ferences between patients treated at home or in hospital, by day or at night. Furthermore, the accumulation of metabolites between dialyses has no apparent effect on this measure.

The findings concerning home dialysis are of particular importance, since the spouse provides one form of control. It is seen that on dialysis nights both patients and spouses lose sleep, but the patients regain their "sleep debt" more than their spouses on non-treatment nights. This suggests a psychological rather than a metabolic cause of insomnia on dialysis. It would add to the evidence showing stress on families of patients being treated with dialysis, particularly where the treatment is conducted in the home. This stress on the spouse would seem understandable in terms of their feelings about the patient's illness, and having responsibility for operating a complex life-support system. But, obviously, other criteria must be considered in deciding on the location for treatment—for example, the additional time the home dialysis patient spends with his family.

Regarding the reliability of these data, Lewis (1969) investigated the accuracy of subjective estimates of sleep with objective (E.E.G.) recordings. He showed that, though subjects are not accurate in their estimates of the quantity of sleep, their estimates do shift in the direction of the objective measures. Thus they are reliable indices of change of sleep. Furthermore, in this study the data from patients in two geographically separate treatment centres showed no significant differences whereas there were significant differences between spouses and patients.

We wish to thank the Directors of the Dialysis Units, Dr. J. S. Robson in Edinburgh and Dr. B. H. Robinson in Birmingham, for permission to study patients under their care. We also acknowledge the criticism and advice of Drs. S. A. Lewis and D. H. Morgan, of the departments of psychiatry at the Universities of Edinburgh and Birmingham respectively.

The study was supported in part by S.H.E.R.T. Grant.

REFERENCES

Gonzalez, F. M., Pabico, R. F., Brown, H. W., Maher, J. F., and Schreiner, G. E. (1963). *Transactions. American Society for Artificial Internal Organs*, **9**, 11.
Lewis, S. A. (1969). *British Journal of Psychology*, **60**, 203.
Menzies, I. C., and Stewart, W. K. (1968). *British Medical Journal*, **1**, 544.
Passouant, P., Cadilhac, J., Baldy-Moulinier, M., and Mion, C. (1967). *Revue Neurologique*, **117**, 525.
Schreiner, G. E. (1959). *Medical Annals of the District of Columbia*, **28**, 316.
Siegel, S. *Non-parametric Statistics for the Behavioural Sciences*, New York, McGraw-Hill, 1956.
Shea, E. J., Bogdan, D. F., Freeman, R. B., and Schreiner, G. E. (1965). *Annals of Internal Medicine*, **62**, 558.
Tune, G. S. (1968). *Ergonomics*, **11**, 183.
Tune, G. S. (1969). *British Journal of Industrial Medicine*, **26**, 54.

# Sleep Habits and Symptoms in Male Medical and Surgical Patients

M. W. JOHNS,* M.B., B.S., B.SC. ; P. EGAN,† ; T. J. A. GAY,‡ B.MED.SC. ; J. P. MASTERTON,§ M.B., DIP.OBST., F.R.C.S.

*British Medical Journal*, 1970, 2, 509–512

**Summary: A questionary survey of symptoms and sleep habits at home among 100 adult male medical and surgical patients showed that the duration of sleep at night was similar to that reported for the general population, decreasing with age from 20 to 50 years and increasing again after 60 years. The duration of daytime sleep increased with age. The degree of sleep disturbance in different patients was compared in terms of the total duration of sleep and the time spent lying awake in bed at night. Increasing age, ischaemic heart disease, and neurotic illness were the main factors associated with long-term disturbances.**

## Introduction

One of the oldest and most widely used therapeutic manœuvres in medicine is to put the patient to bed, to rest, and, in particular, to sleep. Disturbances to sleep are known to be common among psychiatric patients, particularly in those suffering from anxiety and depression (McGhie, 1966; Hawkins and Mendels, 1968), but surprisingly little is known about the sleep habits of patients in different age groups who have physical symptoms. Rudolf (1955) studied the sleep of small groups of patients treated by physicians at home and in hospital, using daily records of the hours of sleep. He suggested that patients with cardiovascular disease slept less than those with gastrointestinal, genitourinary, or respiratory disease. The few patients investigated and the absence of a detailed description of symptoms made this conclusion only tentative. Weiss *et al.* (1962) found that chronic sleep disturbances, as reported in a sleep questionary, increased with age in groups of psychiatric patients, medical patients, and healthy airforce personnel. The psychiatric patients had significantly more sleep disturbance than the medical patients, who did not differ significantly from the healthy controls. Neither the symptoms nor the diagnoses of these patients were described.

