our study concerned only a limited type of schizophrenic illness must be borne in mind when considering its significance.

Summary

A clinical trial is described in the use of acepromazine maleate (notensil) in chronic schizophrenia.

The drug has a limited value.

Side-effects (hypotension and epilepsy) were observed.

The difficulties of making this kind of trial objective are described. The importance of the standard of the placebo is stressed.

We are grateful to Messrs. Bengers for supplying notensil tablets and placebo and for help with the statistical and secretarial facilities. We are grateful also to Mr. R. Bevan, senior psychologist, Hellingly Hospital, and to Mr. P. Slater, of the statistical department of the Institute of Psychiatry, for carrying out a statistical assessment and giving us advice on these matters. In the clinical field we are indebted to many of the staff of Hellingly Hospital, and particularly to our medical superintendent, Dr. David Rice, for having made this study possible.

APPENDIX

Summary of Analysis of Variance (Doctors' Rating Scale—Symptoms)

Source of Variance	Sum of Squares	D.F.	Mean Square Variance
Total variance	1,173.47	151	
Between persons	766.97		
" treatments (treatment/control)	7.17	1	
" sexes	24.17	1	
Sex/treatment interaction	43.00	1	
Residual variance between subjects	692.63		
Variance between trials (first/final)	35.06	1	
Treatment/trial interaction	17.11	1	17.11
Sex/trial interaction	2.95	1	
Sex/treatment/trial interaction	0.90	1	
Residual error	350.48	72	4.868

$$F = \frac{17.11}{4.868} = 3.515. \quad 0.10 > P > 0.05 \text{ on a two-tailed test.}$$

The difference is in the expected direction, that of improvement, but it does not reach a high level of significance.

Summary of Analysis of Variance (Nurses' Rating Scale—Behaviour)

Source of Variance	Sum of Squares	D.F.	Mean Square Variance
Total variance	2,225.26	151	
Between persons	1,831.26		
" sexes	182.48	1	
" treatments	0.94	1	
Sex/treatment interaction	4.95	1	
Residual variance between subjects	1,459.47	72	
Variance between trials	46.42	1	
Treatment/trial interaction	6.74	1	6.74
Sex/trial interaction	1.02	1	
Sex/trial/treatment interaction	0.21	1	
Residual error	339.61	72	4.717

$$F = \frac{6.74}{4.717} = 1.429 \text{ (non-significant).}$$

The assessment showed that, using this method, there was no significant change in the nurses' rating of behaviour following acepromazine therapy.

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DISTURBED RELAXATION OF LIMBS

BY

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In a few individuals relaxation of limbs in the sitting or recumbent positions, or during sleep, is repeatedly interrupted by a train of motor and sensory disturbances. Though the legs are chiefly affected, occasionally the arms also participate in this disorder. These phenomena can be promptly abolished by suspending relaxation and engaging the affected limbs in active movements, and this latter feature constitutes the chief diagnostic touchstone. According to the nature of the main symptom engendered by relaxation, several groups can be recognized, but certain general features apply to most cases.

General Features

After its onset in early adult life, the disorder persists for many years, during which it remains subject to marked fluctuations without ostensible cause. While the distribution is usually bilateral, occasionally only one limb may be affected. Typically the symptoms supervene after relaxing in an easy-chair in the evenings, when travelling, at the theatre or cinema, or when reading or watching television. The symptoms constantly reappear after a period of untrammelled relaxation of the limbs, a period which varies according to the severity of the case. Only by assuming the erect position or by walking can these symptoms be made to disappear completely for a time. The malady shows a pronounced heredo-familial incidence in an appreciable proportion of cases. Pregnancy and anaemia tend to exert a strong aggravating influence. If the testimony of the patient's spouse is available, one often learns that some twitching and jerking of the legs occurs during sleep. This can be of such frequency and severity as to be very disturbing to the other occupant of the double bed.

Cases fall into the following groups according to the nature of the main symptoms: myoclonus, pain and myoclonus, pain, "sleep-pain," and "restless legs."

