconds) this EEG pattern characterized the entire incident. If the incidents were longer, theta, alpha, and beta frequencies against a low-voltage background were characteristic. Most incidents were followed by periods of mixed spindles and slow waves, but approximately one-fourth of the incidents were followed by waking EEG activity.

Visual investigation of the environment, stereotyped movements, nonreactivity, amnesia for the event, and lack of dream recall characterized the sleepwalkers in both studies. Further investigations showed that sleepwalkers up to sixteen years of age exhibited many more episodes of

sudden rhythmical bursts of high-voltage delta activity in slow-wave sleep than did normals. These events occurred both with sleepwalking incidents and at other times, principally with some body movement. Sleepwalking has been induced in sleepwalkers and sometimes in normals by standing the subject up during slow-wave sleep. Sleepwalkers may exhibit more complex gestural movements than normals during slow-wave sleep, and appear to be more confused following forced awakenings from slow-wave sleep.

The etiology postulated for sleepwalking has often depended upon the theoretical persuasion of the writer or on his particular research orientation. Thus the psychologically inclined (see references 5, 212, 252, 295, 299, 309, 320, 325, 365, 380, 391, and 405) have considered sleepwalking to be a neurotic symptom, an immature habit pattern, a form of personality dissociation, or the acting out of a dream. In one case, sleepwalking was a prelude to an acute schizophrenic episode.

On another level, several investigators (see references 10, 115, 192, 319, and 320) have suggested that sleepwalking is a manifestation of epilepsy. There is evidence of a genetic predisposition for the disturbance. Broughton suggested that sleepwalkers are physiologically predisposed to sleepwalk during slow-wave sleep arousals, whereas some other individuals are predisposed to exhibit nocturnal enuresis or night terrors. However, the nature of the specific precipitator of the sleepwalking episode remains

unclear. Jacobson and Kales suggested that both psychological and organic factors are involved in the disturbance. In their view the abnormal high-voltage delta-activity bursts observed in sleepwalking children may represent an organic immaturity factor, and psychological factors may be necessary to precipitate incidents in predisposed individuals.

Sleeptalking

Sleeptalking has long been of interest to physicians and laymen alike because of its supposed reflection of mental activity during sleep. The nocturnal utterances may be simple, mumbled monosyllables, or close approximations of waking, conversational speech, and there are many reports of sleep-talkers responding to a waking individual's questions, commands, or comments.

The incidence of sleep talking has been little studied. One difficulty in deriving realistic figures is that the sleep talker is frequently unaware of this nocturnal behavior. In an early study, Child found that 40 percent of a college sample between the ages of twenty and thirty years reported ever having talked in their sleep. In Gahagan's later study of 559 university students, 61.5 percent reported a past history of sleep talking and 51.2 percent reported that sleep talking still persisted. Goode found 53.1 percent of one group of medical students, 58.5 percent of a second group, 72.2 percent of student

nurses, and 69.2 percent of hospital inpatients reporting histories of the phenomenon. Among fifty-five enuretic marine recruits, twenty-six had talked in their sleep during the past three months, while only fourteen of 135 nonenuretic recruits reported having done so. Since these incidence figures are, in all likelihood, conservative, it would appear that at least a majority of the population has experienced sleep talking at one time or another.

In an extensive review of the literature, Arkin noted that sleepwalking may occur in the absence of any noticeable disorder, or in conjunction with various types of physical or psychological pathology (see references 28, 163, 309, 322, 391, 405, and 418). Based on his clinical experience and research, however, Arkin concluded that sleep talking "is usually benign but may reflect deeper disturbance."

