

Papers and Originals

Royal Free Epidemic of 1955: A Reconsideration

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Summary: From a re-analysis of the case notes of **S**patients with Royal Free disease it is concluded that there is little evidence of an organic disease affecting the central nervous system and that epidemic hysteria is a much more likely explanation. The data which support this hypothesis are the high attack rate in females compared with males; the intensity of the malaise compared with the slight pyrexia; the presence of subjective features similar to those seen in a previous epidemic of hysterical overbreathing; the glove-and-stocking distribution of the anaesthesia; and the normal findings in special investigations. Finally, a deliberate attempt by one of the authors to produce an electromyographic record similar to that reported in Royal Free disease was successful.

In July 1955 an epidemic occurred among the staff of the Royal Free Hospital, London. Its spread was explosive, the number of cases increasing from fewer than five in mid-July to more than 100 a fortnight later. The hospital had to be closed on 25 July; it remained closed until early October. By the time it was all over—in late October—the total number who had been affected was over 300. Two-thirds of them had been sufficiently ill to need admission.

One diagnosis considered in the early stages of the epidemic was glandular fever; negative Paul-Bunnell tests quickly disposed of this idea. Then, when paralyses developed in a number of cases, the question of polio arose; however, all cerebrospinal fluids examined were normal. Puzzlingly, the signs and symptoms failed to add up to any of the usual diagnoses. The consensus was that it was a viral infection of the central nervous system. Fortunately, whatever its exact nature, the disease proved relatively benign and, though a few of the affected suffered some disability for up to a year, no one died of it.

The year after the epidemic, a leading article appeared in the *Lancet* entitled "A New Clinical Entity?". In this article the name "benign myalgic encephalomyelitis" was proposed for Royal Free disease and certain similar illnesses (*Lancet*, 1956). When the medical staff at the Royal Free Hospital wrote their account of the outbreak (Medical Staff, 1957)—referred to hereafter as the Medical Staff report—they also described the illness as an encephalomyelitis. The nature of the infective agent was admitted by all concerned to be obscure, but considerable definition was claimed for the clinical syndrome. To quote the end of the *Lancet* article, "we believe that its characteristics are now sufficiently clear to differentiate it from poliomyelitis, epidemic myalgia, glandular fever, the forms of epidemic encephalitis already described, and, need it be said, hysteria."

The concluding words seem to us non sequiturs. The case for hysteria was not examined in the article; indeed it received no consideration apart from this summary dismissal. In our

opinion the case is a good one, and the purpose of this paper is to obtain a fair hearing for it. Firstly, we present the findings reported from the epidemic and then our interpretation of them.

Analysis of Outbreaks

Epidemiology

The epidemiological study by Crowley *et al.* (1957), of the bacteriology department of the Royal Free Hospital School of Medicine, gives the attack rates as follows:

Males27 out of 950 (2.8%)
Females265 out of 2,550 (10.4%)

These attack rates are for the whole institutional population (staff, students, and patients) and include cases treated on an outpatient basis. By using a rather more rigorous definition of the illness (in terms of timing and days off sick), by excluding the hospital patients, and by excluding all those treated on an outpatient basis, we have obtained the following figures:

Males5 out of 600 (0.8%)
Females193 out of 1,760 (11%)

Prodromal Stage

A list of the initial manifestations is given in Table I of the Medical Staff report, here reproduced as part of our Table I. It will be seen that these manifestations are all subjective complaints. We have placed alongside their table figures for the frequency of these or equivalent complaints among 154 schoolgirls involved in an epidemic of overbreathing (Moss and McEvedy, 1966).

