case, for example, of the skin-sensitizing antibody to ragweed extract (Stavitsky and Arquilla, 1955; Sehon, 1959). Evidence available at the moment, however, does not suggest that circulating antibody to brain plays any fundamental pathogenic part in multiple sclerosis.

Summary

Blood serum and spinal fluid from cases of multiple sclerosis in all stages of the disease and from controls (mainly other neurological conditions) failed to fix complement with an alcoholic brain extract when 5 MHD_{50} of complement was used. The possible causes of discrepant reports in the literature are briefly discussed.

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MULTIPLE SCLEROSIS AND SPINAL-FLUID GAMMA-GLOBULIN

BY

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Although its origin and pathological significance remain uncertain, many workers have confirmed that the gamma-globulin fraction of the spinal-fluid protein is often strikingly increased in multiple sclerosis (Kabat *et al.*, 1942, 1950; Roboz *et al.*, 1953; Yahr *et al.*, 1954; Ivers *et al.*, 1961; Schapira and Park, 1961).

The application and limitations of this method of investigation were discussed by Schapira and Park, who found a mean level of 22.4% (±9.47) of gamma-globulin expressed as a fraction of total spinal-fluid protein in 81 patients with multiple sclerosis, as compared with a figure of 11.1% (±3.18) in 25 control cases: they estimated gamma-globulin by an electrophoretic method, and the increase in this fraction in the cases of multiple sclerosis was highly significant ($P<0.001$). Schapira and Park shared the views of those who had previously reported observations on smaller series of cases that the estimation was potentially helpful in diagnosis.

However, electrophoretic estimation of spinal-fluid proteins is laborious and beyond the scope of smaller laboratories. Papadopoulos *et al.* (1959) described a simple colorimetric method of estimation based on the use of the Folin–Ciocalteu (1927) phenol reagent. It was decided to test this method on the spinal fluids of consecutive neurological admissions to try to assess the comparative value of this very much simpler laboratory test.

Material.—The spinal fluids obtained from 200 successive admissions were first examined by routine laboratory methods, and the total protein and the gamma-globulin were estimated by the method of Papadopoulos *et al.* From a total slightly in excess of 200 a few cases were excluded in which diagnosis remained uncertain.

Results

In all cases the gamma-globulin level was expressed as a percentage of total protein, the value of which ranged from 19 to 500 mg./100 ml of cerebrospinal fluid. The figures for some of the main groups of patients are given in Table 1; cases of multiple sclerosis were regarded as "acute" when symptoms had been present for less than one month.

TABLE I.—*Spinal-fluid Gamma-globulin Levels in Eight Common Neurological Disorders*

Diagnosis and No. of Cases	Gamma-globulin Expressed as % of Total Protein
Acute multiple sclerosis (5)	50, 40, 38, 36, 26
Chronic multiple sclerosis (18)	55, 44, 43, 38 (2), 37, 34, 33 (2), 30 (2), 27, 25, 24, 22 (2), 19, 12
Cerebral infarction (22)	28, 24, 23, 22, 21, 18, 16, 14, 13, 11 (2), 9, 7, 6 (4), 5 (3), 4, 2
Epilepsy (20)	21, 18, 17 (2), 15, 13, 12 (2), 11, 10 (2), 9 (2), 8, 7 (2), 5, 4, 3, 2
Aural vertigo (19)	18 (2), 16, 15, 14 (3), 12, 11, 8 (3), 7, 5 (3), 4 (2), 2
Cervical spondylosis (14)	23, 17 (2), 15, 14, 13 (3), 8 (2), 5, 4 (3)
Motor-neurone disease (8)	19, 18, 14, 7, 5, 3 (2), 1
Vertebrobasilar insufficiency (7)	21, 14, 12, 10, 7, 6, 4
Spinal tumour (7)	25, 18 10, 7, 6, 3, 2

Among smaller groups of patients were six with miscellaneous headaches (16, 9, 6, 6, 5, 3); five each with neurosyphilis (47, 32, 31, 14, 11), chronic polyneuritis (17, 12, 11, 6, 3), and carotid artery stenosis (30, 21, 19, 13, 7). There were four each with presenile dementia (26, 16, 6, 5) and cerebral glioma (29, 26, 25, 12); and three cases of retrobulbar neuritis (37, 18, 15), spontaneous subarachnoid haemorrhage (23, 11, 2), Guillain–Barré syndrome (18, 14, 14), and hypertensive cerebral haemorrhage (13, 6, 3).

The series comprised two cases each of benign intracranial hypertension (11, 9), Krabbe's leucodystrophy (18, 16), syringomyelia (9, 5), subacute combined degeneration (8, 5), aqueduct stenosis (18, 17), temporal arteritis (19, 18), paralysis agitans (18, 6), cerebellar degeneration (23, 7), cerebral fat embolism (11, 9), and haemophilus meningitis (27, 3). Single cases gave figures as follows: subacute inclusion-body encephalitis (33), Stokes–Adams attacks (6), post-pertussis atrophy of cerebral hemisphere (20), migraine (8), syncope (11), progressive myoclonic epilepsy (12), recent poliomyelitis

(18), polyradiculitis complicating measles (31), carcinomatous neuropathy (11), tobacco amblyopia (15), transverse myelitis (20), muscular dystrophy (4), lateral sinus thrombosis (24), acute infantile hemiplegia (13), cerebral abscess (20), cerebral contusion (8).