The discovery of REM sleep and of its relationship to dreaming engendered new interest in the psychophysiological aspects of sleep talking. Kamiya was among the first to perform a polygraphic investigation of sleep-talking. He reported that 88 percent of ninety-eight sleep talking episodes occurred during NREM sleep, and that 71 percent of the episodes were accompanied by body movements. Subsequent investigations usually confirmed the predominance of sleep talking during NREM sleep, although Arkin et al. and Tani et al. described subjects who talked predominantly or exclusively during REM sleep. Several reports indicate that NREM-sleep

speeches are more likely to be accompanied by muscle-tension artifact than are REM-sleep speeches, making it difficult to determine the quality of the EEG activity during the episode. Nevertheless, Rechtschaffen et al. reported that in NREM-sleep speeches a period of stage-2, -3, or -4 sleep would suddenly be interrupted by muscle-tension artifact accompanied by sleep speech. Occasionally a burst of high-voltage slow waves or K-complexes preceded the muscle tension by several seconds. When EEG activity was discernible through the artifact, it was usually in the 7-10 cps range and appeared to be alpha activity. The muscle-tension artifact persisted for ten to twenty seconds beyond the end of the sleep speech. The typical postepisode EEG pattern was that of stage-2 sleep. Cohen et al. described one case of stage-4 sleep speech in which there was no muscle artifact. Analysis of the EEG during the speech suggested that the subject passed briefly into stage 1 during the episode. Schwartz described an episode which occurred during a period of EEG wakefulness which interrupted stage-4 sleep. The subject did not recall the event when questioned about it later.

The nature of the relationship between sleep talking and mentation during sleep has been of interest both for theoretical and for practical reasons. If it could be shown that sleep talking is reliably related to sleep mentation, then content of sleep speeches might prove to be more “pure” than content elicited after involuntary awakenings, and might thus provide a better method of monitoring sleep mentation. After studying a small sample

of sleep speeches, Rechtschaffen et al. tentatively concluded that REM-sleep speeches are characterized by affect in the voice and little relationship to the experimental situation. Ry contrast, NREM speeches are usually flat and unemotional, tend to concern the experimental situation, and are only infrequently followed by reports of mental content with involuntary awakening. In a more elaborate study of the degree of concordance between the content of sleep speeches and recalled mentation, Arkin et al. found that 79.2 percent of REM speeches showed some degree of concordance with mentation, while 45.8 percent of stage-2 speeches, 21.1 percent of stage-3 and -4 speeches and 80 percent of stage-i-NREM speeches exhibited some degree of concordance. Whether the differences in degree of concordance in REM and NREM speeches reflect differences in recall of sleep mentation, in the mechanism of sleep speech, in types of concordance (manifest vs. latent content), or real differences in the amount of sleep mentation in the two types of sleep, remains to be determined.

Nocturnal Enuresis

Nocturnal enuresis refers to bed-wetting in individuals old enough to have acquired voluntary control of micturition. Although most writers consider a child to be enuretic if he wets his bed after three years of age, several studies have shown wide individual differences, as well as possible sex differences, in the age of acquisition of urinary control, suggesting that the

child who acquires control somewhat later than three years should not necessarily be considered enuretic.

The incidence of enuresis has been reported to range from 4 percent for six-year-old Child-Welfare-Clinic patients to 87 percent of idiots. Other incidence figures between these extremes have been reported (see references 8, 38, 55, 91, 167, 207, 234, 244, 280, 281, and 409) for groups of various ages and clinical conditions. Many authors have noted at least a slight predominance of the disorder in males (see references 38, 91, 132, 169, 281, and 392), although Frary found no evidence that enuresis is a sex-linked character. There are numerous observations of a high family history for the disturbance. Frary concluded that it is determined by a single recessive gene substitution, while Hallgren suggested that in "genetic cases" the mode of inheritance may be either by a dominant major gene or by the interaction of polygenes and the environment.