TABLE I.—Incidence of Various Prodromal Symptoms in the Royal Free Epidemic and of Equivalent Symptoms among Schoolgirls Involved in an Hysterical Epidemic

Incidence of Various Symptoms; Royal Free Epidemic	Prodromal Hospital	Incidence of Equivalent Symptoms Among Schoolgirls Involved in an Hysterical Epidemic
Headache	77%	Headache 59%
Sore throat	63%	No equivalent
Malaise	62%	General weakness 40%
Lassitude	51%	
Vertigo	47%	Dizziness 63%
Dizziness	33%	Nausea 44%
Nausea	40%	No equivalent
Pain in limbs	46%	Pain in back or abdomen 44%
Pain in back	32%	Pain in chest or neck 18%
Pain in abdomen	14%	Feeling of panic 25%
Stiff neck	32%	Vomiting <10%
Depression	19%	
Vomiting	12%	
Diplopia, tinnitus, diarrhoea	<10%	

Sensory Symptoms

On discharge from inpatient care the affected were graded into three categories of neurological involvement—slight, moderate, and severe. We have taken 20 cases for restudy of the sensory symptoms: the series is made up of all the 17 cases

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marked severe, plus one (Case 14) whose summary is lost but who must have been considered severe as she was in hospital as a result of the illness for over a year, and plus two (Cases 19 and 20) considered moderate but who had charts of sensory disturbance drawn. The population is, accordingly, made up of two overlapping but complete and objectively defined series: (1) Cases 1-18, the clinically severe cases, and

(2) Cases 2, 4, 10, 14, 17, 19, and 20, the cases for which sensory charts were drawn.

As will be seen from Table II, only 16 of the 20 cases showed an anatomically defined sensory change, and study of this table and of Fig. 1, where the sensory charts are reproduced in facsimile, indicates that of these 16 cases, the distribution of the change in 13 is of the glove and/or stocking type.

TABLE II.—Sensory Signs in Clinically Severe Cases. The Dates in Parentheses refer to the Entry in the Patient's Notes

Case No.	Changes in Arms	Changes in Legs
1	"Glove" (6/9)	"Stocking" (26/8)
2	See Fig. 2	See Fig. 2
4	"Pinprick impaired up to elbow"	"Pinprick impaired up to knee" (16/9). Described as stocking loss in summary
5	"Left hand and foot hypoalgesic" (4/8)	"Both legs anaesthetic up to groins" (14/9)
6	"Peripheral loss arms and legs" (see also note below)	See Fig. 2
9	See Fig. 2	See Fig. 2
10	Nil	"Both legs anaesthetic up to groins" (14/9)
11	See Fig. 2	See Fig. 2
12	Sensation noted to be altered in feet and diminished in finger-tips of right hand the day after an overbreathing attack in which the patient "became hot, [had a] tight feeling in throat, could not breathe, could not take deep breaths, upper part of chest would not work. Respiratory rate went up to 30" (10-11/8)	See Fig. 2
13	See Fig. 2	See Fig. 2
14	"Hypoesthesia of glove distribution both hands" (23/8)	"Pinprick diminished stocking distribution" (25/8)
17	See Fig. 2	See Fig. 2
18	See Fig. 2	See Fig. 2
19	See Fig. 2	See Fig. 2
20	See Fig. 2	See Fig. 2

Cases 7, 15, 16: No note of any sensory impairment.
Case 3: Only note of sensory impairment is "generalized hypoalgesia."
Case 8: Left hemihypoalgesia, including left face.
Case 9: Also loss over left side of face, neck, and shoulder, sparing the nose and corneal reflex.

Motor Symptoms and Signs

According to the Medical Staff report, "The usual initial distribution of weakness was hemiplegic, or less commonly monoplegic or paraplegic, but later the remaining limbs were often affected to some degree. . . . The tendon jerks were preserved. . . . In only two cases were frank extensor plantars encountered. . . . Wasting of muscles was exceptional."

Richardson says: "An important diagnostic feature was the apparent contrast between the severe disturbance of volition and the minimal disturbance of the reflexes. Thus, in two cases of flaccid paraplegia of several months' duration jerks were retained, and in two hemiplegics jerks did not become exaggerated, abdominal reflexes were retained, and extensor plantar responses did not develop."*

* The passage continues: "In fact, frank extensor responses occurred in only three cases and persisted in one." The case in which the plantars became and remained extensor had disseminated sclerosis; she had become ill before the epidemic and died some months after it was over (See below, under histopathology).

