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Isoprenaline and Salbutamol: Trial in asthmatic patients showed these two drugs to be equipotent as bronchodilators but isoprenaline elevated pulse and blood pressure more than salbutamol (p. 65).

Fibrin and Menorrhagia: Level of circulating fibrin degradation products was found to correlate with menstrual phase of cycle, and was high in menorrhagia (p. 74). Leader at p. 61.

Aversion to Smoking: Results of electric aversion therapy seem encouraging (p. 82). Leader at p. 60.

Anaemia in Alcoholics: These patients have an abnormality of iron metabolism, probably due to interference with haem synthesis (p. 86).

Drug-taking Boys: Within four years 9 of 47 delinquent boys originally on soft drugs had progressed to hard drugs (p. 102).

Rifampicin in Leprosy: Experimental and clinical studies suggest that rifampicin has a powerful bactericidal action against *Mycobacterium leprae* (p. 89).

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Hospital Junior Staff: Group Council meets again and reiterates its wish for a standing committee (*Supplement*, p. 9).

"Cures" for Multiple Sclerosis

The natural variation in the clinical course of multiple sclerosis makes a scientific appraisal of the results of treatment exceedingly difficult. At the same time the personal and economic sufferings of its victims are often such that the patients themselves, their relatives, their friends, and their medical advisers are apt to become passionately involved in the urge to produce a cure. Since the cause of the disease remains unknown, no logically based attack can be made on it. Pierre Marie,[1] lecturing in 1892, said that "the causative agent in multiple sclerosis is manifestly of an infective nature. What is its precise nature? No one so far has been able to isolate it but one day this goal will be achieved." Many attempts to discover its cause have since been made, and they have usually been coupled with the recommendation of a new form of treatment. But in 1970 the problem still remains with us.

The only certain criterion of a cure for multiple sclerosis is either the total abolition of relapses or at least a statistically tested reduction in their rate in a large number of patients observed over a period of years. None of the "cures" so far tried has fulfilled this strict criterion. Their authors instead have relied on clinical improvement in established cases as an index of efficacy. The report of a combined trial by centres at Belfast, Leeds, and Manchester on the failure of regular corticotrophin therapy to abolish relapses in 181 treated cases compared with 169 controls, followed up for nearly two years, may be regarded as a methodological model, disappointing though the results must have been both to the patients and to the observers.[2] Likewise Henry Miller and colleagues[3] in a careful trial found that intrathecal injection of tuberculin (P.P.D.) did not have any favourable influence on the course of the disease.

Many proposed "cures" based on improvement of the patients have stemmed from theories differing from the infective hypothesis. Among others T. J. Putnam,[4] following up the thrombotic theory of the disease which had been propounded in the late nineteenth century, reported that 25 patients treated for an average of 18 months had no relapses, but G. A. Schumacher's[5] experience did not support these views. R. L. Swank[6] favoured treatment with a low-fat diet, and the dietary regimen proposed by J. Evers[7] is also based on a belief that raw foods are good while cooked foods are bad for multiple sclerosis. In neither of these treatments have we seen any statistically controlled trials. Swank in fact himself comments on the absence of controls in his series. In any event relapses do not seem to have been abolished or even reduced in number.

The infectious theory of causation has recently received additional attention but to little positive effect. The Russian Margoulis-Shubladze vaccine came on the scene in the 1950s and gave rise in 1958 to a series of questions in Parliament.[8] Interest in this particular therapy subsided rapidly with the disclosure that the vaccine was derived from a virus similar to that of rabies.[9] This remarkable episode exemplified the curious xenophilia characteristic of both press and general public to many problems of medical treatment.

