The clinical significance of disturbed sleep and the use of hypnotics

T. O. CANDLER, F.R.C.S.(Eng.), M.R.C.G.P.
General practitioner, Bideford, North Devon

SUMMARY—This article discusses the causes of sleeplessness and its long-term management. Sleep may be repeatedly disturbed by pain, dyspnoea, micturition, or restlessness. The sleep patterns of the diseases which produce these symptoms are given, with an explanation in physiological terms of why they disturb sleep. A knowledge of these sleep patterns provides a valuable aid to diagnosis. It is concluded that there is only one condition, senility leading to senile dementia, for which long-term night sedation is justified.

Introduction

Acute illnesses disturb sleep. The pain of coronary thrombosis or a whitlow, the dyspnoea of asthma, the delirium of fever, and the hyperactivity of acute mania are so paramount that diagnosis is speedily established, relief provided, and the condition brought under control. The need to promote sleep is short-term, rarely presents difficulty, and is not discussed here.

This paper concerns the chronic and recurrent illnesses that disturb sleep. This is a problem of general practice, and its management is largely empirical. The drugs used tend to produce addiction, and their abuse is causing increasing concern. This paper gives the sleep patterns of some of those disorders which recurrently disturb sleep, and shows how these patterns can be used in differential diagnosis. The sleep patterns described are the patients' subjective impressions, being the only descriptions of sleep available in general practice.

Physiology and pharmacology

In the last 20 years, great advances have been made.[1,8] All-night electroencephalogram recordings have enabled four stages of sleep to be defined: stage one being drowsiness, and stage four ' deep sleep '. The stages occur at definite times of the night. All of us wake one or more times during the night, but this passing from stage one into wakefulness may not reach full consciousness and, especially in the young, will not be remembered. Stage four predominates in the first half of the night and stage one in the second half. During stage one rapid eye movements occur (REM sleep), during which time considerable changes are taking place throughout the body. The best known of these is dreaming, but there is also considerable circulatory activity, shown by rising blood pressure, more rapid and irregular pulse rate, increased cerebral blood flow, irregular and deeper respiration. In the male penile erections occur, these being independent of the content of his dreams. Increased quantities of the pituitary hormones and corticosteroids are found in the blood following a period of REM sleep. Major body movements, such as turning over, may occur. In contrast stage four is remarkably peaceful, the only findings being minor body movements, and demonstrable tone of the voluntary musculature, which is totally absent in REM sleep.

Depriving the body of REM sleep during several nights gives rise to marked personality change, such as irritability, neurosis, aggression and delusions of persecution,

following which, if full sleep is allowed, the body compensates by increasing the amount of REM sleep, which intrudes into the first half of the night at the expense of stage four and the subject may experience nightmares.

Some drugs, and those include most of the commonly prescribed hypnotics, depress REM sleep, and if these drugs are continued nightly for two weeks, the body gradually compensates, and restores the REM sleep to its normal amount. If the drug is stopped at this point there is a rebound effect, with overproduction of REM sleep, often accompanied by nightmares. In the case of alcohol, this rebound effect may be so marked as to break through into consciousness, giving delirium tremens. It has been shown [2] that after giving 15 mgm of nitrazepam (Mogadon) nightly for two weeks, it took 60 days for the rebound effect to wear off, and the all-night sleep profile to return to normal. This, no doubt, in parts account for the difficulty we have in weaning our patients from their hypnotics.

Total deprivation of stage four sleep gives rise to apathy, listlessness, fatigue and depression. Drugs do not appear to influence this sleep, but it is known that sleep-walking occurs solely during it.[8, 10] Exercise in the afternoons increases the amount of stage four sleep.

The average sleep requirements during life change with age. A baby requires 16 hours per 24 hours, waking up only for feeding. Teenagers average nine hours, adults seven or eight hours dropping to five or six hours in old age. These are average times, some requiring more, others less, Churchill's wartime sleep habits being a notable example. Oswald [1] quotes a man keeping fit and active with only three hours sleep per night. Increase above the normal can be achieved by exercise and mental fatigue, but drugs are effective only in the short-term.