A wide variety of physical anomalies has been observed in enuretics, and quite frequently these anomalies have been assigned etiological roles in the disturbance. Various neuromuscular and anatomical abnormalities of the urogenital system have been described (see references 47, 51, 53, 70, 128, 130, 269, 327, and 394). Of particular interest are the observations that the enuretic's bladder capacity may be lower than normal, that some enuretics may have less concentrated urine at night, and that enuretics excrete a larger

amount of urine at night than normals. However, Vulliamy found no differences in nocturnal urine output among enuretics when diet and fluid intake were strictly controlled. Numerous other more or less relevant afflictions have received attention in the literature, including epilepsy. Although high incidences of EEG epileptiform features, and frequent personal and family histories of epilepsy have been reported for enuretics, Poussaint et al. failed to find any clinical evidence of seizure activity in what they considered to be a more representative sample of enuretics.

The psychological characteristics of enuretics have received equal attention (see references 8, 26, 91, 149, 167, 169, 182, 248, 280, 319, 392, and 445). These individuals exhibit a variety of associated behavioral problems, including nail biting, stealing, and truancy, criminal and especially aggressive offenses, thumb sucking, speech impediments, temper tantrums, and sleepwalking. They have been characterized as being temperamental, timid, and sensitive, disturbed in the sexual realm, of loose personality organization, fearful of the opposite sex, lacking inhibitory control, emotionally immature, and passive. In one study it was found that five traits—enuresis, thumb sucking, nail biting, speech impediments, and temper tantrums—occurred more often in combination than in isolation in a sample of children. On the other hand, Lapouse and Monk found no statistically significant relationship between a number of fears and worries and enuresis in a large random sample of children. Werry and Cohrssen concluded that enuretic children

seen by physicians tend to exhibit more psychiatric symptoms than nonenuretics, but they emphasized that more than half of their enuretic subjects were emotionally healthy. This is especially meaningful since they also suggested that children with several behavioral and somatic symptoms are more likely to be brought to a physician and thus load nonrandom samples with disturbed subjects.

Clinical EEG studies of enuretics have generally revealed a high percentage of abnormal or immature EEGs (see references 165, 282, 322, 377, and 411). In addition, Gunnarson and Melin found more EEG abnormalities in enuretics who had never been dry than in those who had experienced a dry period. Contradictory evidence was presented by Ditman and Blinn, who noted no clinical abnormalities in their patients. In a sample of sixty-eight subjects five to sixteen years old, only 10 percent of the EEGs were read as abnormal. Some of these discrepancies may arise from differences in characterizing normal records for a given age.

Deep sleep has been reported as a characteristic of and/or an etiological factor in enuresis (see references 9, 44, 47, 169, 350, and 396), principally on the basis of parents' reports and observations on the difficulty in arousing enuretics after micturition. Sleep EEG studies have revealed that enuresis can occur in all stages of sleep and during periods of nocturnal wakefulness (see references 27, 94, 122, 144, 324, 346, 368, and 424).

Pierce et al. observed an increase in restlessness and a gradual reduction of heart rate to a stable low level during the thirty minutes preceding micturition. Light sleep or waking patterns accompanied the restlessness until a final body movement signaled a change to deep-sleep patterns. Enuresis followed the body movement and slow-wave EEG activity continued throughout micturition.

Gastaut and Broughton's patients typically exhibited a gradual increase in primary spontaneous bladder contractions as they passed from wakefulness to deep sleep during the early part of the night. The "enuretic episode" began with a series of bladder contractions during slow-wave sleep. There followed a series of K-complexes or a burst of rhythmic delta activity in the EEG, and then a body movement. Sleep patterns began to lighten and micturition occurred at some point following the body movement. Micturition could occur at any point along a continuum of increasing vigilance from deep to light sleep or wakefulness. Broughton suggested that this finding may help reconcile some of the earlier, apparently discrepant, observations that micturition can occur in all stages of sleep and wakefulness, although differences in apparatus for signaling the onset of micturition probably contributed to some of the variability in the observations.

There is little evidence that nocturnal enuresis is related in any special way to REM sleep. Only occasional episodes have been observed during this

sleep stage, and, if awakened following micturition, most patients fail to recall dreams. On the other hand, awakenings from REM periods following micturition are more likely to yield reports of dreams of micturition if the bedclothes have been left unchanged, suggesting that dreams of micturition result from incorporation of external stimuli.