Myoclonus Group

A sudden, quick, localized muscle contraction, with or without a movement of the limb, occurs in the legs under the provocative conditions mentioned. The myoclonus is apt to recur in the same situation again and again until the sequence is broken by activity, yet on another occasion a totally different group of muscles may be affected in a similar manner.

Case 1.—A woman aged 39 had for the past 11 years, after relaxing in an easy-chair in the evenings, been subject to sudden recurring muscle twitches, mainly in the left leg—"even in the middle of reading an absorbing book or watching the Mount Everest film." These muscle contractions, which may affect any muscle group of the legs, could be felt and seen; though powerful, they only rarely caused movements of the limbs. Occasionally the resulting jumping of the limb resembled a "knee-jerk." This disorder affected her particularly in bed when about to go off to sleep. Though the jerking "banished sleep," it nevertheless continued to recur at short intervals. She had to remain standing for at least 15 minutes to break the sequence. A shorter period would not suffice, since on returning to bed the muscle twitching reappeared almost at once. She learned to recognize a "non-relaxed sensation"

in the inner groin as a prelude to and concomitant of the myoclonus. While this sensation endured, any handling or touching of the affected limb was apt to "send up a sensation in the groin and might be followed by a jerk." Occasionally myoclonus in her sleep caused her to awaken. Her brother was similarly affected, and often "had to watch television standing up." Her father used to say: "I can't keep my legs still." She recalled that her mother "used to have bad nights because dad could not keep still."

Case 2.—A woman aged 28 said she had "involuntary jumpiness when I sit down and relax." Her legs were affected more than her arms. "My husband says that I am jumping all night in my sleep." A few slight episodes occurred during the past five years, but myoclonus became of disabling degree during her two pregnancies. She was "in an exhausted state at nights" during the first pregnancy, since myoclonus interfered with sleep. "I should imagine if you get it badly you'd commit suicide."

Case 3.—This patient, a woman aged 70, said that, for the past 40 years, if she didn't do anything and sat in the chair or lay down "my legs keep jumping—I must then get up." For the past six months she had similar "jumping" in the arms. Myoclonus became such a hindrance to sleep five years ago that she was given morphine. "If I were to leave off tablets I would get no rest at all."

Case 4.—A man aged 48 said, "After resting I feel as if I am a syringe, and I am sucking up something from the bottom of the legs; this makes my legs kick." Unless he got up and walked about, the myoclonus recurred in precisely the same manner every 30 seconds. Of necessity this interfered with his sleep, and he had to give up driving because, as a consequence of lack of sleep at night, he became liable to fall off to sleep while driving. His mother was probably similarly affected.

Pain and Myoclonus Group

After an adequate period of relaxation of the limbs, pains appear which are described variously as "aching like toothache," "gnawing pain," and "throbbing pain." The pain rapidly mounts in severity and culminates in a myoclonic twitch.

Case 5.—A man aged 77 said that within half an hour of sitting or lying down he experienced a sensation in the region of the right ankle "like a dog gnawing." This sensation heralded the onset of paroxysmal pain—"stabbing"—in the lower part of the right leg. According to him, this "stabbing" caused the leg to kick out. As soon as the "gnawing" sensation appeared he tried to avert the "stabbing" by walking about or, if this was not possible, by standing up and marking time. These disturbances prevented him from obtaining rest and sleep for more than short periods. For many years he received treatment for a minor degree of arthritis of the right ankle. He had been referred to the neurosurgical centre for the purpose of leucotomy, since he had expressed suicidal intentions. Five months later he was readmitted to the centre following a severe head injury. Despite his age he made a complete recovery, and when seen six months after the accident he stated that the right leg had continued to trouble him seriously until the date of the accident. Since then the right leg had been entirely free from the pain, but recently somewhat similar pains, but of lesser severity, had occurred in the left leg. One daughter was reported to be suffering from similar disturbances of her legs when resting.