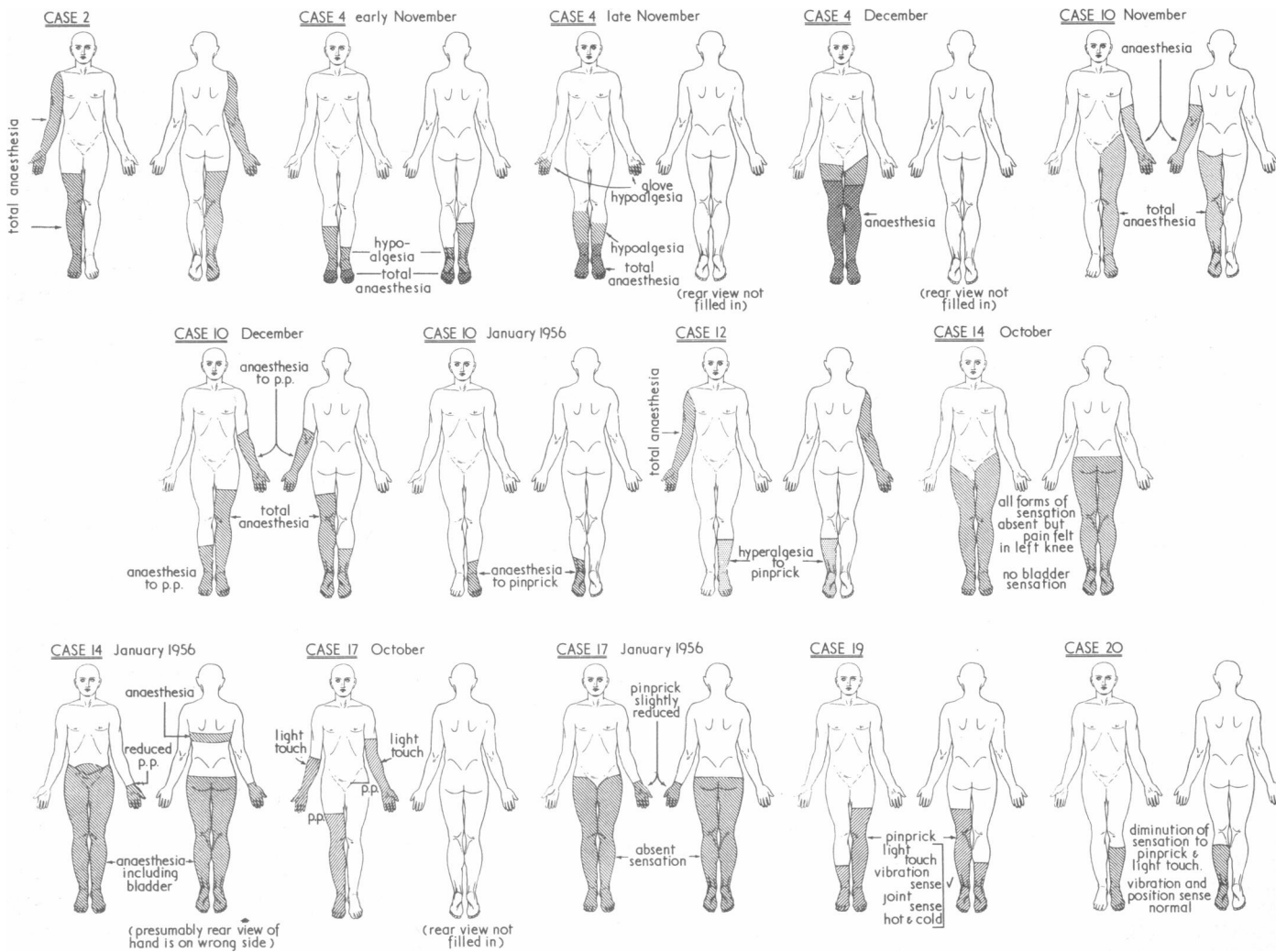


FIG. 1.—Facsimiles of charts of altered sensation. (Bracketed comments are ours.)

Convulsive Episodes

"Fits" of one sort or another, though mentioned only once in the Medical Staff report, appear to have been of relatively frequent occurrence. The clinical notes record convulsive episodes in 10 out of the 18 cases considered to be severely affected.