Disturbances of sleep

Nocturnal pain

Pain which repeatedly disturbs sleep, is indicative of active disease, usually of a serious nature, requiring accurate diagnosis and treatment.

In the skeletal system, this observation is of great assistance in unravelling the rheumatic aches and pains.

The degenerations, such as osteoarthrosis, vertebral spondylosis, tennis elbow, and burnt-out rheumatoid arthritis do not disturb sleep. The patient may have difficulty in getting off to sleep, and need a pillow under the knee, but once asleep, will stay asleep for his usual quota of time. On waking, his degenerate joints will be stiff and painful until such time as they have been mobilised.

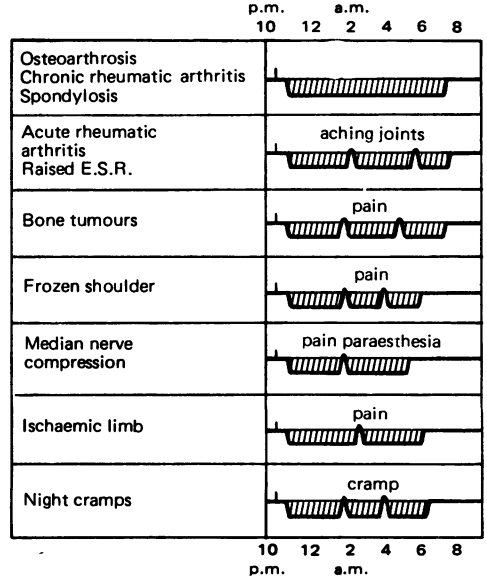

Figure 1
Sleep patterns in some skeletal conditions

In contrast, bone tumours, and secondaries in bone, acute rheumatoid arthritis, and

other conditions with a raised ESR, such as ankylosing spondylitis and polymyalgia rheumatica will give rise to painful nights. The reason is mechanical. Cancer cells, growing in a bony cage, and inflamed joints puffed full with inflammatory exudate cause tension and pain enough to disturb sleep.

Frozen shoulder is usually classified as a degeneration, as the ESR is not raised. The acute phase is painful whenever the joint is moved. There is no effusion present, but inflammation builds up around the joint. Throughout the night, body movements occur, and no matter on which shoulder one lies, or on the back, any movement of the trunk or arm will move the joint, or those muscles that are so involved with the joint. Analgesics may be required to promote sleep, but if hypnotics are prescribed, there is a serious risk of addiction.

Median nerve compression in the carpal tunnel wakes the patient in the small hours with pain and paraesthesiae. Sometimes associated with rheumatoid arthritis of the wrist joint, myxoedema, and toxaemia of pregnancy, most cases have no known cause. It is relieved by immobilising the wrist in a plaster cast at night, and cured by dividing the flexor retinaculum. Why it should disturb sleep is not known. Possibly the horizontal position plays a part causing increased pressure in the subclavian vein, followed by oedema of the arm, but if this were the case, applying a plaster cast would aggravate the condition and not relieve it.

The ischaemic limb is another condition that may disturb sleep. If the block is high in the limb, claudication will probably bring the patient to us, but if it is low in the limb, the foot may reach a pregangrenous stage. At night, when it heats up under the bedclothes, more oxygen is required than the arteries can supply, and pain wakes up the patient. Sleep is promoted by sleeping with the limb cool outside the bedclothes, and by improving the arterial supply, if possible. Analgesics may be required, but I see no need for hypnotics.

Night cramps can be extremely painful and wake the patient up more than once during the night. They are commoner as age advances, and in pregnancy. The cause is unknown. Vitamin B and calcium sometimes help, particularly in pregnancy, but in the elderly, quinine seems to be of most value. Restless legs may delay the onset of sleep, but rarely wake the patient.

