[2] League, R., Parker, J., and Robertson, M., *Lancet*, 1970, **2**, 978.
[3] Shapiro, R. A., and Berland, T., *New England Journal of Medicine*, 1972, **287**, 1236.
[4] Falk, S. A., and Woods, N. F., *New England Journal of Medicine*, 1973, **289**, 774.
[5] Griffiths, P. D., Kell, R. L., and Taylor, W., *Journal of Clinical Pathology*, 1970, **23**, 445.
[6] *British Medical Journal*, 1970, **3**, 662.
[7] Brown, R., *New Scientist*, 1973, **60**, 414.

Signs of Multiple Sclerosis

Walter Moxon (1836-1886), who presented the first two cases of "insular sclerosis" in Great Britain, was guided in the diagnosis by Charcot's triad of nystagmus, scanned speech, and intention tremor.[1] Charcot's approach implied that symptoms are related to the plaques in the nervous system. This view is still widely held, as the following admonition indicates: "We must refuse to diagnose multiple sclerosis if multiplicity be absent."[2] But clinical experience sometimes counters this rule, since cases are seen in which signs and symptoms are indicative of but a single focal lesion. Thus, some 50% of cases of classic retrobulbar neuritis due to the disease never developed any other neurological signs during follow-up periods exceeding ten years.[3-6]

The following are some other well-recognized forms of monosymptomatic presentation of multiple sclerosis: paresis of abducens or facial nerves; facial myokymia;[7,8] trigeminal neuralgia;[9,10] various forms of "internuclear ophthalmoplegia"; vertigo; progressive spastic paraplegia;[11] sensory disturbances, often of symmetrical distribution and not showing any obvious sensory deficit; and Lhermitte's signs (the development of electric-like shocks down the body when the patient flexes the head).[12] Despite even advanced and typical pathological changes in the central nervous system, signs and symptoms may be entirely absent. In some 18% of cases of multiple sclerosis discovered in the course of a large series of consecutive necropsies no relevant symptoms had been noted during life.[13] Again, neuropathological evidence of long-standing disease may be in striking contrast to the brevity of the clinically active phase.[14]

Sometimes such silent cases of multiple sclerosis may betray themselves only during periods of rise of body temperature, whether caused by muscular exercise or fever. It is now generally recognized that transient temperature-related impairment of vision—unilateral or bilateral—must be regarded as a symptom of multiple sclerosis even when other clinical features of this disease are absent.[15,16] This effect of a rise in body temperature intensifying symptoms of multiple sclerosis or provoking new ones forms the basis of a test.[17] Lowering of body temperature may in contrast give temporary relief of symptoms.

Since experimental heating and cooling of nerve tissue result in functional changes opposite to those observed in multiple sclerosis, it has been suggested that the phenomena observed in this disease in response to changes of temperature are due to hormonal influences.[18,19] It is assumed that the hormones concerned are those released during thermal regulation, and it is postulated that they may reduce or increase conduction in regions of central demyelination.[20,21] After G. D. Dawson devised a technique of recording cerebral action potentials it became possible to estimate nerve conduction in man's central nervous system.[22] A delay of cortical responses on stimulation of the median nerve has been detected in 75% of cases of multiple sclerosis.[23-25] A similar delay of cortical responses was also found in cases of multiple sclerosis when a flash of light was used as a visual stimulus.[26,27] A stimulus engendered by the reversal of a checker board pattern has now been used for the study of cortical potential responses in multiple sclerosis, and its value as a diagnostic test is reported on by Dr. A. M. Halliday and colleagues in our Medical Practice section (page 660) this week. A direct comparison of the results obtained with flash and pattern stimuli has previously shown many advantages gained when the pattern stimulus is used,[28] and 93% of patients with multiple sclerosis who gave no history of optic neuritis were found to have delayed cortical responses.

It is difficult to explain these findings, as it is some other clinical phenomena in multiple sclerosis, on the basis of Charcot's "insular" concept. The plaques may perhaps be regarded as representing the "last of a series of changes," some of which may be more widespread than light microscopy would suggest.[29] Indirect support for this inference may be found in investigations proceeding along several different lines.

In biopsy material obtained from the brain of patients suffering from multiple sclerosis thinly myelinated axons with widened nodal gaps have been identified by means of electron-microscopy.[30] Histochemistry has shown abnormal forms of myelin in multiple sclerosis.[31] Reactions produced on cultures of brain tissue by the addition of sera from patients with multiple sclerosis indicate that such sera contain highly specific factors which are toxic to myelin and oligodendrocytes, and also have an inhibitory effect on synapses.[29,32] Whether speculations on these lines will eventually come to be substantiated or refuted the observations made by Halliday and colleagues on visually evoked responses in multiple sclerosis, when scrutinized as they have suggested, should prove of great value in diagnosis—"an art which consists largely of balancing probabilities."[33]