For example:

Case 2.—24 August, "Fit lasting about 20 minutes consisting of throwing limbs about, foaming at the mouth, staring eyes. Said afterwards that she did not know anything about it." 25 August, similar attack, less severe. 8 September, "Query hysterical attack; jerking and throwing herself about."

Case 3.—14 September, "Started having fits. Arms flexed, rigid, shaking. Teeth clenched. Slight breath holding, followed by irregular breathing." Later the same day: "Arms and legs rigid ++, shaking. Breath-holding lasted longer; patient went red, blue, then livid before recovery. Query voluntary."

There is evidence of episodes of overbreathing in the respiration rate records of a further four of the 18 cases.

Special Investigations and Histopathology

Laboratory and other aids proved of no help in diagnosis. The Paul-Bunnell test was negative in 246 out of the 250 patients tested; liver function tests were normal in 115 of the 119 patients tested; the electrocardiogram was normal in 39 out of 42 patients tested; and the cerebrospinal fluid was normal in all 18 cases examined.

Two patients who were thought to have suffered from the epidemic illness died a few months after the epidemic was over. One death was due to an ovarian carcinoma; no lesions were found in the central nervous system of this case. The second death was due to an overdose, and necropsy showed only lesions attributable to disseminated sclerosis.

Comment

We now propose to consider each of the above headings in some detail, suggesting that most of the recorded features fit in with an hysterical aetiology.

Epidemiology

Characteristically epidemic hysteria occurs in populations of segregated females—in girls' schools, convents, and among female factory hands.† At the Royal Free, as at any other hospital, the female population is segregated to a very considerable degree. The attack rate among the females should, according to the hysterical hypothesis, be considerably higher than among the males. There is no dispute that this was so. Moreover, when the more rigorous definition of the illness is used (in terms of timing and days off sick) the difference is even more striking, and fits in well with the hypothesis of an hysterical epidemic. It is surely difficult to associate this epidemic with an infective agent.

Clinical Data

The illness usually began with symptoms "common to the prodromal stage of most infections" (Medical Staff report, p. 896). A minority of the admitted patients did not progress beyond this phase and gradually recovered over a few weeks. About three-quarters deteriorated, entering a phase of central nervous system disturbance which lasted weeks or even

months. For simplicity's sake it is easiest to keep this division into a prodromal stage and a stage of central nervous system disturbance, but it would be wrong to suggest that the two degrees of illness were invariably successive. "A clear division of symptoms into those appearing early and late is not possible" (Medical Staff report, p. 896).

Two further sentences from the Medical Staff report are worth quoting as they appear to be relevant to the whole course of the illness: "The intensity of the malaise, particularly when related to the slight pyrexia in this disorder, requires emphasis." "Spontaneous pain was the commonest sensory manifestation and its part in the clinical picture cannot be over-emphasised."

Prodromal Stages

Comparison of the initial manifestations in the Royal Free disease with the schoolgirls involved in an epidemic of overbreathing (Moss and McEvedy, 1966) showed that the schoolgirls also complained with high frequency of pins-and-needles, feeling hot and cold, and areas of altered sensation, mostly peripheral. Their teeth often chattered, they shivered, 40% were overtly hyperventilating on admission, and a third suffered tetanic spasms. Disorientation, bladder dysfunctions, and specific pareses were occasionally present.

Though paraesthesiae and altered sensations are not tabled in the Royal Free list of prodromal symptoms, the "numbness and coarse tinglings" described later on in the Medical Staff report (p. 897) could be taken as an equivalent phenomenon. Richardson (1956, p. 82) stated: "Initially the neurological symptoms usually consisted of vertigo, generally transient but sometimes persistent, and accompanied by earache and by blurred vision or diplopia. Motor weakness and sensory disturbances of variable distribution and duration followed, and in particular coarse paraesthesiae were experienced" (our italics). Paraesthesiae were certainly common enough among the Royal Free cases to be asked for as a routine on admission; a check on the hospital records indicates that about 40% of those affected experienced them. It is possible that the lowered pain threshold characteristic of the disease caused the paraesthesiae to be tabled as "pains in the limbs."

