MULTIPLE SCLEROSIS

FROM THE STANDPOINT OF GEOGRAPHIC DISTRIBUTION AND RACE *

CHARLES B. DAVENPORT, PH.D.

COLD SPRING HARBOR, L. I., N. Y.

The results of the tabulation of multiple sclerosis as one of the defects found in drafted men are plotted on the accompanying map. It shows that the maximum rate for this disease was found in Michigan and Minnesota, in which there were eighteen persons with this disease per 100,000. The Michigan rate is based on six cases so diagnosed by local boards and on nine at Camp Dodge. Excepting Delaware and the District of Columbia (whose rates depend on one and two cases, respectively), the next highest ratio is that for Wisconsin, fourteen per 100,000, where five cases were found by local boards and six by examiners at Camp Grant. That these states with a high ratio for multiple sclerosis are adjacent states, bordering on the Great Lakes, is of great interest. Since examinations were made at three different camps, the result cannot be ascribed to the idiosyncrasy of a neuropsychiatric examiner at one camp (Fig. 1).

The nearest approach to the distribution of multiple sclerosis found in any other diseases is in goiter, exophthalmic goiter, chorea, varicose veins, varicocele and allied diseases and various heart diseases and defects. The cardiovascular diseases are associated with the tall stature of the men living about the Great Lakes—largely Scandinavians. The resemblance between the distribution of multiple sclerosis and chorea is considerable, except that chorea is abundant also in Texas, Mississippi, Missouri and the states of the North Atlantic coast and of the eastern slopes of the drainage basin of the Ohio River; that is, high rates of chorea are more widespread than of multiple sclerosis. It is rather interesting that especially high rates for chorea, as for multiple sclerosis, are found, outside the Great Lakes region, also in the states of Washington, Mississippi and Maine.

The resemblance of the distribution of multiple sclerosis to that of simple goiter is somewhat striking. In both diseases comparatively few cases are found south of the Ohio River. The maximum rate is found in Michigan, Wisconsin and the extreme Northwest.

Various hypotheses are suggested for these facts. One is that some race inhabits the Great Lakes region and the state of Washington that

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is especially subject to multiple sclerosis as well as goiter, chorea and cardiovascular defects. One thinks of the big Swedes that live in these parts of the country. Probably the cardiovascular defects are associated with the tall stature of men from these localities. The goiter is supposed to be due to the absence of iodin in the potable waters. Whether or not chorea and multiple sclerosis are especially common among Scandinavians cannot be definitely asserted. The matter is considered later in this paper. It is, of course, possible that in the rapid diagnosis of local boards and camps some cases of chorea may have been diagnosed as multiple sclerosis and vice versa.

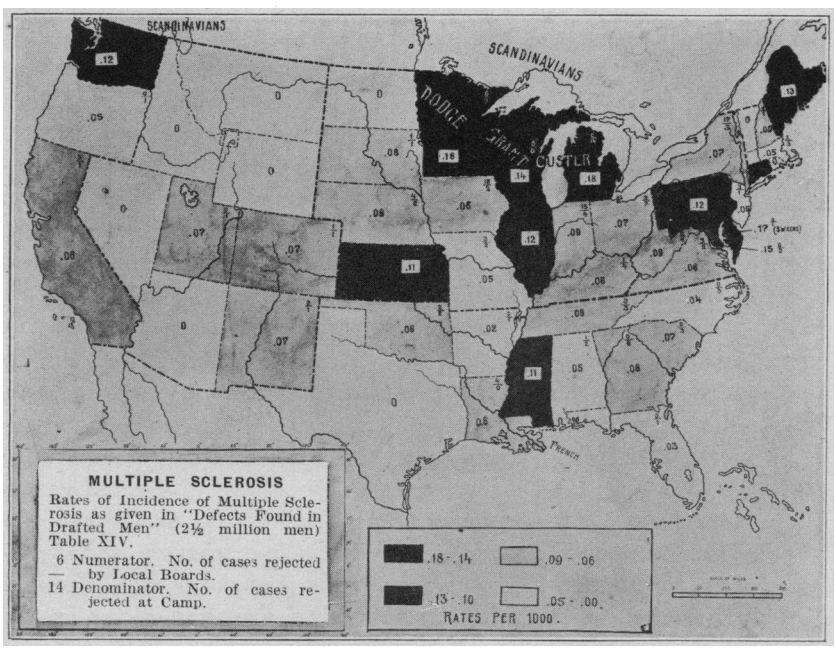

Fig. 1.—Map of the United States showing by states the varying density rate of multiple sclerosis. "Dodge," "Grant," and "Custer" in the Great Lakes region are the names of camps at which the drafted men from those localities were mobilized. (From "Defects Found in Drafted Men.")

