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PROGNOSIS AND TREATMENT OF DISSEMINATED SCLEROSIS

Despite the variable clinical course of disseminated sclerosis, it is commonly assumed that all patients sooner or later become severely disabled. That this fact is regrettably true of the majority cannot be denied, but there is some evidence that a more benign form of the disease may exist. As D. McAlpine[1] has pointed out, there are some patients who make a good recovery from an initial attack of the disease, and relapses may then be mild and infrequent or may cease altogether. Of a series of 586 cases observed at the Middlesex Hospital, 13% of those followed for 15 years showed no disability.[2] L. Alexander and his co-workers[3] have confirmed that the disease exists in severe and mild forms, but point out that there is some overlap between the two. They believe that it is possible, five years after the onset, to predict into which of these two groups any individual patient will fall. This assessment is derived from a complex method—first devised by Alexander in 1951[4]—of allotting a numerical score to the various symptoms and physical signs roughly in proportion to the severity and significance of the resulting disability. Alexander claims that when different observers were asked to calculate the score for any single patient the results were remarkably consistent. By making this calculation at frequent intervals it was possible to obtain a graphic representation of the course of the disease. On this scale a score of 0 would be given if there were no symptoms or physical signs, while a totally disabled patient would achieve a figure of approximately 500. It is now suggested[3] that, if a patient should have a total score of less than 125 after the illness has been in progress for five years, a mild course can be confidently predicted, while if it is over 200 the progress of the disease is likely to be comparatively rapid and the consequent disability severe. Despite the obvious dangers in such a method of assessing disability in a clinically pleomorphic disease—dangers which are even more apparent in simpler indices of severity such as the ten-point scale devised by J. F. Kurtzke[5]—laborious measurements of this type do at least give a degree of objectivity which may be useful in attempts to assess the effect of treatment.

Though there may be some encouragement to sufferers, and to those who care for them, in the knowledge that the disease may sometimes be mild, the discovery of an effective treatment must remain a principal aim of research, since so many patients become crippled at a comparatively early stage. The multiplicity of remedies advocated at one time or another shows how many and varied have been the theories about the aetiology of the disease. Thus numerous bacterial vaccines have been given in the belief that the disease may be infective, as have arsenic and fever therapy.[6] There is little evidence that these methods have any value, though McAlpine[1] continues to advise arsenotherapy in some cases. Because narrowing or spasm of blood vessels has been suggested as an aetiological factor, histamine[7] and other vasodilators such as nicotinic acid have been tried. R. M. Brickner[8] believes that remedies of this type may have some benefit during acute episodes of the disease, but his results have not been confirmed. Many diets have also been devised from time to time, the latest being the low-fat diet of R. L. Swank,[9] but the rationale of this method is far from convincing. Treatment with liver extracts or vitamin B_{12} is extensively used in Britain, though there is little reason for prescribing these remedies and they are probably given *faute de mieux* rather than as rational therapy. Isoniazid, which has also been widely used, has been found to have no significant effect upon the course of the disease.[10] Physiotherapy is occasionally very helpful, though it has no direct influence upon the disease process, simply helping to relieve symptoms, as do drugs such as mephenesin, chlorpromazine, and zoxazolamine, which may sometimes reduce spasticity.

Much publicity has been given to the Russian vaccine which A. Shubladze and S. Gaidamovitch[11] claimed to be an effective treatment. This vaccine was prepared from the so-called E.H.A. virus isolated from cases of disseminated sclerosis in 1942 by Margulis, Soloviev, and Shubladze. At the begin-

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[3] Alexander, L., Berkeley, A. W., and Alexander, A. M., *J. Amer. med. Ass.*, 1958, **166**, 1943.
[4] —— *Arch. Neurol. Psychiat. (Chicago)*, 1951, **66**, 253.
[5] Kurtzke, J. F., *Neurology (Minneap.)*, 1955, **5**, 580.
[6] Cloake, P. C. Humphry Davy Rolleston Lecture, 1946, quoted by D. McAlpine *et al.* in *Multiple Sclerosis*, 1955, Edinburgh.
[7] Horton, B. T., and Wagener, H. P., *J. Lab. clin. Med.*, 1948, **33**, 1611.
[8] Brickner, R. M., *Arch. Neurol. Psychiat. (Chicago)*, 1952, **68**, 180.
[9] Swank, R. L., ibid., 1953, **69**, 91.
[10] Kurtzke, J. F., and Berlin, L., *J. Amer. med. Ass.*, 1957, **163**, 172.
[11] Shubladze, A., and Gaidamovitch, S., *G. Mal. infett.*, 1956, Fasc. II, p. 173.
[12] Dick, G. W. A., McKeown, F., and Wilson, D. C., *Brit. med. J.*, 1958, **1**, 7.
[13] Shubladze, A. K., and Dick, G. W. A., ibid., 1958, **2**, 245.
[14] van Bogaert, L., *Rev. neurol.*, 1932, **2**, 1.
[15] McAlpine, D., Compston, N. D., and Lumsden, C. E., *Multiple Sclerosis*, 1955, Edinburgh.
[16] Pette, H., *Die akut entzundlichen Erkrankungen des Nervensystems*, 1942, Leipzig.
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[18] Glaser, G. H., and Merritt, H. H., *J. Amer. med. Ass.*, 1952, **148**, 898.
[19] Fog, T., *Nord. med.*, 1952, **46**, 1742.
[20] Miller, H. G., and Gibbons, J. L., *Brit. med. J.*, 1953, **2**, 1345.
[21] Smith, H. V., Espir, M. L. E., Whitby, C. W. M., and Russell, W. R., *J. Neurol. Psychiat.*, 1957, **20**, 1.