A sleep questionary was used to describe a pattern of increasingly disturbed sleep with age in healthy adults in Scotland (McGhie and Russell, 1962), and Monroe (1967) showed that different subjective responses to such a sleep questionary by "good" and "poor" sleepers reflect objective differences in sleep measurements. Lewis (1969) suggested that individual subjective reports about a night's sleep tend to underestimate the total sleep time and overestimate the delay to sleep onset as measured by electroencephalographic methods in a sleep laboratory. Nevertheless, the overall correlation between subjective and objective reports of sleep measurements in Lewis's study was significant and justified the use of subjective reports to compare sleep habits in groups of people.

We have designed a questionary to study the usual pattern of sleep in male patients admitted to the general medical and surgical wards of a large teaching hospital in Melbourne. This paper deals with changes with age in the sleep habits of such patients when they are at home as well as the relation between their sleep disturbances and physical and psychological symptoms.

## Methods

*Questionaries.*—The sleep questionary consisted of 28 questions relating to most subjective aspects of an average night's sleep. A range of possible answers was provided from which the patients selected the most appropriate. Detailed information about physical illness and symptoms as well as a rating for neurotic illness was provided by the male version of the Cornell Medical Index (C.M.I.) Health Questionnaire (Brodman *et al.*, 1949; Culpan *et al.*, 1960). This is a self-

*Research Fellow.
†Medical Student.
‡Research Student.
§Associate Professor of Surgery.
Department of Surgery, Monash University, Melbourne, Australia.

administered questionary divided into 18 sections dealing with different physical and psychological symptoms and historical data (see Table III). The relationships between age, symptoms, and various sleep measurements were analysed by means of Student's *t* test, product-moment correlation coefficients, and partial correlation coefficients. Statistical significance was accepted at the 0·05 probability level in a two-tailed test.

*Selection of Patients.*—Patients were selected over a three-week period from the general medical and surgical wards of the Alfred Hospital, a teaching hospital where the mean duration of patient admission is about 10 days. Questionaries were handed out to 137 patients on the basis of their being well enough and co-operative enough to sit up and write the answers to the 223 questions embodied in the two questionaries. One hundred patients returned completed questionaries. No attempt was made selectively to include or exclude any particular diagnostic group of patients. Forty-seven occupied medical beds and 53 were in surgical beds. Their diagnoses covered a wide range of those to be found in general medical and surgical wards of a teaching hospital—from carcinoma of the larynx to appendicitis, and from haemophilia to myocardial infarction. Their ages ranged from 15 to 83 years. The frequency distribution of ages is shown in Table I. Before coming into hospital all patients had been ambulant for most of the day at least. None was receiving psychiatric treatment at the time, though a few had done so in the past.

TABLE I.—*Frequency Distribution of Ages of Patients Studied*

| Age in years | 15–19 | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70+ |
|---|---|---|---|---|---|---|---|
| No. of patients | 6 | 15 | 10 | 17 | 24 | 18 | 10 |

## Results

### Variations in Sleep Habits with Age

The results are summarized in Table II. Elderly patients went to bed earlier but took longer to fall asleep than young patients. On weekdays there was little change with age in the time of finally waking up in the morning, but the delay before getting out of bed increased with age. Most men, especially the younger ones, went to bed later at weekends, woke up later the next morning, and lay awake in bed longer at weekends than on weekdays.

Both the frequency and the duration of awakenings during the night increased with age. Difficulty in getting back to sleep was closely related to difficulty in getting to sleep initially. The commonest reasons for waking up during the night were nocturia (34 patients), "unknown reasons," and "nervous tension." A few patients woke up regularly because of dyspnoea, cough, leg pain, noise, or dreams. No patient in this series reported waking up frequently because of chest or abdominal pain, though a few had been awakened occasionally this way. Thirty-nine patients reported sleeping during the day at some time during the average week. The frequency and duration of daytime sleep increased with age, and this almost compensated for the sleep which each age group tended to lose owing to awakenings during the night (Table II).

