

ROYAL FREE DISEASE, SIXTY YEARS ON
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On 25th July 1955, the Royal Free Hospital closed its doors and remained closed until 5th October. The hospital had been struck by an obscure infectious disease, which became known as Royal Free disease. In total, 292 members of the 3,500 medical, nursing and ancillary staff and 22 patients were affected. In 1956, an article in the Lancet re-named the disease benign myalgic encephalomyelitis (ME). In 1984, another epidemic of a clinically similar disease, in Nevada, USA was named chronic fatigue syndrome (CFS). Since 1934, 62 epidemics of a similar disease have been described globally. Sporadic cases of the disease occur with an estimated prevalence of 2-4 per thousand of the population. The disease may be called ME or CFS, and ME/CFS is the currently favored acronym.

Some 15 years after the outbreak, a paper in the BMJ suggested that mass hysteria was the likely cause. The authors examined the records of some selected patients who were mostly nurses. They did not interview any patients, some of whom were still suffering ill effects from the outbreak. They ignored or dismissed signs of infection and a multitude of neurological signs. Because, in their selected cases, the illness was mostly in young women and no pathogen had been found, they diagnosed the outbreak as mass hysteria. The hysteria hypothesis persists to this day, in spite of many well-documented pathological changes found in patients' immune systems, mitochondrial function, autonomic nervous systems, brains and genomes.

In 1955, the Royal Free hospital group consisted of 5 hospitals and the medical school. Staff from all the hospitals became ill. We, the authors, were medical students at the time. We thought that after 58 years, it would be instructive to find out what happened during the outbreak and discover any long-term after effects of the disease. We put a statement in the Royal Free Association newsletter and the Royal Free Hospital Nurses League magazine asking anyone who was present during the epidemic to contact us. Twenty seven people replied, 6 had suffered from Royal Free disease, 2 had had a short lived illness which was thought to be abortive Royal Free disease and 19 had remained healthy. In 1955, 11 were medical students, 10 doctors, 5 nurses and 1, a physiotherapist.

Our informants told us that initial symptoms and signs of the illness varied, but included fatigue, drowsiness, severe headache, sore throat, vomiting, muscle pain, enlarged posterior cervical glands and a low grade fever. After a few days, symptoms often worsened with severe pain, muscle weakness and sometimes paralysis. Symptom severity ranged from mild to severe. Secondary cases developed the disease after an incubation period of a few days. Most nurses nursing the patients did not develop the disease, but the records of the hospital medical staff, showed that the attack rate was 19% in nurses and 8.3% overall. Only 22 hospital inpatients developed the disease. Tests showed that many patients had a low white cell count and some had atypical lymphocytes, but Paul Bunnell tests were negative. The cerebro-spinal fluid findings were normal, distinguishing the disease from polio. Treatment was mainly supportive, and included insistence on complete bed rest, while symptoms lasted, for severe cases, and convalescence for the same period of time as the duration of symptoms. Too early activity always precipitated a relapse.

Recovery took from a few days or weeks to several months. Some patients with paralyzes and some with several bizarre symptoms were still in the hospital 6 months after the onset of the epidemic. Some of these patients gradually got better and were discharged. A few with persisting paralysis were transferred to a rehabilitation unit. Sadly, one patient committed suicide. Although many of the staff recovered enough to return to work, many continued to feel ill or fatigued for at least a year. Up to now, of the six people known to us, who recovered from Royal Free disease, one has persisting bilateral wasting of the hypothenar muscles, one has Parkinson's disease and one has heart disease. We also had reports of some other people, who had recovered from Royal Free disease, who have various persisting pareses including: weakness of one leg which required an arthrodesis of the knee and ankle; weakness of one hand; foot drop; and ptosis. One person was reported to have had Hodgkin's disease and another severe Parkinson's disease.

At the time of the epidemic, the hospital staff, were baffled about the diagnosis. Initially the disease was thought to be related to polio, but the clinical picture was very different and cerebro-spinal fluid tests were normal. Glandular fever (infectious mononucleosis) was considered, but Paul Bunnell tests were negative. Hysteria was discussed but rejected because the disease was very clearly infectious. However, many hospital staff were understandably anxious about getting the illness and as there was no test for it, some patients were thought to be neurotic, or have exaggerated their symptoms, and some people believed that the disease was psychiatric or not a real illness.

How did the Royal Free hospital cope with an explosive epidemic of a highly infectious obscure illness, which had not been described in the medical text books? "The people running the hospital did not know

what had hit them". The first doctor to get ill was sent to the private wing of one of the smaller hospitals in the group. No infectious disease precautions were taken and a nurse said she caught the disease from him. Later on, staff who felt unwell were told to report to the resident medical officer for the infectious diseases department. The RMO examined them and felt for enlarged cervical nodes. If the nodes were palpable or there was doubt about the diagnosis, the patient was sent for further assessment. In the third week of the epidemic, all the hospitals were closed to new admissions, due to lack of healthy medical and nursing staff and in an attempt at isolation. Following the closing of the hospitals, most of the existing inpatients stayed, but the obstetrics and gynecology wards were cleared in order to admit patients with the epidemic illness. Two of the hospitals remained closed until early October.

Pre-clinical students in the medical school did not develop the disease, but several clinical students became ill. Healthy clinical medical students were sent to various hospitals in and around London and attended clinics and teaching rounds and much enjoyed the experience. Some students were sent away on holiday and some went home to revise for exams. In spite of the interruption in their studies, the healthy medical students managed to qualify on time.

What did we learn from this study? The evidence of those who actually experienced the epidemic showed that Royal Free disease was not "mass hysteria" but was an infectious disease. Mass hysteria does not result in paralysis, persisting for 60 years. Because sporadic ME/CFS can be life-long, we wondered whether some Royal Free disease patients might still be suffering from symptoms of ME/CFS, but if so, they did not contact us. We learnt that ME is spread by casual contact and the incubation period is a few days. Although only a minority of those exposed, develop the disease, the closer the contact with the patient, the more is the risk. Symptoms and severity are very variable, diagnosis is difficult and recovery can take weeks, months or years. There may be permanent muscle weakness. Exposed people who are resting (e.g., the hospital inpatients) are much less likely to develop symptoms and as complete rest as possible is the best therapeutic measure. It is important for patients to have a period of convalescence to avoid recurrences. Fear of contracting the illness in some individuals can lead to difficulties in assessing their symptoms and may result in a diagnosis of hysteria. Suggestions were made for future research.

References: (1) The medical staff of the Royal Free Hospital. An outbreak of encephalomyelitis in the Royal Free hospital group, London, in 1955. *BMJ* 1957; 895-904. (2) Crowley N, Nelsom M, Stovin S. Epidemiological aspects of an outbreak of encephalomyelitis at the Royal free hospital in the summer of 1955. *J of Hygiene (Cambridge)* 1957; 55: 102-122. (3) Leading article, *The Lancet* 1956; 1:789-790. (4) McEvedy CP, Beard BM. Royal Free Epidemic of 1955: A Reconsideration. *BMJ* 1970; 1:7-11.