Case 6.—A woman aged 44 said: "For some years, directly I sit down and relax I get neuralgia pain in the right leg below the knee; the pain gets to a pitch and then makes the leg jump; the pain and jumping continue until I start moving about, and this relieves them."

Case 7.—A woman aged 63 for many years had "a fidgety, nervy feeling" in her calves after sitting for more than three hours, or during a long train journey. "It would stop if I walked across the room." Recently these symptoms appeared more readily, and were much more

intense—"as if something tearing the calves." "If I don't get up and walk, legs jump of their own accord—walking is the only thing that stops it. Massaging the legs is of no help, but a hot bath may relieve it. I call it torture—though it does not make me feel ill it spoils all my pleasure." She had been told that jerking of the legs continues in her sleep. "I always wake up with the fidgety feeling in the legs." One sister and two nieces were similarly affected. Following medication with phenobarbitone she improved considerably, but relapsed for no apparent reason. Examination revealed anaemia of moderate severity—haemoglobin 67%, colour index 0.66. Injections of "imferon" produced a dramatic relief of her symptoms.

Case 8.—This patient, aged 39, had had four pregnancies during the past 14 years. During each of them the following symptoms occurred, causing her much distress, mainly because of interference with sleep. A "heavy ache" appeared in the limbs, culminating in a "spontaneous jerking" which was immediately preceded by a "sensation" spreading down the affected limb. The legs were principally affected, but the arms were also involved, though to a much less extent. "It seems to come on when I am relaxed, if I sit down in the evenings or in bed. When it starts I can't stop it except by getting up." The symptoms made their appearance between the third and sixth months of her pregnancies and endured in a greatly diminished form for varying periods after the confinements.

Pain Group

As the following cases illustrate, pain similar in character to that in the previous group can occur in the absence of myoclonus during waking hours. Myoclonus, however, is commonly present during sleep—a feature common to all the groups into which the disorder has been subdivided for the purpose of classification.

Case 9.—A man aged 54 first began to be troubled with recurring pain in his left leg shortly after partial gastrectomy for dyspepsia two years previously. "I can't sit still—no time before left leg starts aching—pain like toothache at its worst within half an hour. As soon as I lie down it starts. I walk round the bedroom night after night. Once I manage to get to sleep I am all right. My wife says that it is the left leg that keeps kicking out at night when I am asleep."

Case 10.—This patient, a man aged 58, had since his youth, and especially during the past 10 to 15 years, had "throbbing, heavy, burning pain in both legs from the knees down; terrific ache, immediately relieved by standing and walking; not too bad during the day because I am concentrating on the paper work." Crural pain was also present on awakening in the mornings. His daughter, a young medical practitioner, was also similarly afflicted. She said: "I am afraid to sit down in the evenings. Once I sit down I become aware of a burning pain in the legs. It used to be in my right leg only. I've got to get out of bed in the mornings to be relieved of the pain—I can't have breakfast in bed."

Case 11.—A woman aged 51 complained of pains in the legs—"no trouble during the day—I get them when sitting down in the evenings, but mostly in bed. It starts with a throb in the calves and gradually gets worse—becomes a gripping neuralgia pain. Suddenly goes to such a pitch I have to get out of bed, then it goes quite quickly. Sometimes I go to sleep and it wakes me up; at other times it starts directly I lie down." According to her husband her legs kick out in her sleep.

"Sleep-pain" Group

As already mentioned, the appearance of symptoms on relaxation is always delayed, the latency period varying from case to case. Evidently this latency period may be so long as not to give rise to any overt manifestations during waking hours. In these cases the pain is felt only immediately on waking in the mornings, or the pain may awaken the sufferer in the night. Weir Mitchell (1897) described

this variant, which he named "sleep-pain." "I find in my notebook some half-dozen cases of pain in the legs, never known during the day, and needing sleep as a conditioning factor. Whenever I have spoken of this disorder to the patient he is apt, if intelligent, to say: 'No; not pain; it is distress.' The cases are alike. A man is well in the day, walks, works, does as do others. Some time after he falls asleep he is awakened by aching in the legs, from the soles half-way to the knees. There is but one remedy—motion. He rises, walks for ten minutes, is eased, goes to sleep, and in an hour or two awakens to feel the distress and repeat the relieving exercise." Weir Mitchell then gives a well-documented case history.