The use of hypnotics increased with age, so that one in five of the patients over 50 years took them regularly. Only 15 of the 31 patients who took hypnotics frequently or occasionally could give information about the type of tablet, the commonest ones named being barbiturates (nine patients), of which amylobarbitone was the single drug most often used. Three patients took aspirin as a hypnotic rather than as an analgesic.

The mean total duration of sleep for all patients was 53·7 hours per week (standard error 1·15 hours). The lowest individual amount reported was 21·5 hours and the highest 88·9 hours per week. The relation between age and the total duration of sleep per week, night sleep per week, and the total number of hours spent in bed at night per week is shown in Fig. 1. The total sleep and night sleep decreased from 15-19 years to a minimum at 50-59 years and then rose again after 60 years. The duration of night sleep, but not that of total sleep, was significantly less at 50-59 years than at either 20-29 years or 60-69 years. The increasing difference with age between night sleep and total sleep reflects the increasing amount of daytime sleep in older age groups. The total time spent in bed at night (either asleep or awake) fell gradually to a minimum at 50-59 years, and then rose fairly steeply.

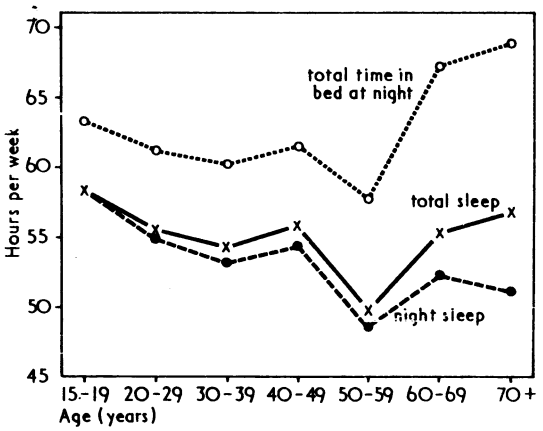


FIG. 1.—Mean duration, in hours per week, of night sleep, total sleep, and total time spent in bed at night at different ages.

All of the patients in the present series who usually slept less than a total of 35 hours per week complained of sleep disturbance, and many of those who slept between 35 and 55 hours per week also felt sleep-deprived, particularly if they lay awake in bed at night unable to sleep. Sleep disturbance in any particular patient may be due to long delay before getting off to sleep initially, to frequent awakenings and delay

TABLE II.—*Variations with Age in the Sleep Habits of Male Patients*

| Sleep Habits | Age in Years | | | | | | | Correlation with Age (r) | Statistical Significance (P) |
|---|---|---|---|---|---|---|---|---|---|
| | 15–19 | 20–29 | 30–39 | 40–49 | 50–59 | 60–69 | 70+ | | |
| Time of going to bed on weekdays (p.m.) | 10·0 | 11·15 | 10·15 | 10·05 | 10·10 | 10·00 | 9·15 | −0·36 | <0·001 |
| Time of going to bed at weekends (a.m.: p.m.) | 12·25 | 12·15 | 10·45 | 10·55 | 10·50 | 10·15 | 9·50 | −0·57 | <0·001 |
| Time of falling asleep on weekdays (p.m.) | 10·20 | 11·40 | 10·45 | 10·30 | 10·40 | 10·25 | 10·20 | −0·26 | <0·01 |
| Time of falling asleep at weekends (a.m.: p.m.) | 12·50 | 12·40 | 11·10 | 11·20 | 11·20 | 10·40 | 10·55 | −0·41 | <0·001 |
| Time of morning awakening on weekdays (a.m.) | 7·0 | 7·0 | 6·30 | 6·30 | 6·15 | 6·30 | 6·15 | −0·17 | N.S. |
| Time of morning awakening at weekends (a.m.) | 8·30 | 9·0 | 7·0 | 7·30 | 6·45 | 6·55 | 6·30 | −0·39 | <0·001 |
| Delay before getting up on weekdays (minutes) | 14 | 18 | 23 | 20 | 12 | 28 | 56 | +0·21 | <0·05 |
| Delay before getting up at weekends (minutes) | 33 | 42 | 40 | 33 | 28 | 46 | 55 | −0·03 | N.S. |
| Number of night awakenings per week | 1·4 | 0·7 | 2·6 | 4·0 | 4·2 | 11·0 | 8·5 | +0·33 | <0·001 |
| Total duration of night awakenings (hours per week) | 0·3 | 0·3 | 2·0 | 2·0 | 3·7 | 5·1 | 5·3 | +0·36 | <0·001 |
| Total duration of daytime sleep (hours per week) | 0·0 | 0·1 | 1·0 | 0·8 | 0·9 | 3·1 | 3·2 | +0·40 | <0·001 |

