CHAPTER 10

Depth of Sleep and Enuresis: a Critical Review

PHILIP GRAHAM

Introduction

When higher cortical function ceases because of injury to or disease of the brain, incontinence of urine is an inevitable result. It might, therefore, be thought that nocturnal urinary incontinence (enuresis) arises during sleep because of a relative diminution of cortical function. However, normal sleep is not a halfway stage between wakefulness and coma. It is a complex phenomenon, with its own characteristic cyclical neurophysiology and its own associated mental content (dreams), which have no exact parallel in waking life.

Evidence as to the relationship between depth of sleep and enuresis arises from three main sources: clinical observations, EEG recordings, and measurements of eye movements. Clinical observations have in general been limited to the child's arousability—how easy it is to wake him up. There is a common-sense assumption that those children who are more deeply asleep are more difficult to rouse, but there is, in fact, no necessary connection between arousability and other measures of depth of sleep. Lightly sleeping enuretic children might resist arousal because it carries for them more unpleasant connotations (a cold lavatory seat situated in a toilet at the end of a draughty unlit corridor) than it does for non-enuretic children. Theoretically, there is no reason why other clinical observations of depth of sleep, such as gross body motility, should not have been made. In practice, however, arousability has been the sole clinical criterion of depth of sleep to have been examined.

Real possibilities for an increase in knowledge have arisen from advances in electroencephalographic (EEG) techniques, which have allowed continuous monitoring of a sample of brain wave activity during sleep. These observations have usually been linked with measurements of eye movements, which are now known to be closely linked to particular phases of the sleep cycle (Dement and Kleitman 1957). Dement and Kleitman recognise four stages occurring cyclically in normal sleep. In Stage I, the brain waves are predominantly of low voltage, and there is an absence of spindle activity. Rapid eye movements are invariably present, and, if the subject is woken during this phase of sleep, he is likely to report that he has been dreaming. Dream phenomena are unlikely to occur in other phases of sleep. In Stage II, spindle activity is present, but there is still a low voltage background. In Stage III, high voltage slow waves become more common, but there is still some spindling. In Stage IV, at least half the EEG record is made up of high voltage slow waves. It is, therefore, possible to compare the brain wave activity of enuretic children with that of non-enuretic children, to examine the phases of sleep when wetting occurs, and to record the effect of different types of drug and other treatments both on brain wave activity and on enuresis, in a manner which should allow conclusions to be drawn about the way in which the three

variables (*i.e.* sleep patterns in normals and enuretics, the relationship between sleep phase and enuresis, and the effects of treatment of enuresis on the type of sleep) are related.

As a result of these recent advances in knowledge and technique, it is reasonable to expect knowledge in this area to increase considerably over the next decade. Indeed, the research opportunities are so obvious that it would be surprising if definitive work were not at present being undertaken. At this particular stage, however, published work does not allow us to answer many questions with certain answers, as the following review attempts to show.

Do Enuretic Children Sleep More Deeply Than, or Otherwise Differently From, Non-enuretic Children?

As mentioned above, clinical observations in this field have been limited to the measurement of arousability. Many authors have commented on their belief (which seems in the main to derive from parental descriptions, rather than direct observation) that enuretic children are especially difficult to rouse. There is an obvious possible source of error here, since parents will, in general, have had less cause to wake their non-enuretic children, and any impression that their enuretic children are more difficult to rouse is likely only to a limited extent to be founded on direct objective comparison.

The two most substantial studies of arousability have come to diametrically opposite conclusions. Bostock (1958) reported an experiment in which an attempt was made to compare the arousability of seven enuretic and twelve non-enuretic children using a standard auditory stimulus produced by a buzzer. The enuretic children took an average 418 seconds to reach a waking state, whereas the non-enuretic children took 319 seconds. The author concluded that this provided sufficient support for his view that enuretics sleep more deeply than others, though statistical evidence is not provided. Bostock developed an elaborate evolutionary theory to account for his finding. He postulated that, in the six months after birth, infants go through a period of 'exterior gestation', in which there is a need for an uninterrupted sleep rhythm. Mothers who attempted to impose unnatural sleep patterns, or insisted on early pot-training, produced a habit of withdrawal by the child into deeper sleep, which itself resulted in later enuresis. In fact, the evidence suggests that early pot-training is, if anything, associated with a lower incidence of later enuresis (Blomfield and Douglas 1956). This, therefore, seems to be another example of a theory based on a faulty observation being used to explain an unproven hypothesis.