Richardson also remarked on "the tendency for the limbs to develop spasm in response to sensory stimulation" while the Medical Staff report refers to "severe and prolonged painful muscle spasms."

As to emotional state, "disproportionate depression and emotional lability" were frequently present at the start of the illness (Medical Staff report, 1956, p. 895).

It will be seen that there is a fair case for regarding these symptoms as the subjective complaints of a frightened and hysterical population whose overbreathing was intermittent and covert but sufficient to bring their limbs to the threshold for tetanic spasm. On this view the sore throat—which is described as "mild"—would be partly a complaint, partly an objective but incidental finding to be related to the statement in the Medical Staff report (p. 898) that "a small outbreak of streptococcal sore throat affected a group of nurses." The much lowered pain threshold which was such a pronounced feature of the epidemic could well cause a positive reply to a routine inquiry for sore throat.

The objective changes one might expect in the prodromal stage of an infective illness were only exceptionally present; pyrexia over 100°F. (40°C.) in 4.5%, erythrocyte sedimentation rates over 20 mm. in the hour in 1.5%. The white blood count was said to show a "tendency for a low-normal neutrophil count, with a high-normal lymphocyte count... in about half the cases." As this was no more than a tendency (which could well have been balanced by an opposite tendency in the other half of the cases) it appears that all white counts were within normal limits.

† The literature is surprisingly thin. Specific instances are (for girls' schools) Schuler and Parenton (1943), Tan (1963), Moss and McEvedy (1966), McEvedy *et al.* (1966); for convents Huxley (1952); for factory hands Kerckhoff and Back (1968).

Sensory and Motor Features

It seems fair to say that the characteristic pattern of sensory loss is a classically hysterical one. Moreover, any explanation of the finding of normal reflexes surely places the onus on the organicist to prove that the condition is not hysterical, for traditional diagnosis regards normal reflexes as proof that a paralysis is functional. Indeed, the formulations quoted fit so readily into the hysterical hypothesis that an organic theory seems worth considering only if other evidence can be brought in to support it. Some have seen such evidence in Richardson's electrodiagnostic investigations. As the point is crucial, it is worth considering the results of his careful (and carefully reported) studies in some detail. He found that:

- (1) With one exception the muscles tested satisfied the criteria of normal innervation.
- (2) With one exception (the same) no fibrillation potentials were found in the muscles with established paralysis.
- (3) Nerve conduction was within normal limits in all cases tested. "The medial popliteal reflexes, even after eight months of flaccid paraplegia, were found to be normal."
- (4) Some of the electromyograms taken from the affected muscles showed a peculiar bunching of the action potentials, groups of roughly half a dozen spikes being separated by electrically quiet intervals.

The first three points are obviously no help to the organicist. The fourth point is taken by Richardson to indicate no more than "a severe disturbance of volition," a lesion that is surely characteristic of hysteria. A hasty reader, however, might get the impression that the peculiarity demonstrated was unphysiological and that the electromyograms therefore provide support for the organicist. Neither statement is true, and the first is easily disproved by experiment.

Though motor units fire rhythmically, different units are rarely in phase and the electromyographic picture obtained with increasing muscular activity is a fairly steady filling in of the trace as asynchronous rhythms are superimposed. The peculiarity observed in the Royal Free cases lies in the synchronous firing of the motor units; macroscopically the effect would presumably manifest as a fast tremor. In practice it is quite easy to obtain this type of trace by encouraging one's rigid outstretched arm to tremble, Fig. 2 shows a trace of

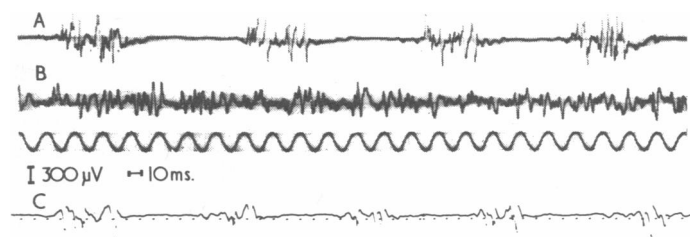


FIG. 2—Trace A: Weak tibialis anterior muscle on maximum sustained volition. Trace B: Normal contralateral tibialis anterior on maximum sustained volition. These two traces are photocopied from Fig. 6 in the Medical Staff report. Trace C: Normal extensor digitorum. One of us obtained this trace by extending his arm rigidly and encouraging his natural tremor.