before getting back to sleep during the night, to early morning awakening, or, as is often the case to a combination of these factors, each of which increases with age. A single measurement—the total time spent lying in bed awake at night, which includes each of these three factors—can be used, along with the duration of sleep, to compare the degree of sleep disturbance in different patients. The total time spent lying awake in bed at night, and hence the degree of sleep disturbance, increased progressively with age ($r = +0.266$, $P<0.01$; Fig. 2).

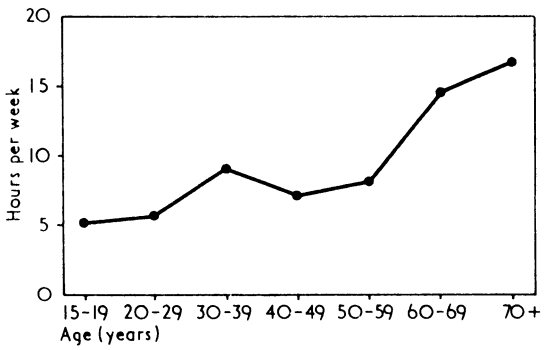


FIG. 2.—Number of hours per week spent lying awake in bed at night at different ages.

## Variations in Symptoms with Age

There were significant increases with age in the number of symptoms of eye and ear disease and of cardiovascular and genitourinary disease. By contrast, the number of symptoms referable to the nervous system decreased with age. The latter symptoms were mainly of functional illness, such as headaches, stammering, and feeling of faintness. None of the scores in other C.M.I. sections changed significantly with age.

## Symptoms and Sleep Disturbances

The relationships, as indicated by partial correlation coefficients, with constant age, between the number of "yes" answers in each section of the C.M.I. and various measurements of sleep in hours per week are shown in Table III. The duration of night sleep was significantly reduced at all ages when there were many cardiovascular symptoms. Day sleep increased in such patients, but this did not entirely compensate for lost night sleep, so their total sleep was also reduced. There was a highly significant correlation between cardiovascular symptoms and increased amounts of time spent in bed awake at night. The total time in bed at night, both awake and asleep, was not significantly correlated with scores in any of the C.M.I. sections. There was therefore a statistical association between cardiovascular disease and sleep disturbance.

Some patients reported frequent night awakenings but did not suffer from significant loss of sleep. They were usually able to get back to sleep quickly after waking during the night and generally obtained more daytime sleep than average. This was so with nocturia as a result of prostatomegaly and with dyspnoea as a result of bronchial asthma. Musculoskeletal symptoms were associated with increased day sleep, but not with significant disturbance to night sleep. Symptoms of nervous origin and a feeling of fatigue were associated with decreased amounts of night sleep without a compensatory increase in day sleep. Patients with these symptoms obtained less sleep overall and spent more than the average amount of time awake in bed at night. Those who lay awake in bed at night for many hours also reported greater frequency of illness of various kinds (J section, Table III). In section L, relating to habits, which is specially concerned with the use of tobacco and alcohol, decreased amounts of regular exercise and difficulty in getting off to sleep, the number of "yes" answers was correlated with the time in bed awake at night. The number of psychological symptoms as indicated by the score in C.M.I. sections M-R was not significantly correlated with any of the sleep measurements. The total C.M.I. score (sections A-R), which gives an indication of neurotic illness, was related to increased time awake in bed at night.