Boyd (1960) examined 100 enuretic children aged five to fifteen years, and compared them with a similarly-sized control group, matched for age and sex. The children were woken by calling their names, and, if they did not respond, by shaking them gently by the shoulder. The enuretic children, who took, on average, 16 seconds to wake up, were quicker to rouse than the non-enuretics who took 20.5 seconds, though the difference was not statistically significant. This study appears to be methodologically superior to that of Bostock, but, of course, the results do not exclude the possibility that there may be a sub-group of enuretic children whose incontinence is associated with particularly deep sleep. If there is such a sub-group

(and there is no good clinical evidence for its existence), it is likely not to be characterised by brain dysfunction, for Boyd (1963) found that abnormal EEGs were no more common in her deep than in her light sleepers.

Clinical observation may have led to contradictory conclusions on this issue, but it must be admitted that, as yet, EEG studies have not yielded much more information. Pierce (1963) reports that enuretic children have less rapid eye movement (REM) activity, and consequently dream less, than do non-enuretics. He claims, interestingly (though without providing adequate quantitative data), that if each episode of enuresis is counted as a period of REM activity the dream-lack of enuretic children is accounted for. However, there seems to be no other EEG information as to the relative amounts of time spent in the four sleep stages by enuretics compared with non-enuretic children, and before accepting Pierce's findings one would need a great deal more quantitative data.

Broughton (1968) suggests that the quality of sleep of the enuretic patient may differ from that of the non-enuretic in other ways. He found that the mean pulse rate of an enuretic group was higher than that of a control group, although mean respiration rates did not differ. He suggests, mainly on the basis of this finding, that enuresis and, indeed, a whole range of other disorders (*e.g.* sleepwalking and nightmares) which occur during sleep are produced by a disturbance of the arousal mechanism. In our present stage of knowledge, it would seem premature to conclude that the quality of the sleep of the enuretic child does differ significantly from normal, but certainly Broughton's work provides an interesting pointer in this direction.

Does Bedwetting Occur in any Particular Phase of the Sleep Cycle?

There are no clinical observations of any substance, although some authors do mention a tendency of some enuretics to wet during the first two to three hours of sleep. The first report on this subject (Ditman and Blinn 1955) provided evidence from EEG studies of three children aged five to seven years and 22 naval recruits aged seventeen years or more. The children wet during deep sleep (Stages III and IV), whereas the young adults were physiologically awake at the time of enuresis, showing a considerable amount of alpha rhythm (a form of rhythmic activity occurring especially during waking life when the eyes are closed, and arising from the posterior part of the brain). The young adults also showed a change in psychogalvanic response (PGR) and a rise in heart rate during the period between five and thirty minutes before wetting, possibly indicating a rise in anxiety level. Ditman and Blinn concluded that enuresis in the young is the result of physiological immaturity, whereas in the young adult it is more likely to occur as a result of a hysterical dissociative reaction.

Quite apart from the very small number of children involved in their study, there are other reasons for doubting these authors' findings and conclusions. The development of alpha rhythm is itself a maturational phenomenon, and even in the waking life of five- to seven-year-old children, alpha rhythm is likely to be a great deal less well-formed than in the adult. Differences between adults and children in the timing of wetting episodes may not reflect different physiological or psychological mechanisms, but rather the same mechanisms occurring at different phases of development. The assumption that PGR and heart rate changes are due to increased levels of

anxiety is unimpressive, without data about the changes in these variables which might occur in normal subjects at the time of waking. Characteristically, the sleeping pulse is slower during sleep than during the waking state, though Broughton (1968) suggests this may not be so for enuretics.

Broughton and Gastaut (1963), in a very brief communication, also report that enuretic events begin in Stage IV sleep. However, in their study of seven five- to ten-year-old children they report a characteristic sequence of events occurring over a period of about three minutes. Whilst in Stage IV sleep,the child begins to show whole body movement, sleep rapidly lightens, there is a change in heart rate, tachypnoea, and (in boys) penile erection. Enuresis occurs about three minutes after the commencement of this train of events, and is *followed* by a period of REM and dream activity. These workers also carried out simultaneous intra-vesical recordings, and found that bladder contractions occur more commonly and more powerfully in the bladders of enuretic than in non-enuretic children. They postulate that the basic defect in the enuretic child is either a congenital absence of central inhibitory mechanisms preventing bladder contraction, or (and this is the explanation they appear to favour) there is a peripheral vesical abnormality involving an over-excitable muscular lining to the bladder. They feel that dreams must be unimportant as precipitants of enuresis, because dream activity follows the enuretic episode. Without more evidence, it is difficult to evaluate this study, but certainly the method of simultaneous intra-vesical, EEG and eye movement recording contains definite promise.