RATE OF MULTIPLE SCLEROSIS IN URBAN AND RURAL POPULATION

For the United States as a whole, the defect rate found in the draft was, for multiple sclerosis, 10 per 100,000 of the population examined. The urban rate was 12 per 100,000 and the rural rate 8 per 100,000; thus the urban rate was one-half greater than the rural rate. For four large cities (combined) the rate was 14; the rate for each city was: Philadelphia, 23; Boston, 16; New York, 13, and Chicago, 11.

SECTIONS AND GROUPS OF SECTIONS

The rate per 100,000 men examined in the draft is shown in Table 1.

TABLE 1.—RATES PER 100,000 FOR MULTIPLE SCLEROSIS ("DEFECTS IN DRAFTED MEN")

For southern, prevailingly *white* agricultural communities	7
For southern, prevailingly *colored* agricultural communities	6
For northern agricultural communities, prevailingly native white	8
For northern agricultural communities, prevailingly foreign	10
For mining sections	7
For maritime sections	10
For mountain sections	2
For the "mountain whites" of the South	7
For Indian sections	1
For Scandinavian sections	16
For German and Austrian sections	10
For Finnish sections	29
For French-Canadian sections	8

The high ratios found in Scandinavian and Finnish sections are probably significant. However, both Finnish sections are in the Great Lakes region, which is a region with a high rate of multiple sclerosis.

RACIAL DISTRIBUTION

In 1902, the incidence of multiple sclerosis in New York City among patients with nervous diseases was considered low. The rate was from 2 to 7 per 1,000, except that Dr. Onuf found, among 500 to 600 cases, 14 per 1,000, and Fraenkel found 18 per 1,000 among Jews at the Montefiore Home.

In 1903, Taylor and Myers, in Boston, found only 1 per 1,000 among nearly 10,000 nervous cases. They called attention to the great difficulties of diagnosis. If patients with certain ataxic paraplegias, diffuse degenerations and spastic paraplegias were included, the rate would be increased to 4 per 1,000.

Van Wart, in 1905, on the basis of 500 nervous cases in New Orleans, found a rate for multiple sclerosis of 44 per 1,000 and concludes that in Louisiana and the surrounding states multiple sclerosis is an extremely frequent disease. But this may well be due to the idiosyncrasies of the examiners. Perhaps a prevailing tradition is responsible for the high rate for this disease in Mississippi at the time of the draft.

For other countries the rate is said to be much higher than the 2 to 7 per 1,000 in New York City. Thus the Bramwells (1903, 1915) find a rate first of 20, and later of 32, in Scotland and the North of England. Williamson is said (Collins and Baehr, 1914) to have found a rate in Manchester of 27 per 1,000 and the National Hospital for Paralyzed and Epileptic in London of 60 per 1,000 "nervous cases";

but in this hospital the patients with nervous cases were a more rigidly selected lot than in many of the other instances, so that multiple sclerosis formed a larger proportion of the population than in other hospitals. According to Jelliffe (1904), Jolly of Berlin found 8 per 1,000 multiple sclerotic patients among nearly 10,000 patients with nervous diseases; and Sanger of Hamburg about 10 per 1,000.

Various authors, such as Jelliffe (1904) and Collins and Baehr (1914), give statistics concerning the racial constitution of patients with multiple sclerosis. But in a country whose racial composition changes so rapidly it is difficult to compute satisfactory racial rates. Also, there is reason for thinking that there is a racial selection for particular clinics. Thus, private patients are more likely to include an excess of native Americans and Germans, and the hospital clinics of the later immigrants. The excellent provision made for Jewish patients in special hospitals for that race diminishes the Jewish rate in the general hospitals.

TABLE 2.—RATES OF VARIOUS FOREIGN NATIONALITIES IN NEW YORK AND AMONG PATIENTS WITH MULTIPLE SCLEROSIS

1	2	3	4	5
Name of Nation	Number in Greater New York, 1920, per Thousand	Proportion of Total Foreign-Born Population of 1,990,000	Number of Cases of Multiple Sclerosis Listed in the Four Hospitals	Proportion of Entry of Column 4 to 70 Foreign-Born Patients
Russia	480	24.1	9	12.9
Italy	389	19.6	11	15.7
Germany	194	9.8	12	7.2
Ireland	203	10.2	8	11.5
England	71	3.6	5	7.2
Sweden	33	1.7	3	4.3
Norway	24	1.2	3	4.3