In the dyspepsias, night pain is of diagnostic importance; oesophageal reflux and duodenal ulcer disturb sleep, gastric ulcer does not.

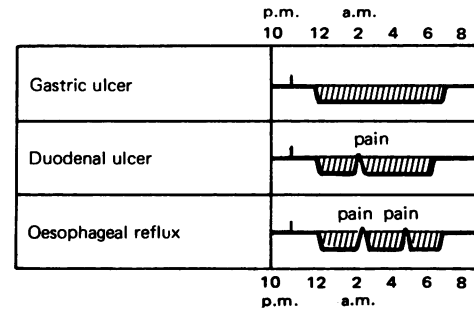

Figure 2
Sleep patterns in some gastrointestinal conditions

It has long been known that the night pain of duodenal ulcer is associated with a high acid curve secreted at night, and relief can be obtained by vagotomy. It has now been established that this acid is secreted during the REM phases of sleep.[10] It does not occur in a normal stomach, or in one with a gastric ulcer. Hypnotics and sedatives, which temporarily inhibit REM sleep, will temporarily improve the night pain, and promote sleep, but after two weeks the body will restore the REM sleep to normal, and the night pain will recur. Withdrawal of hypnotics will give the rebound increase of REM sleep,

with increased pain and loss of sleep. For these reasons, hypnotics should be given sparingly to a duodenal ulcer patient.

In my view the night pain that disturbs sleep is a warning sign that this ulcer is liable to perforate or bleed, and demands proper treatment of the ulcer, if necessary with specialist assistance. It should not be allowed to lumber on in the mouldering morbidity of general practice, dulled by antacids and sedatives.

The night pain which wakes a patient with oesophageal reflux differs in several ways from that in duodenal ulcer. It is substernal, rather than epigastric and, if referred to the back, is higher up the thoracic spine. It is not caused by REM sleep but by the horizontal position, with acid flowing through the lax cardia into the oseophagus. Sleep is promoted by sleeping in a more upright position—difficult to achieve—and a generous supply of antacids or anti-reflux agents, especially at night. Fortunately thoracic surgeons seem prepared to operate on these unfortunate patients more readily than in the past. I do not think hynotics play a part in treatment, and if used, there is a danger of addiction, and of inhalation pneumonia.

Nocturnal dyspnoea

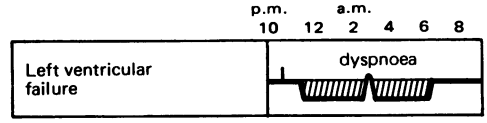

Figure 3
Sleep pattern in left ventricular failure

The first symptom of left ventricular failure may often be waking up at night short of breath. Some patients interpret this as a night cough, while others feel claustrophobic, throw the windows wide open and take gasps of fresh air. Relief is obtained by walking about, or sitting on the edge of the bed with the legs hanging down, so that blood accumulates in the veins, reducing the venous return to the heart. Some old ladies find this out for themselves, and our first indication that they are in LVF is that they sleep all night in their chairs.

The explanation for these attacks occurring during sleep is mainly due to the horizontal position. In this position, the action of the diaphragm is impeded, vital capacity is reduced, and blood pools in the lungs. During the day fluid, which may not be demonstrable as clinical oedema, will have accumulated in the tissue spaces of the legs. In the horizontal position this filters back into the veins. With the reflexes dulled during sleep and a failing left ventricle, oedema of the lungs appears.

This explanation has been given in the textbooks for many years, but it seems to me that the trigger that initiates an attack of LVF might be the arrival of a REM phase, with its great circulatory surge. I can find no articles in the literature to support this, but it has been established that anginal pain, occurring at night in association with ischaemic heart disease, occurs during REM sleep.[10] It seems reasonable to infer, therefore, that nocturnal attacks of left ventricular failure may also be triggered by the arrival of REM phase.