Two of the cases described by Purdon Martin (1946) in his paper on "unexplained pains in the legs at night" can be clearly recognized as presenting typical features of "sleep-pain." Furthermore, it was noted in these cases that similar pains were apt to occur occasionally during the evenings under conditions of relaxation.

"Restless Legs" Group

In his excellent monographs on "restless legs," Ekbom (1945, 1950) states that the only clinical description of this condition he could trace in the past medical literature was one given by Theodor Wittmaack in 1861. Wittmaack evidently recognized the three essential elements of this syndrome: (1) A crural sensation defying description—"eine nicht näher zu beschreibende Empfindung—ohne allen Schmerz—ohne Ziehen." (2) Restlessness of the limbs—"als wäre ein Geist der Unruhe in die Beine gefahren." (3) The occurrence at rest—"theils gegen Abend, besonders aber in Bett bis zum Einschlafen."

Minor forms of this disorder are undoubtedly common—Ekbom (1945) put it as high as 5% in a representative control group of the population—and rarely it can occasion a considerable amount of distress, when relief can only be obtained by getting up and walking up and down. The heredo-familial character, the exacerbating influence of pregnancy and anaemia, as also myoclonus in sleep—features which have already been mentioned as characteristic of the disorder as a whole—also apply to this group. Ekbom (1945) mentions the case of a soldier suffering from restless legs, "who sometimes kicked so violently during his sleep that his neighbours in the tent had to put up planks to protect themselves."

There is a unanimity among patients that some form of disagreeable sensation in the legs precedes the movements, that this sensation is unlike anything experienced in ordinary life, and that movement of the legs affords some relief. "It feels like internal itching," "it feels as though my legs were tied, so that I have to move them," testified some of Ekbom's (1945) patients; and these analogies help to convey something of the nature of this sensation. All agree that, while the desire to move the legs can be resisted for a while, a point is quickly reached when this becomes impossible.

The "restlessness" implied in the name is in the main of voluntary nature. Myoclonic jerking can, however, occur also during the waking state. Allison (1943), from personal experience, described the movements which occur in this syndrome—called by him "leg jitters"—as follows: "A combination of voluntary movement and involuntary jerks of the affected limbs. It has no relation to the sudden leg-jerk which sometimes occurs at the moment of going off to sleep." These references to myoclonus are of some importance, as they help to bridge the various subgroups.

"Dyslysis"

Underlying the graded series of cases presented here, there is clearly a neurological disorder showing several uniform features. That relaxation rather than immobility of the limbs is the provocative factor can be inferred from the fact that in most cases the symptoms may be absent or minimal while the sufferer is engaged in his business,

even if the limbs remain immobile for a long time, as when the job is of a sedentary nature. Bearing in mind that the disorder is one attendant upon relaxation of the limbs, it may be justifiable, to avoid circumlocution, to speak of "dyslysimelia," making use of the classical Greek word "lysimelia" denoting a state of relaxation of limbs as in sleep or death. For reasons of brevity "dyslysis" may, however, be preferable.

Provocative and Aggravating Factors.—Excepting for pregnancy and anaemia, no obvious precipitating or aggravating factor could generally be discovered in the cases of dyslysis reviewed. In one case the onset of myeloid leukaemia was followed by a pronounced exacerbation. In a case of disseminated sclerosis of recent onset much distress was caused by dyslysis shortly afterwards.