Pierce (1963), in a study of ten enuretic boys aged between five and nine years and ten young enuretic adults, also noted that enuresis and dreaming never seemed to appear together. In contrast to Broughton and Gastaut, he reports that the initial dream occurs, on average, 2¼ hours after the enuretic episode in both children and young adults. The content of the dreams of enuretic children is said to vary depending on whether or not the child wets the bed that night. On bed-wetting nights, content is mainly concerned with situations involving dependency (the receiving of gifts, food, affection), whereas on non-wetting nights the child is said to have dreams filled with violent content. Again no data are provided, and the study is impossible to evaluate. This is particularly exasperating in view of the fascinating yet improbable nature of some of the findings.

The three studies cited so far in this section emphasise the regular pattern of sleep events associated with the act of bedwetting. More recent studies, however, have cast doubts on this regularity, and point instead to the wide range of sleep circumstances in which wetting can occur. Weinmann (1968) examined child enuretics up to the age of six years with telemetric EEG recordings. He found that some wet in the lighter and some in the deeper stages of sleep—there was no definite pattern. He also noted (and this is a factor little dealt with by other investigators, although it may be important) that after a wetting episode, sleep was fitful and restless for the rest of the night, unless the subject's night clothing was changed.

Ritvo *et al.* (1969), who studied seven boys aged between eight and ten years, found that all their subjects wet sometimes in Stage III or IV sleep, especially in the first part of the night (non-arousal enuresis), and sometimes during lighter phases of sleep (arousal enuresis). Some children also wet in the morning when physiologically

awake (awake enuresis), and these were the ones showing neurotic conflicts. They postulated a physiological basis for the symptoms, which could lead to the development of emotional disturbance and an associated alteration in the type of enuretic events which occurred.

This study is the most adequately reported of those reviewed, and its findings do lead one to believe that enuretic events can occur in all phases of sleep except Stage I, when REM activity is occurring. However, it is difficult to see how the authors could possibly establish a link between a particular pattern of enuresis and the presence of neurotic disorder with such a small number of subjects, and this does vitiate some of their conclusions. Clearly, this work is time-consuming and expensive (the seven subjects of these last experiments are reported upon by an equal number of investigators), but it will not be possible to draw conclusions of this nature without the examination of a large number of children.

Indeed, very recently, Evans (1971) has reported preliminary findings in six adolescent and three adult enuretic subjects. Nineteen enuretic episodes were recorded, and all of them occurred in Stages III or IV sleep. The episodes were preceded by muscle twitching and tachycardia. It seems likely that Evans's study will provide the best evidence available of the association between sleep events and bedwetting episodes, but sufficient detail is not yet available to draw definitive conclusions. In any event, it appears that he has not yet investigated any pre-adolescent enuretic patients.

Do Effective Treatments of Enuresis Act by Altering the Quality or Depth of Sleep?

Detailed evaluation of drugs and conditioning methods of treatment are reported elsewhere. It is assumed here that the alarm apparatus, imipramine, amitriptyline, and, to a lesser extent, amphetamine, are sometimes effective methods of treatment. All these methods of treatment may affect sleep. Does their therapeutic efficacy have implications for the possible rôle of deviant sleep patterns in the aetiology of enuresis?

Two of these three drugs (amphetamine and, to a lesser extent, imipramine) are known from clinical evidence to produce insomnia and to lighten sleep. By contrast, amitriptyline causes drowsiness, which, particularly in the early stages of treatment, is often quite severe (Shepherd *et al.* 1968). No EEG evidence is available of the effect of amitriptyline or amphetamine on sleep. However, EEG findings (Ritvo *et al.* 1967) from a study comparing the effects of imipramine and a placebo in seven enuretic boys aged nine to eleven years suggest that imipramine reduces time spent in REM sleep, increases time spent in Stage II sleep, and increases time from onset of sleep to the first REM epoch. It is possible that any of these phenomena could be relevant for the understanding of the effectiveness of imipramine in enuresis.