[1] Hospital Practice, *Lancet*, 1875, **1**, 471 and 609.
[2] Kennedy, F., *Research Publications Association for Research in Nervous and Mental Diseases*, 1950, **28**, 524.
[3] Kurland, L. T., Auth, T. L., Beebe, G. M., and Kurtzke, J. F., *Transactions of the American Neurological Association*, 1963, **88**, 231.
[4] Collis, W. J., *Archives of Neurology*, 1965, **13**, 409.
[5] Bradley, W. G., and Whitty, C. W. M., *Journal of Neurology, Neurosurgery, and Psychiatry*, 1968, **31**, 10.
[6] Taub, R. G., and Rucker, C. W., *American Journal of Ophthalmology*, 1954, **37**, 494.
[7] Andermann, F., Cosgrove, J. B. R., Lloyd-Smith, D. L., Gloor, P., and McNaughton, F. L., *Brain*, 1961, **84**, 31.
[8] Matthews, W. B., *Journal of Neurology, Neurosurgery, and Psychiatry*, 1966, **29**, 35.
[9] Olafson, R. A., Rushton, J. G., and Sayre, G. P., *Journal of Neurosurgery*, 1966, **24**, 755.
[10] Chakravorty, B. G., *Archives of Neurology*, 1966, **14**, 95.
[11] Bramwell, B., and Dawson, J. W., *Edinburgh Medical Journal*, 1916, **17**, 411.
[12] Brody, I. A., and Wilkins, R. H., *Archives of Neurology*, 1969, **21**, 338.
[13] Georgi, W., *Schweitzerische medizinische Wochenschrift*, 1961, **91**, 605.
[14] Russell, D. S., *Lancet*, 1964, **1**, 978.
[15] Earl, C. J., *Transactions of the Ophthalmological Societies of the United Kingdom*, 1964, **84**, 215.
[16] *British Medical Journal*, 1972, **2**, 122.
[17] Davis, F. A., *Journal of the Mount Sinai Hospital*, 1966, **33**, 280.
[18] Paintal, A. S., *Journal of Physiology*, 1965, **180**, 20.
[19] Heiss, W. D., Heilig, P., Heyer, J., *Experimental Brain Research*, 1968, **4**, 321.
[20] Hopper, C. L., Matthews, C. G., and Cleeland, C. S., *Neurology*, 1972, **22**, 142.
[21] McDonald, W. I., and Sears, T. A., *Brain*, 1970, **93**, 583.
[22] Dawson, G. D., *Journal of Neurology, Neurosurgery, and Psychiatry*, 1947, **10**, 137.
[23] Namerow, N. S., *Bulletin of the Los Angeles Neurological Society*, 1968, **33**, 74.
[24] Baker, J. B., Larson, S. J., Sances, A., and White, P. T., *Neurology*, 1968, **18**, 286.
[25] Namerow, N. S., *Neurology*, 1968, **18**, 1197.
[26] Richey, E. T., Kooi, K. A., and Tourtelotte, W. W., *Journal of Neurology, Neurosurgery, and Psychiatry*, 1971, **34**, 275.
[27] Namerow, N. S., and Enns, N., *Journal of Neurology, Neurosurgery, and Psychiatry*, 1972, **35**, 829.
[28] Halliday, A. M., McDonald, W. I., and Mushin, J., *Lancet*, 1972, **1**, 982.
[29] Bornstein, M. B., in *Central Nervous System*, ed. O. T. Bailey and D. E. Smith, p. 70. Baltimore, Williams and Wilkins, 1968.

Br Med J: first published as 10.1136/bmj.4.5893.626 on 15 December 1973. Downloaded from http://www.bmj.com/ on 22 September 2020 by guest. Protected by copyright.

[30] Suzuki, K., Andrews, J. M., Waltz, J. M., and Terry, R. D., *Laboratory Investigations*, 1969, **20**. 444.
[31] Feigin, I., and Popoff, N., *Journal of Neuropathology and Experimental Neurology*, 1966, **25**, 166.
[32] Bornstein, M. B., and Crain, S. M., *Science*, 1965, **148**, 1242.
[33] Osler, W., *Aequanimitas*, 3rd edn., p. 38. London, H. K. Lewis, 1939.

Hodgkin's Disease and Schools

The claim by N. J. Vianna and colleagues[1] that Hodgkin's disease is an infective condition with a carrier state, a long incubation period, and transmission by person-to-person contact was the subject of previous comment in these columns.[2] The hypothesis was based on finding that a surprising number of cases of the disease in Albany, New York State, could be linked. Arresting though it was to learn that 31 cases could be linked, it was difficult to assess this finding, particularly since the group of cases investigated was largely identified by following up leads of possible links from case to case. That the authors could find no links between 18 cases of a non-infective condition (burns) which were each identified in a quite different way did not help to evaluate the observations about Hodgkin's disease. This shortcoming was pointed out[2] and the need for a carefully controlled study stressed, preferably in an area where no one had suspected clustering of the disease.