Etiological theories of nocturnal enuresis are varied and plentiful (see references 9, 20, 26, 42, 43, 47, 70, 91, 94, 113, 122, 132, 144, 149, 165, 167, 169, 170, 248, 249, 279, 280, 288, 289, 322, 324, 327, 350, 368, 377, 392, 394, 396, 409, 419, 427, and 445), and the classification scheme used by Werry and Cohrssen is helpful in considering them. Genetic theories are based on the high familial incidence of the disorder. Maturational theories derive from observations of physical or psychological immaturity in enuretics. Data concerning physical or psychological abnormalities in enuretics give rise to the pathological theories, while the numerous and varied observations of psychological disturbances in enuretics have produced psychogenic theories. Poor habit training has been ascribed an etiological role by some authors. As Werry and Cohrssen noted, these categories are not mutually exclusive and several writers (see references 51, 149, 169, 346, and 394). have emphasized the multiple etiologies of nocturnal enuresis.

Sleep EEG studies have given rise to several explanations of this disorder. Ditman and Blinn and Bental stressed the discrepancy between

behavioral reactivity and EEG sleep before and during the enuretic event. Ditman and Blinn suggested that enuretics are in a dissociative state, while Bental hypothesized that the enuretic child develops a "will" to remain awake in order to avoid wetting the bed. This will is reflected in the waking EEG activity accompanying behavioral sleep. Pierce et al. and Schiff considered the enuretic event to be a dream equivalent or variant. On the basis of their data, Ritvo et al. concluded that there are three types of enuretic events: (1) awake enuresis occurs during EEG wakefulness; (2) nonarousal enuresis occurs during stages 2, 3, or 4 and is not preceded by arousal phenomena; and (3) arousal enuresis occurs during stages 2, 3, and 4 and is preceded by arousal phenomena. According to Ritvo et al., all patients appear to have a pathophysiological substrate for enuresis, but psychological factors are probably very important in the maintenance of enuresis in patients exhibiting predominantly awake and arousal enuresis.

Broughton suggested that enuresis is a slow-wave-sleep arousal phenomenon, similar to sleepwalking night terrors. In Broughton's opinion, slow-wave-sleep arousals occur in all individuals but enuretics are physiologically predisposed to enuretic attacks during the arousals. Finley has also viewed enuresis as an arousal defect within the CNS.

Bruxism

Bruxism, or teeth grinding, is of interest to the physician primarily because of the damage it may cause to the teeth and related structures, but it causes an unknown amount of annoyance to the sufferer's close associates. Although most writers consider diurnal and nocturnal bruxism to be a single entity, Reding et al. suggested that they are separate phenomena. Nocturnal bruxism is typically characterized by rhythmic patterns of masseter EMG activity which is frequently accompanied by sounds of teeth grinding, while diurnal bruxism is idiosyncratic and silent, except in individuals with organic brain lesions. Reding et al. noted that the two phenomena occur during different states of consciousness, and that if nocturnal bruxists are awakened they appear to have no awareness of their teeth grinding. In one sample of forty-five nocturnal bruxists, none gave evidence of diurnal bruxism.

Among periodontal patients 78 percent have been described as bruxists. In studies of somewhat more representative samples, Reding and his associates have reported the following incidence figures: 5.1 percent of 2290 undergraduate and graduate students between the ages of sixteen and thirty-six years reported current bruxism; 5.5 percent of 1157 laboratory school students ages three to seventeen years reported to be current bruxists by parents, and 15.1 percent reported to have either current or past histories; and 8 percent of 2168 undergraduate and graduate students reported current or past histories. Bruxism appears to affect people of all ages, but seems to decline in incidence with increasing age. There is some evidence that bruxism

is a familial disorder.