Miss Louise A. Nelson has ascertained the birthplace of seventy foreign-born patients with multiple sclerosis from the records of Montefiore Home, Neurological Institute, St. Luke's Hospital and Post-Graduate Medical School. According to the bulletin of the United States Census Bureau, the number of foreign-born persons per 1,000 in Greater New York for the leading countries is as given in column 2, Table 2. The proportion that each number makes of the 1,990,000 foreign-born persons for the seven leading nationalities is given in column 3. The number of cases of multiple sclerosis in these same nationalities found by Miss Nelson is given in column 4. The proportion that each is of the seventy foreign-born patients with multiple sclerosis is given in column 5. Were the patients distributed among the nationalities in the same ratio as the whole foreign population, columns 3 and 5 should be closely similar. Actually they show striking differences. Thus the number of cases among the Russians and Italians are far below expectation. The number of cases among the Irish are

slightly above expectation; the English and Germans have about twice as many cases of multiple sclerosis as expected; Sweden has about 2.5 times and Norway about 3.6 times as many cases as expected. Without laying any stress on the exact multiples, we have relatively more Scandinavians with multiple sclerosis in the hospitals named than we would expect were patients of all nationalities equally likely to go to these hospitals and were the rate of incidence the same in all nationalities. While we cannot assume the first to be true, still there is no obvious reason why it should not be approximately true. If this be granted, it would follow that there is probably an exceptionally high incidence of multiple sclerosis among Scandinavians. Incidentally it may be said that Jelliffe's figures also seem to show that there are more Scandinavian than Russian patients in a New York City clinic. When we recall that in the draft statistics the rate for multiple sclerosis is high in states with a large proportion of Scandinavians, it does not seem unwarranted to suggest that the Scandinavian race may be especially subject to this disease.

It is only right to add that a visit to the Swedish Hospital, Brooklyn, since the foregoing was written, did not reveal any cases of multiple sclerosis there nor listed on the records of the hospital. However, this hospital does not receive many nervous cases.

The negro race is not immune from this disease; although, as indicated by Table 1, it—including mulattoes—is probably less subject to the disease than the white race. Miura (1911) states that the disease is infrequent in Japan, while amyotrophic lateral sclerosis is common.

HEREDITY

If there is any racial tendency in multiple sclerosis in the strict sense of the word, there is an hereditary factor. Usually inquiry of the patient elicits no evidence of the disease or any similar disease in other members of the family. In other cases positive evidence of recurrence in the family is obtained. Multiple neurofibromatosis is hereditary; hence, if multiple sclerosis is a primary hyperplasia of the glia, it might well be hereditary also.

Since it is impossible at this time to make such an assertion, it will suffice to consider the pedigrees of a number of families containing one or more cases of diseases regarded as probable multiple sclerosis.

The most famous instance is that first described by Pelizaeus (1885), and continued twenty-four years later by Merzbacher (1909). This pedigree chart (Fig. 2) is shown herewith (from Arch. Rassen-u. Gesellsch.-Biol., 1909). Some authors doubt the diagnosis in this case and would classify the condition as an hereditary type of "cerebral diplegia."

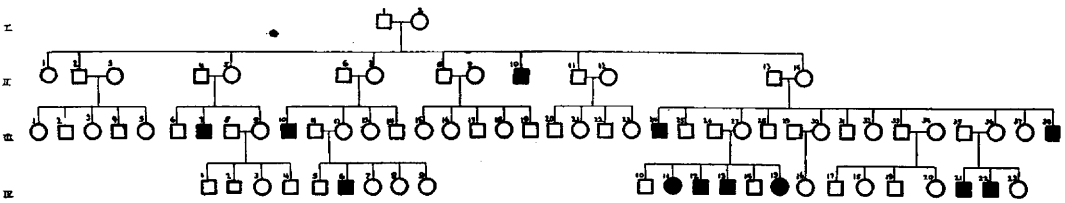

Fig. 2.—Eickhold pedigree of multiple sclerosis of Tübingen and vicinity, Germany. The squares represent males and the circles females. The dark symbols indicate those affected with the disease. The earliest generation is represented by the top line. Merzbachers, Arch. Rassen u. Gesellsch., Biol. VI, 1909.

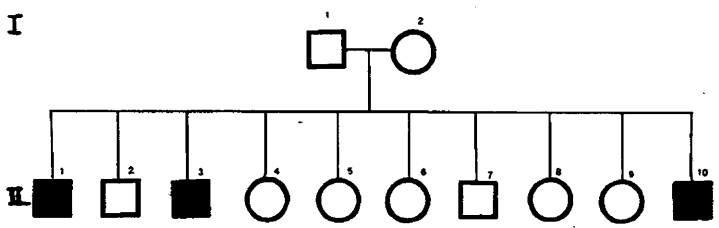

Fig. 3.—Pedigree of multiple sclerosis, showing three sibs affected. Pauly et Bonne, Rev. de méd., Paris, 1897.

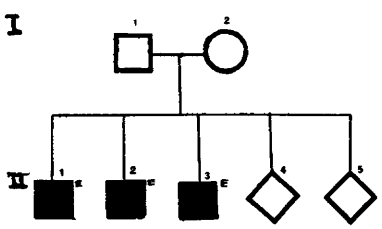

Fig. 4.—Pedigree chart of parents and their children; a Bohemian family. The three dark symbols represent three sons with multiple sclerosis and epilepsy. There are also two normal children and two who died in infancy. Abrahamson, J. Nerv. & Ment. Dis. **33**:200, 1906.