Right ventricular failure does not cause dyspnoea at night, although the horizontal position allows the oedema in the legs to be excreted, waking the patient several times to pass water.

Right and left ventricular failure often merge, blurring the symptoms described above. In both, however, sleep is promoted by resting the ventricles and removing excess fluid. Diuretics by day and an afternoon nap, lying horizontal with the feet up, will do more to give a good night's sleep than hypnotics.

Patients with dyspnoea associated with diseased lung, such as emphysema, and

chronic bronchitis, in my experience do not complain of lack of sleep, and if given hypnotics, respiration may be depressed and CO_2 retention may be induced.

Nocturnal micturition

Getting up several times at night to pass water is one of the classical presenting symptoms of an enlarged prostate.[5] It may also be the presenting symptom of diabetes and right ventricular failure.

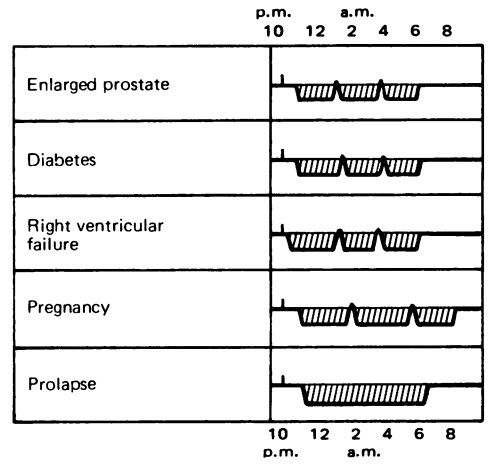

Figure 4
Patterns of nocturnal micturition

In women, the latter stages of pregnancy are renowned for disturbing sleep. Prolapse without infection does not disturb sleep, although the patient will often have to pass water on rising, sometimes with stress incontinence. The reasons for this are essentially mechanical through pressure on the bladder or obstruction at its neck.

It is not possible to evaluate urinary infection in women without the aid of the pathological laboratory, whose report showing the number of pus cells or bacteria present in the urine enables a true cystitis to be distinguished from urethritis. I thought, before starting this investigation true cystitis would disturb sleep, but urethritis might not. This is not so—both may disturb sleep, and each may be present without sleep disturbance. It seems that the acuteness and severity of the infection is the deciding factor, and not the anatomical site.

Enuresis does not usually wake the patient. It has been shown to occur mainly during stage four sleep, although the patient may not wake until the next REM phase, when the wetness of the body may focus the dreams on an enuretic content.[1, 10]

Restless sleep

The elderly

In managing the sleep of the elderly, it is important to realise the amount of sleep required by any individual diminishes as the years go by and at 80 may be as little as five hours.[1, 10] This seems to be independent of the afternoon nap favoured by many old people. In fact if this afternoon rest is carried out for cardiac reasons, a better night's sleep can be expected.

Another point is that the arousal time in the elderly is reduced. Arousal time is that period of time that elapses between the cessation of stage one sleep, i.e. drowsiness, to being fully awake and conscious. Teenagers are often not fully awake until they have finished their breakfast, or even morning coffee, but old people may be wide awake within 15 secs. All of us pass out of stage one into wakefulness one or more times each night, and old people tend to wake more often. With this short arousal time, old people will remember these waking moments. A shorter, more wakeful night is normal for the elderly, and our job as general practitioners is to help our patients to accept this, and not blanket them with hypnotics whose pharmacological action will be neutralised by the body within a few weeks.

As the years go by, the amount of stage four sleep gradually diminishes. With the onset of senility, it becomes fragmented, and disappears completely when senile dementia occurs.[8] This fragmentation of stage four sleep appears ten or more years before there is clinical evidence of senility, so that those of us in their 50s who are experiencing increased forgetfulness, and loss of mental agility will be sorry to learn that the EEG evidence was present in their late 30s and 40s.