Differential Diagnosis

Dyslysis can manifest itself during waking hours, during sleep, and during predormitium, which Weir Mitchell (1897) defined as follows: "As we are falling asleep the senses go off guard in an orderly and well-known succession—this interval I desire to label *prae-dormitium*." The symptoms of dyslysis commonly occur during waking hours, but may exceptionally occur only during sleep. However, in none of the cases reviewed here or quoted by others has there been an *exclusively* predormitial incidence. A great variety of sensory and motor disturbances are known to occur, often with regularity, during predormitium; but these phenomena, because of their *exclusively* predormitial incidence, should provisionally not be grouped with dyslysis. A further noteworthy nosographic point is the absence in dyslysis of tactile paraesthesiae such as pins-and-needles and numbness.

Acroparaesthesia.—The cardinal feature of this syndrome is the occurrence of paraesthesiae, with or without associated pain, in the upper limbs after the affected limbs have remained immobile for some time, either at rest or during activities in which there is little or no movement, as when writing, knitting, holding a newspaper or telephone receiver, etc. These symptoms as a rule are conspicuous at a time when objective sensory abnormalities are minimal or entirely absent. In early cases the immobility of the limbs has to be long-sustained so that the incidence is purely nocturnal, symptoms causing the patient to awake from sleep, or else the incidence is matutinal, symptoms becoming evident for a short time immediately on awakening in the mornings. Apart from the difference of the limbs principally involved—arms in acroparaesthesia and legs in dyslysis—there are also other diagnostic differences—for example, absence of tactile paraesthesiae in dyslysis, to be borne in mind.

Predormitial Myoclonus.—A sudden start of one or more limbs occurs not infrequently when falling off to sleep, and may arouse the sleeper. Weir Mitchell (1897) mentions the case of a woman whose sleep was rendered impossible by a series of such "explosions" each night. "Just as she begins to lose herself an arm, a leg, or the whole body suddenly moves with violence. As she awakens, hands and feet, or either alone, twitch for a few moments. Then she settles herself to sleep anew, only to repeat the same process." Because of the *exclusively* predormitial incidence these cases should be differentiated from dyslysis.

Nocturnal Burning Legs.—The descriptive name applied to this syndrome by Tinel (1937) was "causalgie nocturne spontanée de vieillards." It should be added that these distressing thermal paraesthesiae in the feet and legs eventually become continuous, disappearing only when walking. The thermal character and unremitting nature of the paraesthesiae during rest help to distinguish this condition from dyslysis.

Cases of dyslysis vary considerably in severity, but, clinically, two phases can be generally recognized: (1) latency phase, and (2) phase of overt clinical manifestations. During the latter phase there occurs rarely the phenomenon of sensory precipitation of myoclonus (Case 1).

Treatment

Most patients find that phenobarbitone appreciably relieves the symptoms of dyslysis. One patient who had been given phenobarbitone for some other condition reported that, while this treatment failed to effect the improvement expected, it considerably relieved her symptoms of dyslysis. Case 7 at first improved on phenobarbitone, but relapsed later. Iron therapy for the control of anaemia relieved dyslysis in a most dramatic fashion.

Conclusion

From the physiological point of view the disturbance of relaxation of limbs described in this paper is best regarded as "inhibition of inhibition." An analogy is provided by an experiment in which a recurrently elicited knee-jerk in a cat is first inhibited by ipsilateral sensory-nerve stimulation, and later this inhibition is "inhibited" by stimulation of the bulbar reticular formation (Bach, 1950).

The following points may perhaps indicate that dyslysis is a manifestation of a raised excitatory state referable to bulbar reticular activity: (a) exceptionally high voltage of motor unit potentials were observed during minimal effort contractions; (b) pronounced susceptibility of dyslysis to the influence of lowered oxygen tension; (c) the occasional sensory precipitation of myoclonus; (d) a partial improvement obtained in most cases with phenobarbitone.

Summary

A disorder characterized by disturbed relaxation of limbs at rest is described.

Cases are divided into the following groups, in accordance with the chief clinical features: myoclonus group, pain and myoclonus group, pain group, "sleep-pain" group, and "restless legs" group.

Legs are usually, but not always, the only limbs affected in this disorder, which often shows a heredo-familial incidence and tends to have a long, fluctuating course. Myoclonus during sleep is common.