A primary difficulty in studying bruxism has been the reliable and artifact free monitoring of teeth grinding. In early work it was concluded that bruxism is temporally related to REM sleep. This conclusion has been revised with the use of stricter criteria for the detection of bruxism episodes. The latest evidence indicates that bruxism occurs predominantly during stage-2 sleep. There is no change in the nature of sleep or in the relative proportions of sleep stages when bruxists are compared to controls. The bruxism episode, which lasts an average of nine seconds, is often preceded by a K-complex or a K-complex wave without a spindle. During the episode, trains of alpha or a temporary change toward lower-voltage, fast, random activity, without K-waves or spindles, may occur. Heart rate may increase just before or during the episode, and subcutaneous blood vessels are constricted. Pulse rate and respiration may also change. Forearm and palm electrodermal potentials have been observed during a number of episodes. Sound stimuli during the various stages of sleep have provoked teeth grinding in some subjects. There is evidence that teeth grinding is not associated with any specific manifest content during stage-2 sleep.

Diurnal and nocturnal bruxism have been attributed to a variety of causes, including genetically determined behavior patterns, local or intraoral factors, lesions of the CNS, and psychological factors (see references 131, 136,

173, 290, 378, 397, 408, 413, and 420). Several authors have suggested that psychological disturbance is a necessary condition for the disorder and that dental problems are precipitating factors.

The oral expression of aggression has been one of the most common psychological interpretations of bruxism. However, in a study of bruxists, presumably of both the diurnal and the nocturnal type, Frisch et al. failed to find a significant relationship between degree of dental evidence of bruxism and mode of expressing aggression as determined by the Rosenzweig Picture-Frustration Study, an instrument designed to measure responses to frustration. Reding et al. concluded that nocturnal bruxists and their controls do not show any statistically significant personality differences as measured by the MMPI and the Cornell Medical Index.

On the basis of their sleep EEG and psychological studies of nocturnal bruxists, Reding and his associates concluded that none of the factors listed above plays the primary etiological role in bruxism. They proposed instead that nocturnal bruxism is a partial arousal phenomenon similar to the slow-wave-sleep arousal phenomena (sleepwalking, enuresis, and night terrors) described by Broughton. Satoh and Harada extended this explanation by proposing that bruxism often occurs if the dopaminergic nigrostriatal system excessively drives the areas controlling jaw movements during the transition from sleep to wakefulness. This hypothesis is indirectly supported by a report

that administration of dihydroxyphenylalanine, the precursor of dopamine, to an individual suffering from Parkinson's disease provoked bruxism.

Jactatio Capitis Nocturna

Jactatio capitis nocturna, or sleep rocking, is a motor-behavior pattern consisting of rhythmical movements of the head or body prior to or during sleep. Evans, who extensively reviewed the literature concerning this rather rare disorder, concluded that the movements may be regular or intermittent bursts of activity and that they may appear to be voluntary, even though the individual is usually unable to recall the episode the next morning. Mental retardation and daytime tics, and rocking movements may characterize some sufferers, but more commonly they exhibit symptoms of behavioral disorders. Most patients have rocked from the second six months of life, and the disturbance may persist into adulthood.

Only a few cases of sleep rocking have been studied in the sleep laboratory. Gastaut and Broughton found that the onset of rocking associated with going to sleep is typically signaled by several slow nystagmoid eye movements. The episodes usually appear during stage-1 sleep and produce no significant EEG, cardiac, or respiratory changes. Baldy-Moulinier et al. observed one case where rocking movements seemed to facilitate the return to sleep after periods of wakefulness.

Rocking movements during sleep have been observed in all phases of sleep. Slow-wave sleep episodes begin rather abruptly, and seem not to produce noticeable changes in heart rate or respiration. Although Gastaut and Broughton observed no important modifications in the EEG during the episodes, Oswald found that periods of slow waves and spindles were interspersed with periods of low-voltage activity as the episode ran its course.

Episodes of REM-sleep rocking also occur. In one of his cases, Oswald found that rocking episodes were most frequent and violent during this stage. As with episodes occurring during other stages, there were no significant EEG or heart-rate changes during these REM-sleep episodes.