Royal Free type, a normal trace (same case), and a trace produced in a deliberate and not unsuccessful attempt to simulate the first by one of us.

Far from being unphysiological, this type of trace suggests that the weakness is produced by a process similar to that used in its simulation—a "maximum effort" in which agonist and antagonist counteract each other.

It is interesting to note that in his classic work on hysteria Janet (1907) observes of hysterical tremors that they characteristically show a regular rate averaging between 5 and 9 a second (p. 129); he prints a smoke drum trace of such a

tremor on p. 130. The rate in the Royal Free cases falls at the upper end of this range.

The final clinical feature of Royal Free diseases were the convulsive episodes. We suggest that hyperventilation as a result of anxiety was the primary disorder underlying these, that the resulting paraesthesiae increased the anxiety, and that the "fits" were probably partly tetanic and partly a direct expression of overwhelming anxiety.

Special Investigations

The few abnormal results of the laboratory investigations cannot be regarded as significant in an illness so difficult to define; inevitably, a minority of the cases included in the series will have been suffering from illnesses other than the epidemic affliction. For example, one patient became jaundiced. This male doctor satisfies the epidemiological criteria we have used to define the affected population; but it is difficult to read through the notes of his case without feeling that at any other time he would have been diagnosed as an uncomplicated case of infectious hepatitis. Jaundice was not part of the picture of the epidemic illness, and the malaise he felt is more simply explained as a consequence of his hepatitis than as due to a superadded "viral encephalomyelitis."

Discussion

The manifestations of encephalitis are extremely variable and at first sight a diagnosis of encephalitis seems logical in an illness with such protean central nervous system symptomatology as "Royal Free disease." Inherent in the diagnosis, however, are expectations which, despite the large number of cases, were never in any instance borne out. Encephalitis is a serious illness; in at least some cases one would expect a high temperature and prolonged disturbance of consciousness. One would expect a mortality. One would expect, at least in some cases, involvement of the meninges and alterations in the cerebrospinal fluid. The culture of an infective agent, if viral, could only be hoped for, but some signs of its effect in post-mortem material would seem likely.

In the Royal Free epidemic the temperature rose above 100°F. (40°C.) in only 9 out of 200 cases. This could well be within normal limits for this population over a three-month period. There were no sustained comas and no deaths. There was complete failure to obtain objective evidence of any inflammatory response in the blood or cerebrospinal fluid. There was an equal failure to elicit clinical signs of the type classically expected in organic dysfunctions of the central nervous system.

The hypothesis of an hysterical epidemic seems to us to fit well with these and other findings. The greater susceptibility of the segregated female would explain the failure of the epidemic to propagate beyond the institutional population or, within the institution, to affect significantly the males and the patients. It would explain the other epidemiological findings and also the observation that non-residence had a protective effect (Crowley *et al.*, 1957, p. 110). Not only the negative but also the positive clinical findings—the prodromal complaints, the glove and stocking anaesthesias, the flaccid paralyses with preserved reflexes, the paroxysms of hyperventilation, and the high incidence of difficulty in micturition (26%; Medical Staff report, p. 897)—fall into place as part of this picture.

Many people will feel that the diagnosis of hysteria is distasteful. This ought not to prevent its discussion, but perhaps makes it worthwhile to point out that the diagnosis of hysteria in its epidemic form is not a slur on either the individuals or the institution involved. Whereas it is true that sporadic cases of hysterical disability often have disordered personalities, the hysterical reaction is part of everyone's potential and can be elicited in any individual by the right set of circumstances.

The occurrence of a mass hysterical reaction shows not that the population is psychologically abnormal but merely that it is socially segregated and consists predominantly of young females.

Our reassessment has been possible only because of the generous help we have received from the medical, administrative, and nursing staff of the Royal Free Group of Hospitals. We would like to place on record our appreciation of this co-operation, which has been truly unstinting. Our views are, of course, entirely our own.