TABLE III.—*Partial Correlation Coefficients, with Age Constant, between Symptoms Relating to Particular Bodily Systems and Sleep*

| C.M.I. Section | Partial Correlation Coefficient Between Number of "Yes" Answers in C.M.I. Section and Hours per Week of | | | |
|---|---|---|---|---|
| | Night Sleep | Day Sleep | Total Sleep | Time Awake in Bed at Night |
| A, Eyes, Ears | O | O | O | O |
| B, Respiratory | O | O | O | O |
| C, Cardiovascular | − | ++ | − | +++ |
| D, Digestive | O | O | O | O |
| E, Musculoskeletal | O | +++ | O | O |
| F, Skin | O | O | O | O |
| G, Nervous System | − − | O | − | ++ |
| H, Genitourinary | O | O | O | O |
| I, Fatigability | − − | O | − − | +++ |
| J, Frequency of Illness | O | O | O | ++ |
| K, Miscellaneous Diseases | O | O | O | O |
| L, Habits | O | O | O | + |
| M–R, Mood and Feelings | O | O | O | O |
| Total A–R | O | O | O | + |

O .. $r<0.197$, N.S.
+/− .. $r=0.197-0.257$, $P<0.05$.
++/− − .. $r=0.257-0.324$, $P<0.01$.
+++/− − − .. $r>0.324$, $P<0.001$.

## Discussion

The pattern of sleep at home in this sample of Australian male patients was very similar to that described for "healthy" adults in Great Britain (McGhie and Russell, 1962; Tune, 1968, 1969). The mean duration of total sleep per week for 240 men and women in Scotland, as determined by daily subjective reports for eight weeks, was 53·2 hours (Tune, 1968) and compared with 53·7 hours per week in the present study. The variation in total sleep with age, decreasing to a minimum at 50-59 years and then increasing again after 60 years, was the same as that derived from daily reports (Tune, 1968, 1969) as well as from detailed electroencephalographic studies (Webb and Agnew, 1968). The validity of both subjective methods of obtaining information about sleep habits (daily records and sleep questionaries) would seem to be enhanced by these results. The overall similarity between patients and "healthy" subjects in most aspects of both their sleep habits and their use of hypnotics also suggests that for most of the patients in the present study the presence of physical symptoms did not of itself produce much long-term disturbance from the "normal" pattern of sleep, a conclusion similar to that of Weiss *et al.* (1962).

The total duration of sleep may vary from day to day, especially in young adults, but is much more constant in any individual when considered over a week. In the present study, particularly in men under 40 years, those who slept less than the average amount on week nights slept significantly longer than average at weekends, and vice versa. The overall effect was for each group to approach more closely the mean amount of sleep for the whole week at that age. It would seem preferable, therefore, to describe sleep duration in terms of hours per week, as in this study, rather than hours per 24 hours.

After middle age there is a steady increase in the amount of daytime sleep and a decrease in night sleep, despite an increased time in bed at night. This is due to increasing disturbance to sleep with age—increased delay in getting off to sleep, more frequent and longer awakenings during the night, and earlier morning awakening. The change is very prominent in patients with chronic brain syndrome (Feinberg, 1967). In some respect this represents a gradual return to the polyphasic pattern of sleep seen in children, presumably as a result of degenerative changes in the central nervous system.

The present analysis of symptoms and sleep disturbances showed that men with chronic symptoms of cardiovascular disease (particularly ischaemic heart disease), as well as those complaining of multiple physical symptoms as a result of neurotic illness, have significantly increased degrees of sleep disturbance at all ages. This is manifested in the reduced duration of sleep and increased time spent awake in bed at night. As a diagnostic group the patients with ischaemic heart disease reported the most sleep disturbance. Some of these patients had evidence of significant neurotic illness, presenting as anxiety, depression, or multiple minor complaints which often follow acute episodes of heart disease. They may also have had a disorder of their sleep mechanisms as part of a more widespread disorder of their diurnal rhythms which is manifested, for example, in decreased or absent diurnal variation in plasma corticosteroid concentrations (Knapp, 1969).

As was suggested by Weiss *et al.* (1962), gastrointestinal, genitourinary, musculoskeletal, and respiratory symptoms alone did not usually cause significant long-term sleep disturbance, though there may be exceptions to this. When such symptoms were also associated with neurotic illness, however, they tended to be associated with sleep disturbance. It is not possible to say whether any of the symptoms arose as a result of long-term sleep deprivation.

We thank Professor H. A. F. Dudley for help in the preparation of this paper.

Requests for reprints should be addressed to Dr. M. W. Johns, Department of Surgery, Monash University Medical School, Commercial Road, Prahran, Victoria 3181, Australia.