Evans noted that both organic and psychological etiologies have been proposed for this disturbance. Evans himself suggested that the rocking movements relieve anxiety associated with sleep, and produce sleep through autohypnosis, much as the rhythmic stimulation employed by Oswald produced sleep in an experimental situation. Oswald also considers sleep rocking to be motivated, and suggested that it may reflect the use of a previously learned mechanism to relieve unhappy thoughts during sleep. Gastaut and Broughton have categorized the disorder as an unconscious, semipurposeful automatism which is liberated with the depression of cortical and subcortical systems during falling asleep and during sleep.

Sleep-Modified Disorders

In sleep there are many physiological changes which might account for modifications of various medical complaints. The changes may or may not be sleep dependent, i.e., they may be circadian. During REM sleep, pulse rate, respiration rate, and blood pressure increase and show greater variability, penile erections occur, and there are increases in plasma and urinary levels of 17-hydroxycorticosteroids, brain temperature, oxygen consumption, unit neuronal discharge rates, antidiuretic hormone activity, and urinary 3-methoxy-4-hydroxymandelic acid. Many other physiological changes occur during sleep, but this list should make the point sufficiently clear.

Several cardiovascular and respiratory disorders are exacerbated during sleep. There is great variability in the EEG sleep patterns of angina patients, and nocturnal angina attacks, evidenced by ST-segment depression on the electrocardiogram, appear to occur predominantly during REM sleep. Clinically it has been noted that myocardial infarctions occur with a high frequency during sleep. In our laboratory preliminary evidence suggests that myocardial infarct patients maintained on an intensive-care ward are sleep-deprived, either because of discomfort or because of disturbances produced when therapeutic procedures are carried out. We have also noted that these patients often show increases in premature ventricular contractions during REM sleep.

Paroxysmal nocturnal hemoglobinuria is a rare disease affecting both sexes. It is most common between the ages of twenty and fifty and is usually fatal. Hemolysis is increased during the sleep of victims.

Left ventricular failure is commonly associated with pulmonary edema at night and results in episodes of paroxysmal nocturnal dyspnea. The mechanism appears to involve an increase in plasma volume and a shift of blood from the lower extremities to the pulmonary circulation on assumption of the supine position. The resultant increase in pulmonary blood promotes pulmonary congestion and produces pulmonary edema.

Paroxysmal nocturnal headaches are also called cluster headaches because they tend to occur in series. The patient usually awakens during the night with a severe, throbbing, unilateral headache, which may be accompanied by vomiting, watering and redness of the eyes, and stuffiness of the nose. The disorder appears to result from a periodic dilatation of the extracranial vessels in the territory of the external carotid artery.

Emphysema patients, who exhibit increased alveolar $C0_2$ tension and decreased arterial oxygen saturation during the waking state, suffer their most difficult periods soon after awakening. The fact that these patients show abnormal increases in alveolar CCL tension and decreases in arterial oxygen saturation while asleep may explain these postawakening exacerbations.

Sleep EEG studies of asthmatic children have shown that these patients have decreased stage-4 sleep, frequent awakenings, and decreased total sleep time. Asthmatic episodes are confined to the last two-thirds of the night. In asthmatic adults episodes occur throughout the night, with no relation to any specific sleep stage. The patients have shorter total sleep times and less stage 4 than controls. Johns et al. found that patients experiencing dyspnea as a result of bronchial asthma reported frequent night awakenings without significant loss of sleep, and more daytime sleep than average.

Snoring is the nocturnal emission of various grunts, snorts, wheezes, buzzes, and gurgles. The immediate cause of these noises is vibration of the soft structures in the nose and throat accompanying mouth breathing during sleep. It has been estimated that one in eight persons snores most of the night. In 1961 over 300 antisnore devices were recorded in the U.S. Patent Office. Diverse etiologies have been suggested, including structural abnormalities of the upper respiratory tract, sleeping position, allergies, overheated or overventilated rooms, and psychological factors. There are no known polygraphic studies of snoring. Since the etiology of this extremely common disorder is apparently mixed, such a study might help to differentiate the various types of snorers, as well as determine whether or not snoring is confined to any particular sleep stage.