ning of this year Professor G. W. Dick and his co-workers[12] in Belfast reported that the virus from which the Russian vaccine was made was indistinguishable from rabies virus and that the vaccine might therefore be dangerous. A few weeks ago Professor Shubladze expressed his agreement with the findings of the Belfast workers in a letter[13] signed also by Professor Dick and published in this *Journal*. As a treatment for disseminated sclerosis this vaccine therefore no longer has any standing.

That disseminated sclerosis might be an allergic reaction of the nervous system to a variety of sensitizing agents was first suggested by L. van Bogaert[14] in 1932. Quite apart from the similarity between histological changes in the nervous system in this disease and those of acute encephalomyelitis, there is now more clinical evidence to support this view, to which an increasing number of workers subscribe.[2 15 16 17] Certainly there is evidence that relapses may follow non-specific infections, as they may follow fatigue, trauma, or emotional stress.[1] It is therefore not surprising that A.C.T.H., cortisone, and related remedies should have been tried in disseminated sclerosis. Results have been conflicting. G. H. Glaser and H. H. Merritt[18] reported that some of their 33 cases improved, as did T. Fog,[19] but H. G. Miller and J. L. Gibbons[20] concluded from their experience in 7 cases with acute neurological episodes that A.C.T.H. had no effect. However, Alexander and his co-workers,[3] using their "scoring" method of assessing disability, now believe that A.C.T.H. has a significantly beneficial effect upon the course of the disease. But no similar benefits were seen after treatment with cortisone or prednisone, and the authors suggest that the improvement was due to some adrenal hormone other than cortisone, a view which must be accepted with some reserve. It was also found that weekly blood transfusions reduced the liability to relapse, possibly through some factor in the donor's blood which enabled the patient to resist further encroachments by the disease process. In the absence of adequate controls it is impossible to be certain that these methods have a real place in treatment, but there is an increasing body of opinion which now favours a course of A.C.T.H., cortisone, or prednisone during acute episodes of the disease.

A lack of controls also makes it difficult to assess the findings of H. V. Smith and her co-workers,[21] who reported that intrathecal injections of purified protein derivative (P.P.D.) of tuberculin might modify the course of the disease. Their observation that Mantoux-positive cases of disseminated sclerosis show a modified reaction in the cerebrospinal fluid when P.P.D. is injected, as if a cortisone-like substance were being spontaneously produced, is of the greatest interest, but it is difficult to see exactly why treatment with P.P.D. should arrest the disease. Possibly it may act by producing widespread vasodilatation in the central nervous system. It is apparent that this is one of several methods of treatment arising out of recent research work which merit investigation in a series of carefully planned controlled trials. With the lively interest now being taken in disseminated sclerosis the patient with this disease and the doctor who must care for him may now discern a glimmer of hope.

THE DEAF CHILD

The possibility that her child may be born deaf is not one that usually occurs to the mother. Only if she is intimately connected with the problems of deafness, or if she has a fear of a hereditary tendency, is she likely to make observations on her child's reaction to sound. Fortunately only a few children are born with a defect of hearing, probably not more than one per thousand, but even so it is by no means a negligible problem. Deafness alone is serious enough, but it always has accompanying defects of speech and general development if it is not treated at an early stage. Thus the problem of early diagnosis is of fundamental importance.

The detection of deafness is not easy early in a child's life, for in the first few weeks the general behaviour of normal and deaf babies is much the same, but about the age of 4 weeks a normal child first becomes responsive to sounds associated with natural life such as the mother's activities and attentions and the sounds of other children. Later the normal child's response becomes more versatile, though not always predictable, for a given sound may not evoke the same response in all situations.[1-3] It is in observing these reactions that the parent is in a privileged position; indeed, many of the young deaf children referred to clinics are first discovered by parents because they noted abnormal responses at these early stages.

Deafness in early childhood may be due to a number of causes which include hereditary factors, prenatal infection, effects of chemotherapy, and mishaps at birth. Collaboration between doctors, parents, and audiologists can assure that, should one of these causes be suspected, adequate investigations can be carried out. In recent years school medical

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[4] *Educational Guidance and the Deaf Child*, 1957, edited by A. W. G. Ewing, Manchester University Press.
[5] Ewing, I. R., and Ewing, A. W. G., *Opportunity and the Deaf Child*, 1947, University of London Press.
[6] —— —— *Speech and the Deaf Child*, 1954, Manchester University Press.
[7] International Congress on the Modern Educational Treatment of Deafness (Proceedings in press), 1958, Manchester.