In my opinion, senility, with its organic brain degeneration, is the only condition where regular and prolonged night sedation is justified. It must be remembered that a minor disorder, such as a full rectum, mild infection, or anaemia, may give rise to confusion, agitation and restlessness in the elderly, and the choice of the wrong sedative, which interferes with REM sleep, or its sudden withdrawal with the rebound increase of REM sleep, may have similar effects. The modern tranquillisers interfere with the physiology of sleep less than the older hypnotics, and in senility are undoubtedly superior, but they should be used sparingly, and in the smallest effective dose.

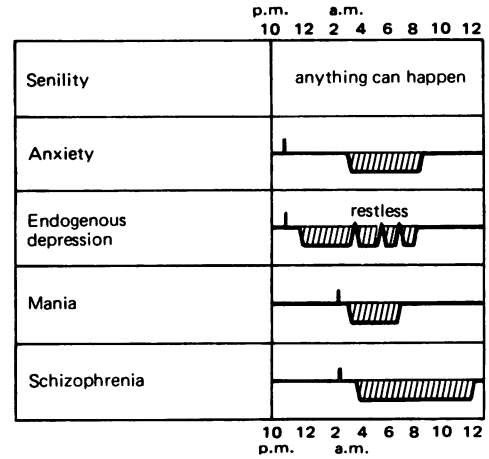

Figure 5
Sleep patterns in psychiatric conditions

Anxiety

Anxiety and reactions to stress are fairly easy to diagnose, and the sleep pattern of difficulty in getting off to sleep adds confirmation. Management of the sleeping problem consists essentially of relieving the anxiety or stress, if one can, but until that is achieved, some night sedation may be required. In acute anxiety, heavy doses of the older hypnotics may be required, but in my view, they should be given, like morphia, from the doctor's bag, for one or two doses. For longer use, newer anti-anxiety drugs, such as diazepam (Valium) and chlordiazepoxide (Librium) are better. They are less addictive, easier to withdraw, and have the added advantage that overdosage is not usually lethal.

Depression

Endogenous depression can be extraordinarily hard to diagnose, the patient concealing misery behind that part of the body that happens to be below par, but the sleep pattern of ease in getting off to sleep, but tossing and turning the second half of the night, is usually present. To my mind, there are only two signs of endogenous depression—the first is tossing and turning in the second half of the night; the second is attempted suicide. The presence of the first should put us on our guard.

Hypnotics have their maximum effect half to four hours after ingestion. Logically they should be given to depressed patients when the patient first wakes, in the middle of the night, but if this is done, drowsiness continues unacceptably into the morning. Before the days of the modern antidepressant drugs, this problem was overcome by giving doses of hypnotics at bedtime, and many of my patients who were so treated are still addicted to large doses of barbiturates.

Modern antidepressant drugs have transformed the treatment of depression, but take time to have their effect—ten days or more before the sleep pattern begins to return to normal—some of them also have a sedative effect. In my experience the sleeplessness of the mildly depressed is best treated by giving the antidepressant drugs mainly at night.

It must be explained that it may be several days before improvement in sleeping can be expected. This is accepted by the patient, and I find no need for hypnotics. In the severely depressed who may be suicidal, there may be a need for heavy night sedation, but these patients should be in hospital.

Mania

With the first attack, mania is usually advanced before it reaches us, by which time it may seem that the patient hardly goes to sleep at all. Late to bed and early rising is the sleep pattern of this disease—three to four hours sleep, or less, being all that is required to rejuvenate these over-active people. This knowledge is useful for the early detection of relapses and I now tell my patients that when the ' late to bed and early rising ' start again, they should come and see me, and not wait until their relatives have to send. It is an instruction they understand and do not resent.