Various neuromuscular conditions are exacerbated during sleep. In

acroparasthesia, or carpal tunnel syndrome, the patient awakens in the later part of the night with pain, tingling, and numbness in the first three or four digits of one or both hands. Attacks last for thirty minutes or more and are more frequent in women than men. This disorder appears to result from compression of the median nerves in the carpal tunnel at the wrist.

Night cramps, usually of the calf, occur increasingly with age, and also during pregnancy. They are thought to result from a serum calcium deficiency in pregnant women, but the etiology in the elderly is unclear.

Tired-arm syndrome affects middle-aged women, who awaken with pain in the forearm and may detect a weakness in the hand. Excessive muscular exertion has been attributed a causative role.

The elderly are primary sufferers of nocturnal pseudohemiplegia. This disorder is characterized by numbness and immobility of one arm or one side of the body upon awakening at night or in the morning. It is of short duration and is possibly some form of pressure palsy.

Familial periodic paralysis is characterized by episodes of muscular weakness and eventual flaccid paralysis. Onset is usually at night, and the attacks can last as long as several days. The apparent cause of the paralysis is an exaggeration of the normal loss of plasma potassium to the muscles, and the resulting decrease in muscle membrane excitability.

The restless-legs syndrome was first described by Wittmaack as anxietas tibiarum, which is defined in *Dorland's Illustrated Medical Dictionary* as "a painful condition of unrest leading to a continual change of position of limbs, and due to an increase of the muscular sense." This disorder has been briefly described by several authors, but Ekbom has presented the most detailed discussion. He coined the term "restless legs" for this syndrome and differentiated two clinical forms, asthenia crurum parasthetica and asthenia crurum dolorosa. The disorder is frequently familial in nature and sleep disturbance is an almost constant concomitant. Our recent study of a patient confirmed the findings of Lugaresi et al. that the motor disturbances occur every twenty to thirty seconds. We also noted that the EEG burst activity signaling the limb movements became progressively stronger over a period of five to ten minutes until the patient awoke. During REM sleep the myoclonic jerks subsided, but movements of the toes continued to occur periodically. It has been proposed that restless legs is a somatic form of anxiety or a manifestation of disturbed lower-limb circulation. Several authors have attributed the disorder to disturbances in the reticular formation.

Several additional medical conditions have been shown to occur or be exacerbated during sleep. Microfilaria of Wuchereria bancrofti can be found in the blood most frequently between midnight and 2 a.m. Patients suffering from diabetes mellitus show a fairly wide variation in blood-sugar concentrations during sleep, whereas in normal individuals there are only

small variations in blood-sugar levels.

A sleep EEG study of patients with duodenal ulcers revealed that the high nocturnal secretion rate of gastric acid by ulcer patients is particularly exaggerated during REM sleep. The authors suggested that content of dreams may determine the magnitude of the secretion rate.

Hypnalgia, or psychogenic pain during sleep in children, is attributed to underlying emotional disturbance.

Painful nocturnal penile erections may awaken men at night and induce a special type of sleep disturbance. They appear to be REM-related phenomena.

Nocturnal proctalgia, or proctalgia fugax, is an early morning pain seeming to arise from the rectum. It is more common in men than in women, is reported most frequently by people twenty to fifty years old, and is often a familial disorder. It has been attributed to segmental cramp of the puboccocygeus muscle.

From this very brief review of some sleep-modified disorders it is clear that many sleep-related phenomena have yet to be studied by sleep researchers. With further study it may become necessary to reclassify some of these disorders as secondary sleep disorders. In any case, there can be no

doubt that sleep research has contributed in many ways to a better understanding of numerous clinical conditions, and there is every reason to expect a similar contribution in the area of the sleep-modified disorders.

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