The electromyographic study was carried out at the Department of Electromyography at the Middlesex Hospital by kind permission of Dr. Pamela Fullerton. The expertise needed to make the recordings was supplied by Dr. Ian Wilkinson.

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Concept of Benign Myalgic Encephalomyelitis

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Summary: The reports of the 15 recorded outbreaks of benign myalgic encephalomyelitis have been reviewed and in one instance the original clinical data studied. We believe that a lot of these epidemics were psychosocial phenomena caused by one of two mechanisms, either mass hysteria on the part of the patients or altered medical perception of the community. We suggest that the name "myalgia nervosa" should be used for any future cases of functional disorder which present the same clinical picture.

Acheson (1959), in a review article on benign myalgic encephalomyelitis, enumerated 14 epidemics that he considered belonged in this category. A fifteenth has been reported since (Daikos *et al.*, 1959). The term "benign myalgic encephalomyelitis" was proposed in 1956 (*Lancet*, 1956), so the dozen outbreaks before this date have received the label retrospectively. The outbreaks, however, have so many features in common that the case for regarding at least the epidemic form of the illness as a unitary phenomenon is a very fair one.

In the preceding paper (McEvedy and Beard, 1970) we have presented the evidence for regarding one of the most striking epidemics in the series—the Royal Free Hospital outbreak of 1955—as an hysterical phenomenon. Can this formulation be applied to any or all of the other 14? After looking at the published reports on these epidemics (which we review below with our comments), and in one instance studying the original clinical data, our conclusion is that two mechanisms are at work, both psychosocial. We believe that between them they account for the phenomenon of benign myalgic encephalomyelitis.

Hospital Outbreaks

Of the 15 recorded outbreaks of benign myalgic encephalomyelitis eight have occurred among hospital nurses. The leading points about these eight are set out in Table I. We will look at two of them in some detail—the Los Angeles epidemic of 1934, because an excellent report on it has been published by the United States Public Health Service (Gil-

liam, 1938), and the Middlesex epidemic of 1952, because this is our hospital and we have had access to the clinical notes made at the time.

Los Angeles Outbreak of 1934

As shown in Table I, the Los Angeles outbreak occurred at a time when a poliomyelitis epidemic was under way in that area. The influx of poliomyelitis cases led to the opening of five emergency wards at the Los Angeles County Hospital during May 1934. A further 10 were opened in June; these were largely filled with suspected cases that had occurred among the younger members of the nursing staff of the hospital. The attack rate among the nurses was extraordinarily high (12% as compared with 0.073% for the population of Los Angeles City and County). Moreover, it soon became apparent that the illness that had broken out among the nurses was not poliomyelitis. Whereas the cases admitted from outside had the clinical, laboratory, and necropsy findings characteristic of poliomyelitis, the nurses had: (1) temperatures fluctuating between 97 and 98°F. (36.2 and 36.7°C.); (2) more sensory than motor disturbance, with paraesthesiae, muscle tenderness, and general hyperaesthesia prominent; (3) muscular weakness only rarely associated with atrophy; (4) an unusually high frequency of "insomnia, emotional upsets, other disturbances of the sensorium, joint changes, trophic changes, oedema, cystitis, and menstrual disturbances"; (5) a normal cerebrospinal fluid; (6) a clinical course marked by relapses that were often as severe as the original illness; and (7) no mortality. This is the clinical picture that has since been termed benign myalgic encephalomyelitis.

One point of interest is the immunity of a second hospital that lay within the same grounds as the County Hospital. The staff of this institution (the County Osteopathic Hospital) had a very different age and sex distribution from the County Hospital proper. At the Osteopathic Hospital 44% of the staff was male (as compared with 27% at the County Hospital); of the females only two out of five were under 30 years old (as compared with three out of five at the County Hospital). By no means all the local institutions achieved this immunity. Leake *et al.* (1934) mentioned "a sharp focus in May in the Ruth Protective Home, an institution for infants, children, and young women, located about 3 miles' east of the city limits." Eleven out of about 100 inmates required admission.

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