Pregnancy and anaemia greatly aggravate this condition.

During the phase of overt manifestation of symptoms, sensory precipitation of myoclonus may occur.

Differential diagnosis and treatment are discussed.

"Dyslysis" is suggested as a name for this syndrome.

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"The speed with which people grow old depends as much on social factors as it does on purely physical processes. Ageing is quickened by such things as the loss of interests due to compulsory retirement or frailty; loss of relatives and friends due to the inevitable result of living longer; loss of financial security due to a decline in income or in the value of money; loss of emotional security due to changing environment; loss of status through ceasing to be primarily a contributor to society; and loneliness. Singly or collectively, these are responsible for much of the frustration, disappointment, anxiety, depression, and unusual behaviour amongst elderly citizens."—*Notes on Mental Frailty in the Elderly*, a booklet prepared by the National Old People's Welfare Council for the guidance of those concerned with the care of the elderly. The *Notes* (price 1s.) are obtainable from the National Council of Social Service, 26, Bedford Square, London, W.C.1.

STAPHYLOCOCCAL SPINAL MENINGITIS

BY

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During the years 1949–56, 115 cases of pyogenic meningitis were admitted to the isolation ward of the Cumberland Infirmary (Table I). Comparison of the

TABLE I.—Pyogenic Meningitis, 1949–56

Type of Infection	No. of Cases	No. of Deaths
Meningococcal	61	3
Influenzal	15	1
Pneumococcal	16	3
Pyogenic. No growth on culture	16	—
Staphylococcal	7	1
Total	115	8

figures in Table I with other published series showed an unusually high incidence of staphylococcal infection. These cases presented as meningitis without any obvious local sepsis, but, because of their probable relationship to staphylococcal epidural abscess, the term "staphylococcal spinal meningitis" is used to describe them.

Literature

The first proved case of staphylococcal meningitis was described by Galippe in 1889, following suppuration of the jaw. Anthony (1892) reported the first "cryptogenic staphylococcal meningitis" in a robust soldier aged 23. Neal (1924) and MacNeal *et al.* (1943) collected small series of cases, and Teng and Meleney (1950), in an exhaustive review of the literature, recorded 88 cases with recovery.

In approximately one-third of the published cases the source of infection has been described as "haematogenous" or unknown. The infecting organism, in all but a small minority, has been a coagulase-positive *Staphylococcus aureus*, but *Staph. albus*, *Staph. citreus*, and a mixture of organisms have been incriminated. The possibility of contamination of cerebrospinal fluid (C.S.F.) samples makes evaluation of all reported cases difficult, but the criterion adopted has been the presence of staphylococci in direct smears, and their growth on culture, in cases of pyogenic meningitis.

Prior to 1932 the only successes in treatment were reported from France, where it was recognized that many of the so-called primary infections were secondary to latent spinal infection. This type of case was called "la forme rachidienne primitive," and treated by laminectomy and drainage (Sicard and Paraf, 1925; Benoit, 1929; Chavany and George, 1929). Benoit (1929) recognized the danger that lumbar puncture may precipitate generalized meningitis and cautioned against unnecessary spinal taps.

Staphylococcal bacteriophage (Schless, 1932) was given intrathecally with some benefit, and sulphonamides alone (Tolan, 1943) assisted recovery in one case, but it was the introduction of penicillin by intrathecal and intramuscular injection, used in conjunction with sulphonamides, that first gave a prospect of cure in the majority of cases (Evans, 1944; McCune and Evans, 1944; Worth, 1945; Johnson and Walker, 1945). With the emergence of penicillin-resistant strains of organism, other antibiotics have been used with success. Intrathecal and intramuscular bacitracin (Teng and Meleney, 1950; Teng, 1950), chlortetracycline (Almklov and Hansen, 1949), and intrathecal and oral chloramphenicol (Anderson and Ellis, 1951) have all been proved of value in small numbers of cases.

Because of the high incidence of spinal block in cases of staphylococcal meningitis, streptokinase-streptodornase by