The mean values and standard deviations of gamma-globulin expressed as a percentage of total protein in spinal fluid for 23 patients with multiple sclerosis (acute and chronic) and 177 patients with other neurological complaints are shown in Table II. With a standard error of 1.93, the difference between these means is highly significant ($P \ll 0.001$). The five cases of neurosyphilis had a mean of 27.0, with a standard deviation of 14.71. The remaining 172 cases had a mean of 12.2

TABLE II.—*Mean Values and Standard Deviations of Spinal-fluid Gamma-globulin Expressed as a Percentage of Total Protein*

	Mean	Standard Deviation
Multiple sclerosis	32·9	±10·16
Others	12·7	±7·95

(S.D. ±7.34). With a standard error of 3.44 the difference between these two means is highly significant ($P<0.001$). There was no statistically significant difference between the means of the multiple sclerotic and neurosyphilitic cases ($P>0.2$).

The group of miscellaneous conditions with a mean of 12.7 plus two standard deviations reaches a value of 28.6. Eight of the 177 cases, or 5% of the distribution, lie outside this value, and three of the eight patients making up this proportion gave positive serological tests for neurosyphilis. Of the multiple sclerotic group, 15 of the 23 patients had a higher gamma-globulin fraction than 28.6%.

Discussion

These results indicate that, using the colorimetric method of Papadopoulos, a figure of more than 28.6% of gamma-globulin expressed as a fraction of total spinal-fluid protein is highly suggestive of multiple sclerosis, provided serological tests for neurosyphilis are negative. Levels above 28.6% are found in only about 5% of all other neurological cases, and in a still smaller proportion of those most easily confused clinically with multiple sclerosis, such as subacute combined degeneration, cervical spondylosis, and especially spinal tumour. On the other hand, a "normal" figure (below 28.6%) by no means excludes the diagnosis of multiple sclerosis, such figures being found in one-third of such cases. In this series there was no correlation between gamma-globulin level and duration of symptoms. The Lange curve was "paretic" in only 3 of the 23 cases.

These observations establish that, despite its limitations, estimation of spinal-fluid gamma-globulin can be a useful aid in the recognition of multiple sclerosis, and that at the present time it is the best laboratory test available in this connexion. The colorimetric method yields generally higher levels and a wider scatter than the electrophoretic techniques previously described, but it is simple and rapid enough to permit its employment as a routine laboratory procedure.

Summary

The results of colorimetric estimation of the gamma-globulin content of the spinal fluid in 200 unselected neurological patients are presented and considered in relation to clinical diagnosis. The value of a positive finding in the differentiation of multiple sclerosis from other neurological disorders is confirmed, and it is suggested that the method is suitable for routine laboratory employment.

We are indebted to Professor A. L. Latner and Dr. Henry Miller for suggesting this investigation and defining its scope and purpose, and to Mrs. D. Weightman, of the Department of Industrial Health, for the statistical analyses.

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Medical Memoranda

An Unusual Injury

A haymaking machine (syn. haykicker. Welsh: chwalwr) designed to throw up and turn cut hay consists of a number of steel prongs which stick out from a bar. A series of bars are attached to a central spindle which rotates as the machine is pulled forward. The bar is about 3 ft. (90 cm.) long (Fig. 1). Older machines, made partly of wood and possessing no guard, were designed to be drawn by a horse. Nowadays they are drawn by tractors and consequently subjected to much greater stress.

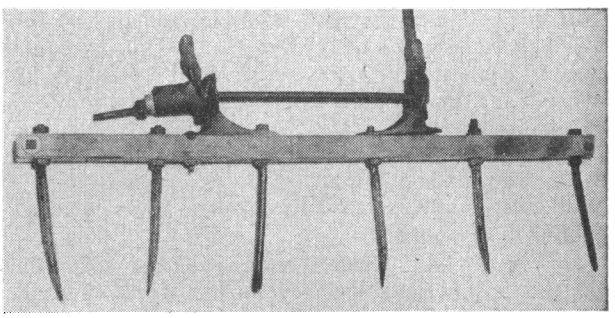

FIG. 1.—Photograph of part of haymaking machine.

Case Report

On June 24, 1961, a young fit man aged 18 was driving a tractor hauling such an old type of haymaking machine. Noticing the exhaust of his tractor beginning to turn red, he leaned forward to switch off the engine, when he heard a loud bang and experienced a sudden pain in his back. He was knocked off his seat on to the ground, where he lay in a prone position. He felt a heavy weight on his back and was unable to breathe properly because of pain.

He managed to attract the attention of his sister, who was driving another tractor. She helped him to his feet and walked him over two fields to the farmhouse. From there an ambulance brought him, in the standing position, to the casualty department of the West Wales General Hospital. The situation at the time is shown in Fig. 2. (1) The upper prong of the bar had caused a laceration over the left mastoid and the superficial bony table was fractured. (2) The second prong had entered the chest wall but lay