It is also possible—and this is discussed in other Sections—that these drugs exert their effect by a peripheral rather than by a central action. Both amitriptyline and imipramine have marked anticholinergic action, resulting in relaxation of the smooth muscle of the bladder and contraction of sphincter. Imipramine, for example, has been found to exert a beneficial influence on urinary control in cases of 'neurogenic bladder' where, of course, it can only be exerting its effect by a peripheral rather than a central action (Williams 1971). Amphetamine is a sympathomimetic amine, which also produces relaxation of the vesical smooth muscle and sphincter contraction.

The fact that so many differing attempts (see other Sections) have been made to fit the effectiveness of the buzzer method of treatment into one or other theoretical model of behaviour suggests that none is totally satisfactory. It is, therefore, reasonable to consider whether the fact that the treatment works can be explained by its effect on sleep pattern rather than by any form of conditioning. We have probably all had the experience of repeatedly wakening during the night when we have set the alarm for a particularly important occasion. Could this 'expectancy arousal' phenomenon produce lightening of sleep throughout the night rather than, as the conditioning models suggest, just at the time of bladder filling. Experimental evidence is needed to provide information on the all-night effect on sleep patterns of subjecting the enuretic child to a loud auditory stimulus at the time of wetting.

Conclusions

It is uncertain whether enuretic children are less or more easy to rouse than non-enuretics. It appears that bedwetting can occur during any sleep phase except during REM sleep, although in adults there is increasing evidence that Stages III and IV are the most vulnerable phases. It has not been possible to show that children have characteristic patterns relating bedwetting to sleep rhythms, although this has been claimed to be the case. It is, therefore, as yet logically impossible to investigate whether children who characteristically wet in one phase of sleep differ in other ways from those who wet in other sleep phases. Finally, the efficacy of the various methods of drug treatment of enuresis possibly has little to do with the effect of these drugs on sleep patterns—peripheral rather than central effects are as likely. It is also conjectural whether buzzer alarm treatment works through a general effect on sleep throughout the night or because it generates a specific conditioned sleep response to bladder filling.

REFERENCES

Blomfield, J. M., Douglas, J. W. B. (1956) 'Bedwetting—prevalence among children aged 4-7 years.' *Lancet*, **i**, 850.

Bostock, J. (1958) 'Exterior gestation, primitive sleep, enuresis and asthma: a study in aetiology.' *Medical Journal of Australia*, **ii**, 149, 185.

Boyd, M. M. (1960) 'The depth of sleep in enuretic school children and in non-enuretic controls.' *Journal of Psychosomatic Research*, **4**, 274.

Broughton, R. G. (1968) 'Sleep disorders: disorders of arousal?' *Science*, **159**, 1070.

—— Gastaut, H. (1963) 'Etude polygraphique de l'énurésie nocturne.' *Revue Neurologique*, **109**, 246.

Dement, W., Kleitman, N. (1957) 'Cyclic variations in EEG during sleep and their relation to eye movements, body motility and dreaming'. *Electroencephalography and Clinical Neurophysiology*, **9**, 673.

Ditman, K. S., Blinn, K. A. (1955) 'Sleep levels in enuresis.' *American Journal of Psychiatry*, **111**, 913.

Evans, J. I. (1971) 'Sleep of enuretics.' *British Medical Journal*, **3**, 110.

Pierce, C. M. (1963) 'Dream studies in enuresis research.' *Canadian Psychiatric Association Journal*, **8**, 415.

Ritvo, E. R., Ornitz, E. M., La Franchi, S., Walter, R. D. (1967) 'Effects of imipramine on the sleep-dream cycle: an EEG study in boys.' *Electroencephalography and Clinical Neurophysiology*, **22**, 465.

—— —— Gottlieb, F., Poussaint, A. F., Maron, B. T., Ditman, K. S., Blinn, K. A. (1969) 'Arousal and non-arousal enuretic events.' *American Journal of Psychiatry*, **126**, 77.

Shepherd, M., Lader, M., Rodnight, R. (1968) *Clinical Psychopharmacology*, London: English Universities Press.

Weinmann, H. M. (1968) 'Telemetric recording of sleep rhythms in enuretic children.' *Electroencephalography and Clinical Neurophysiology*, **24**, 391.

Williams, D. I. (1971) Personal Communication.