Later another infective theory came to the fore. P. Le Gac,[10] interested in rickettsial disorders as a result of his work in the French Colonial Service, advanced the view that multiple sclerosis is an infectious disease produced by a rickettsia. In support of his theory he gave serological data on 27 cases, 23 of which showed positive agglutination reactions to various forms of rickettsiae. He suggested that the lesions in multiple sclerosis are a form of rickettsial endarteritis with local tissue anoxia, subsequent nerve damage, later neuroglial phagocytosis, and finally replacement of nerve tissue. In a later paper he[11] mentioned 14 negative agglutinations out of a total of 52 patients and explained that certain patients "who are suffering from a physiological deficiency state are unable to produce antibodies and so give negative reactions". Putting this theory into practice, he treated a number of patients with a regimen aimed at neutralizing the organism with broad-spectrum antibiotics given in successive months for the first twelve days in each month.[12] Simultaneously he urged what he called the "elimination of toxins" by hot seaweed baths, the stimulation of the cardiovascular system by camphor and nikethamide, and restoration of the patient's general state by the administration of calcium, testosterone, and an infusion of Quinton's plasma (diluted sea-water). Cure was said to be aided by acetylcholine injections and by draughts of sweetened infusions compounded of wild cherry stalks, maize whiskers, and couch grass, while further benefit might result from taking the well-known natural Vitel water. Le Gac has also suggested that amyotrophic lateral sclerosis, Parkinsonism, and other diseases of the nervous system are due to rickettsial infection and may respond to this regimen.

The investigation reported by Professor E. J. Field and Miss Mavis Chambers[13] at page 30 of the *B.M.J.* last week is therefore to be welcomed for its careful analysis of the scientific basis of the rickettsial theory. It seems that the serological evidence adduced by Le Gac is open to considerable doubt and that the findings in normal controls do not differ significantly from those in cases of multiple sclerosis. Field and Chambers draw attention to the fact that Le Gac has so far not produced any reports of controlled trials and also to the evidence provided by a number of patients who have received the treatment but have not had any significant alteration in the course of their disease. This clinical evidence can be supported by other clinical neurologists who have seen such cases. It seems, therefore, that the twin scientific and therapeutic supports of the Le Gac theory are fragile.

In the face of a disorder that is ill understood and so tragic in its effects many serious and well-intentioned people, both lay and medical, press clinicians to carry out clinical trials of various remedies. The "try-anything" philosophy is indeed very understandable, and it is difficult to produce arguments to counter it. But future attempts must begin with a scientifically reasonable idea (and Le Gac's idea was reasonable) and then proceed to thorough therapeutic trial as exemplified by the three-cities trial of corticotrophin.[2]

Is the present position all dark? So far there is indeed no cure, but treatment is helpful. Though relapses cannot be abolished, the residual effect of an acute attack can be minimized. The relation between intercurrent infection and relapse of the disease may be indirect and involve immune mechanisms.[14] Some workers[15 16] have commented on the apparent rapidity with which acute relapses in multiple sclerosis appeared to respond to the administration of cortisone, prednisone, or corticotrophin. M. D. Rawson and colleagues[17 12] studied the clinical evolution of two groups of cases of retrobulbar neuritis and showed that the response in 25 treated cases was both more rapid and better than in 25 controls. This was a double-blind trial and appears to be statistically valid at least for the short-term result. If the results of treating retrobulbar neuritis can be generalized to acute attacks elsewhere in the nervous system, it does seem reasonable to give the patient a short course of corticotrophin in one form or another as advised by Rawson and his colleagues.[18] But, as Millar and his colleagues showed,[2] continuous corticotrophin therapy (at least in a dosage of 20 units per day) was not effective in abolishing relapses. In addition we know that vitamin B_1 and vitamin B_{12} are essential components of myelin. On the assumption that myelinated fibres have been only partly destroyed by the disease process it may be reasonable to give a short course of both vitamins for two or three months after any acute attack.

Apart from these suggestions the treatment of multiple sclerosis must be symptomatic, with management of spasticity, bladder symptoms, and such other disabilities over which the patient may be helped. Meantime the struggle to find the real cure goes on, and the criteria by which it is tested should be rigorous and strictly observed.

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Learning and Aversion

Aversion therapy is one of a number of treatments based on principles of learning. It sets out to inhibit patterns of behaviour which the patient finds undesirable and wishes to control, and it does so by linking the behaviour pattern repeatedly with an unpleasant stimulus, so that a conditioned reflex is established.

The best-known form of aversion therapy is still the use of apomorphine or emetine in the treatment of alcoholism. Administration of apomorphine, which acts as an unconditional stimulus for nausea and vomiting, is repeatedly asso-