Schizophrenia

Many investigations into the sleeping habits of schizophrenics have been carried out.[11] The general impression is that their sleep differs from normal, but the results are inconclusive. This may be because the surveys have all been carried out in the artificial atmosphere of the psychiatric hospital, and on advanced cases, or perhaps the term schizophrenia includes more than one psychiatric disorder.

In 20 years of general practice, I have had three cases of schizophrenia labelled by the psychiatrist. All of them presented as morning lie-abeds. ' I have to force him to get up and out of bed so as to get him to work on time ' was how one housewife put it. As the withdrawal from the world gradually progressed, his sleep pattern became more abnormal until he was ' mooching around in the living room and kitchen until three in the morning, and not getting up till past lunchtime.' Three cases are not enough on which to generalise, but I suspect that ' late to bed and lie-abed in the mornings ' is the sleep pattern for schizophrenia in the community.

Discussion

A knowledge of those disorders which repeatedly interrupt normal sleep is helpful in diagnosis. Rheumatic aches and pains occupy a large proportion of consultations in general practice and part of the skill is to pick out for full investigation those that conceal serious disease, such as bone tumours. The sleep pattern enables one to do so.

When I first entered general practice, I rapidly discovered that orthopaedic surgeons, if they did not operate on my patients, either put them in plaster, or mobilised them with manipulations and exercises. I found it difficult to understand what factors influenced the surgeon's choice, and he could not always explain it. The answer lies in the sleep pattern, extended to include the first few hours of activity. A good night's sleep, followed by morning pain and stiffness which eases after moving around for an hour or so, will respond to mobilisation. A good sleep, followed by morning pain and stiffness which gets worse on moving around demands immobilisation, while a night repeatedly disturbed by pain demands the fullest investigation. Treatment and investigation can be initiated in general practice, and often concluded without specialist assistance.

Depression conceals and manifests itself in strange ways, but the sleep pattern of tossing and turning the second half of the night is usually present, as the following case demonstrates:

Mrs S. aged 52. Housewife. She complained that her rheumatism had started waking her at night. I knew she had a degenerated lumbar disc, and early osteoarthrosis of the hip, and thought it unlikely that anything fresh had occurred. Enquiry showed that she went to sleep all right, but woke up three or four times in the second half of the night, with pain in her hip. This pattern, without the pain, is typical of endogenous depression. She was given amitriptyline 25mg (Tryptizol) each night. She reported that improvement began after taking the ' sleeping tablet ' for ten nights, and had cleared in two weeks. Asked about her rheumatism, she replied that she still had that when she got up in the morning, but her exercises soon cleared the stiffness and pain.

This case illustrates how depression may lurk behind a simple malady, causing disturbed nights, which disturbed rheumatic joints which then hurt. It also shows that a small dose of an antidepressant each night in the mildly depressed can restore sleep, but it has to be given for at least ten days before relief occurs. The patient must be warned of this, or she will cease to take them. There is no need in these early cases for the three times a day routine. Provided the sleep has improved, it seems reasonable to give the antidepressant for six weeks. They are non-addictive, and there is no difficulty in weaning the patient.

Depression in children is being increasingly diagnosed. I have recently had two cases. A child aged ten developed a behaviour disorder at home and at school. He went through the paediatrician to the child guidance clinic, and improvement did not begin until antidepressants were started. After a month the mother, who was a nurse, volunteered that his bed was now much easier to make, just pulled straight, whereas before it had been in a great tangle each morning.

The second child, aged five, had for two years woken up in the small hours, and mother had had to get up and go to the child's bedroom and comfort her for three quarters of an hour. On questioning, mother stated the child was a restless sleeper, and the bed had to be completely remade each morning. After amitriptyline 10mg each night for a fortnight, they had their first unbroken sleep and, after a further month, there were no more tangled bedclothes.

Two cases are not enough on which to generalise, but restless sleep in children, as shown by tangled bedclothes, may be a sign of depression.