REFERENCES

Brodman, K., Erdmann, A. J., Lorge, I., and Wolff, H. G. (1949). *Journal of the American Medical Association*, **140**, 530.
Culpan, R. H., Davies, B. M., and Oppenheim, A. N. (1960). *British Medical Journal*, **1**, 855.
Feinberg, I. (1967). *Research Publications, Association for Research in Nervous and Mental Disease*, **45**, 211.
Hawkins, D. R., and Mendels, J. (1968). *American Journal of Psychiatry*, **123**, 682.
Knapp, M. S. (1969). *Journal of the Royal College of Physicians of London*, **3**, 398.
Lewis, S. A. (1969). *British Journal of Psychology*, **60**, 203.
McGhie, A. (1966). *British Journal of Medical Psychology*, **39**, 221.
McGhie, A., and Russell, S. M. (1962). *Journal of Mental Science*, **108**, 642.
Monroe, L. J. (1967). *Journal of Abnormal Psychology*, **72**, 255.
Rudolf, G. de M. (1955). *Medical Press*, **233**, 324.
Tune, G. S. (1968). *British Medical Journal*, **2**, 269.
Tune, G. S. (1969). *British Journal of Medical Psychology*, **42**, 75.
Webb, W. B., and Agnew, H. W., jun. (1968). *Progress in Clinical Psychology*, **8**, 2.
Weiss, H. R., Kasinoff, B. H., and Bailey, M. A. (1962). *Journal of Nervous and Mental Disease*, **134**, 528.

# Use of Vaccinia Virus in the Treatment of Metastatic Malignant Melanoma

I. HUNTER-CRAIG,* M.A., M.CHIR., F.R.C.S. ; K. A. NEWTON,† F.R.C.P., F.F.R.

G. WESTBURY,‡ M.B., F.R.C.S., M.R.C.P. ; B. W. LACEY,§ M.D., F.R.C.PATH., F.I.BIOL.

*British Medical Journal*, 1970, 2, 512–515

**Summary: Of 19 patients with proved metastases from malignant melanoma treated by inoculations of smallpox vaccine, intradermal deposits disappeared completely in six out of ten cases. Five of these remained well 2 to 22 months after initial treatment. The response was limited strictly to the site of inoculation. The mechanism of action of vaccinia virus in malignant melanoma is not clear.**

## Introduction

It has been known for many years that viruses might inhibit the growth of malignant tumours. DePace (1912) aroused interest in the clinical use of viruses with his description of a woman who gained remission of her cervical carcinoma following rabies vaccination for a dog-bite. Since then various workers using live virus have attempted to reproduce this effect, though mostly with negative results, and Southam and Moore (1952) have stressed the great obstacles to any practical use of viruses.

Pack (1950) suggested that rabies vaccine might inhibit the course of malignant melanoma. Other workers have used standard smallpox vaccine (vaccinia virus) in malignant melanoma, and have reported regressions of both cutaneous and visceral lesions (Burdick, 1960; Belisario and Milton, 1961; Burdick and Hawk, 1964; Milton and Lane Brown, 1966). We report our experience with vaccinia virus in the treatment of selected cases of malignant melanoma.

## Method

As a rule small cutaneous lesions were cleaned with spirit, allowed to dry completely, smeared with smallpox vaccine (Lister Institute sheep lymph containing about $2 \times 10^8$ pock-forming units per ml.), and either scarified or pricked repeatedly with a needle. Sometimes the vaccine was injected into the lesion with a Pan Jet‖ adjusted to deliver 0·1 ml. per shot intradermally. Bulky cutaneous lesions, subcutaneous deposits, and on one occasion a lymph node metastasis were infiltrated with up to 3 ml. of a one in three dilution of vaccine from a tuberculin syringe. Informed consent was obtained from the patients undergoing this procedure.

One patient was inoculated intravenously with about $2 \times 10^8$ pock-forming units of sheep-derived vaccinia virus kindly supplied by Dr. H. G. S. Murray (Lister Institute). This preparation had been freeze-dried with sorbitol and

* Consultant Surgeon, Redhill Group of Hospitals, Redhill, Surrey.
† Consultant Radiotherapist, Westminster Hospital, London S.W.1.
‡ Consultant Surgeon, Westminster Hospital, London S.W.1.
§ Professor of Bacteriology, Westminster Hospital, London S.W.1.

‖Available from Schuco International London Ltd., Halliwick Court Place, Woodhouse Road, London N.12.