Both these requirements are met by a new study recently reported by Vianna and A. K. Polan in which confirmatory evidence for the hypothesis is offered.[3] This evidence comes from pupils, students, and teachers in schools and colleges in Suffolk and Nassau counties of New York State. Two approaches were used to analyse the data. In the first it was possible to link to the eight high schools which had a new case in a pupil or teacher in the period 1960-4 no fewer than 10 cases diagnosed in the years 1965-9, but only nine cases were linked to the remaining 195 schools which had no cases during 1960-4. In the second approach the 20 schools which had at least one case in the study period were found to have produced additional (or "secondary") cases in 21 students and seven teachers after the first (or "primary") case, whereas the numbers expected were 9·3 students and 0·9 teachers. It was also noted that the high schools in which Hodgkin's disease occurred tended to be larger than the average, for the annual rate for schools with a total enrolment of 1,500 or more was 23·8 per 100,000, but it was only 5·3 for smaller schools.

This work may be of importance to our understanding of Hodgkin's disease. However, it is also likely to disturb both patients and their contacts. It therefore demands close attention. A crucial question is whether the clustering of disease in certain schools could be due to some overlooked methodological bias. Thus it might be postulated that there may have been a consistent tendency to overlook cases in certain areas and schools. Not only would this have to be on a very large scale (entirely out of accord with the reported thoroughness of the search for cases), but it would still not explain the repeated observation of secondary cases of this rare disease in schools with "primary" cases.

Nevertheless, one point deserves comment. The number of cases of Hodgkin's disease (at all ages) found by Vianna and Polan in the two counties seems surprisingly low, indicating a rate of 1·9 per 100,000 compared to 2·6 in New York State excluding New York City.[4] More importantly, the numbers of cases found in Suffolk and Nassau in the age group 10-19 seem particularly low. The annual rate appears to be below 0·6 per 100,000, though the corresponding figure for the whole state (excluding New York City) in 1959-61 was almost three times greater (1·6).[4] Such differences must raise the question of cases being overlooked. On the other hand the annual incidence rates calculated for the high school children aged 13-17 of 5·3 and 23·8 per 100,000 according to the size of school are very high indeed—being appreciably greater than the rate of 2·3 reported for New York State in 1959-61 in the slightly older age group 15-19.[4]

As the authors themselves state, studies of this type should be interpreted cautiously. It would be helpful if the apparent discrepancies referred to above could be explained, but in any case there would still remain an urgent need for other workers to apply similar methods in other areas. Details of schooling are not difficult to obtain even in the case of deceased patients, so the results of further studies on similar lines may be expected in the near future, together with the results of a carefully controlled study in the Oxford region.[5]

To counter anxiety in patients and their contacts as a result of this work it is right to observe, firstly, that the whole question is still open, and secondly that the risk of developing Hodgkin's disease, even if it is increased almost three-fold in certain schools as this work suggests, is still very low. At ages 10-19 in England and Wales the annual incidence rate in the years 1963-6 was estimated as being less than 0·02 cases per 1,000 persons.[6] From the point of view of prevention the present evidence gives little indication of whether Hodgkin's disease may be infectious before or after diagnosis. At least one pair of cases in the Albany series suggests evidence of infectivity before diagnosis, but in general Vianna and Polan's data do not allow this question to be investigated.

[1] Vianna, N. J., *et al.*, *Annals of Internal Medicine*, 1972, 77, 169.
[2] *British Medical Journal*, 1972, **4**, 564.
[3] Vianna, N. J., and Polan, A. K., *New England Journal of Medicine*, 1973, **289**, 499.
[4] Doll, R., Payne, P., and Waterhouse, J., *Cancer Incidence in Five Continents*, Vol. 1. U.I.C.C., Springer-Verlag, 1966.
[5] Kinlen, L. J., Pike, M. C., and Smith, P. G., *British Journal of Preventive and Social Medicine*, 1973, **27**, 66.
[6] Doll, R., Muir, C., and Waterhouse, J., *Cancer Incidence in Five Continents*, Vol. 2. U.I.C.C., Springer-Verlag, 1970.

Neonatal Kidney Tumours

Though typical nephroblastomas composed of a mixture of embryomatous tissues are encountered in early infancy,[1] the majority of renal neoplasms originating in the fetus and found during the first few weeks of life differ in structure and in biological behaviour. In gross appearance these neonatal tumours are unencapsulated and infiltrate and replace some 50% to 90% of the renal parenchyma. The cut surface has a pale, whorled appearance resembling that of a uterine fibroid, and areas of haemorrhage and necrosis, so common in nephroblastomas, are not seen. Histologically, tissue composed of elongated, spindle-shaped cells of both fibrous and leiomyomatous type predominates, but thin-walled vascular sinusoids are evident, as are foci containing glomeruli and renal tubules, which are sometimes dysplastic and immature. These epithelial elements are believed to represent portions of kidney tissue which have become entrapped within the neoplasm. The whole appearance is that of a mesenchymal proliferation of a diffuse rather than a unicentric origin.[2]

Clinically, the presenting feature is most often an abdominal mass which is detected on routine neonatal examination.

Br Med J: first published as 10.1136/bmj.4.5893.626 on 15 December 1973. Downloaded from http://www.bmj.com/ on 22 September 2020 by guest. Protected by copyright.