Long-term night sedation can only be justified in those unfortunate patients with organic degeneration of their brain cells—the senile and the senile dements. The vast number of patients who attend every month to collect their supply of sleeping tablets is a monument to our failure to understand and treat their problems—or to just bad doctoring.

This counsel of perfection is indeed hard to achieve. In 1968, I resolved not to allow any ' new ' patients to become hooked on hypnotics, but in four years, eight have done so. Apart from one who took the sleeping tablets prescribed for his demented wife, delay in diagnosis was the deciding factor.

Mr W. aged 59. Teacher. In 1956, he had a partial gastrectomy for gastric ulcer. In 1964, he developed chronic iron-deficiency anaemia, due to failure to absorb iron, and has been on parenteral iron ever since. In 1969, he started feeling unwell, with vague aches and pains and lassitude. Clinical examination was negative. The extensive investigations produced a mass of normal tests, the orthopaedic surgeon manipulated his cervical spondylosis with no benefit, until finally, after two years, evidence of malabsorption was found. During this time, he demanded treatment, which had to be symptomatic. He knew we did not know what was the matter with him. He worried, became depressed, and did not sleep. With the help of locums, rota doctors and several trips to hospital, he became hooked on nitrazepam (Mogadon).

Mrs M. aged 67. Housewife. She was always inclined to send for a doctor rather more often than she should. In 1968 she came to see me, or sent at unusual times with increasing frequency. She usually complained of cough, headache, rheumatism or just fatigue. A colleague thought she had myxoedema, and twice went through all the thyroid and many other tests, with normal results. After two years, she suddenly said ' I know what the matter with me is, and as my doctor you ought to know. Its my husband —he's a terrible man, etc.' Again it took two years before her problem was understood, during which time she was treated symptomatically. She is now hooked on nitrazepam (Mogadon), and applies every month for her regular supply. We rarely see her, although she still lives with her husband—a classic example of what Michael Balint *et al.*[13] called the ' peaceful repeat prescription.'

Conclusions

All of us have, from time to time prescribed an analgesic for a pain without making a proper diagnosis, but should that pain persist, we would feel negligent if a full investigation were not carried out.

Failure to sleep should be viewed in a similar manner. No longer should one be

content to treat a symptom empirically with prescriptions repeated every month. Every symptom has a differential diagnosis. This article attempts the differential diagnosis of disorders that chronically disturb sleep.

Acknowledgements

My thanks are due to my colleagues, Drs D. Barlow, M. George and T. A. Medway for their helpful criticism and suggestions, and to Mrs M. Raymont for her secretarial assistance.

REFERENCES

1. Oswald, I. (1970). *Sleep*, Harmondsworth: Penguin Books.
2. Oswald, I. & Priest, R. G. (1965). *British Medical Journal*, **3**, 1095.
3. Hillman, H. (1972). *Update*, **5**, 690–706, 867–880, 1309–1318.
4. Seiler, E. R. (1972). *Practitioner*, **208**, 271–276.
5. Southwell, P. R., Evans, C. R. & Hunt, J. N. (1972). *British Medical Journal*, **2**, 429–431.l
6. Brezinova, V. & Oswald, I. (1972). *British Medical Journal*, **2**, 431–433.
7. Johnson, I. & Clift, A. D. (1968). *British Medical Journal*, **4**, 613–617.
8. Segal, L. & J. *Insomnia.*
9. Simpson, R. G. (1969). *Practitioner*, **202**, 259–268.
10. Kales, A. & Kales, J. (1970). *Journal of the American Medical Association*, **213**, 2229–2235.
11. McGhie, A. (1966). *British Journal of Psychiatric Medicine*, **39**, 221.
12. McGhie, A. & Russell, S. M. (1962). *Journal of Mental Science*, **108**, 642–644.
13. Balint, M., Hunt, J., Joyce, D., Marinker, M. & Woodcock, J. (1970). *Treatment or diagnosis.* London: Tavistock Publications.