Another considerable pedigree is contributed by Batten and Wilkinson, 1914. As in Merzbacher's report, chiefly males are affected, and the tendency is passed on by mothers who are not themselves affected. This reminds one of the ordinary sex-linked type of heredity. Numerous hereditary data for the disease have been collected by Klausner (1901) and Röper (1913).

Recurrence of the disease in two generations is not common in typical multiple sclerosis, and when it does occur, the mother and child are usually affected. Such is the case of Eichhorst (1896). A woman

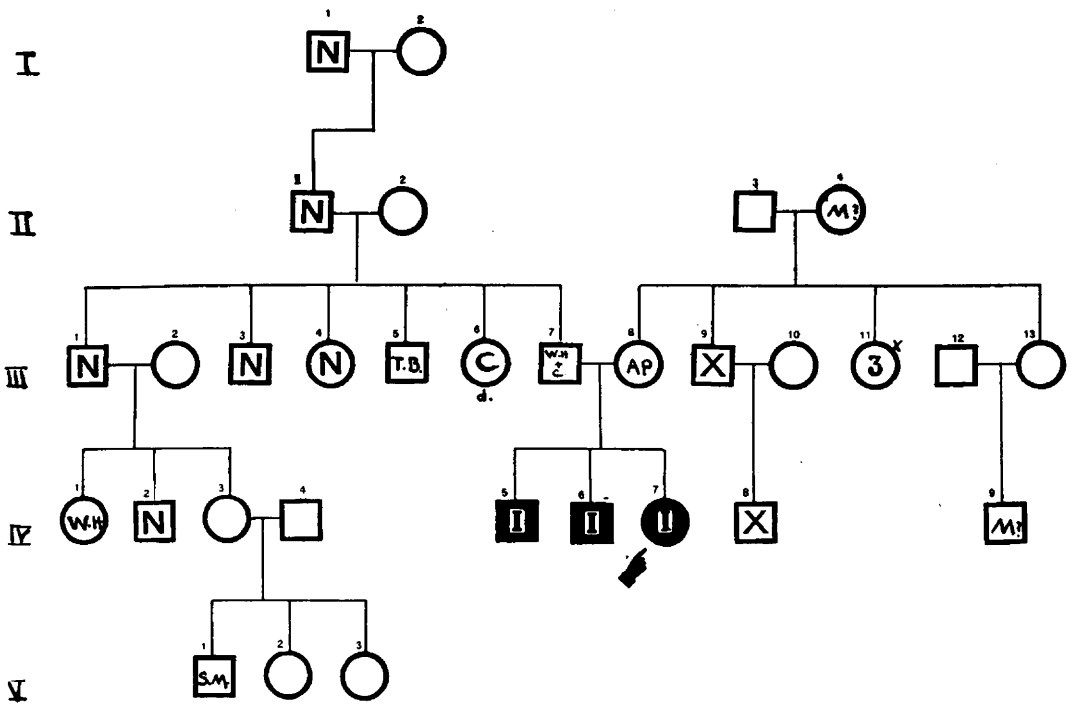

Fig. 5.—Pedigree chart of multiple sclerosis in case of R. J., Central Islip State Hospital. *N* indicates normal; *M?* mentally questioned; *AP*, died of apoplexy; *T.B.*, tuberculosis; *C*, cancer; *W.H.& C.*, weak heart and cardiac disease; *S.M.*, spinal meningitis; *I*, insanity; *X*, little known; dark symbols, multiple sclerosis.

first noticed weakness in the legs, which finally no longer would hold her, and tremor set in. Speech became disturbed and scanning. There was horizontal nystagmus. The optic papillae looked pale. Intention tremor developed. Multiple sclerosis all along the cord was found at necropsy. Her son showed tremors shortly after birth in 1879; he developed weakness of the leg in 1887, then diminished vision, nystagmus and scanning speech. Necropsy revealed sclerotic changes in the

cord only, as in the mother. Groups of atrophic nerve fibers were found, especially in the anterior roots. The mother had three normal children.

Klausner (1901) gives an account of nervous "heredity" in thirty-one of his patients. In one (No. 10) the arms and legs of the mother had been paralyzed for sixteen years, and the daughter began to have symptoms of multiple sclerosis at 18 years of age.

In one of Röper's (1913) cases a mother had paralysis agitans and two sons had typical symptoms of multiple sclerosis.

According to Bramwell (1915), Lenot described an instance in which both mother and child had multiple sclerosis. One of the patients at the Montefiore Home, November, 1921, had a similar history, with paralysis in the grandmother.

Cestan and Guillain (1900), describe the case of a boy of 15 years with paraplegia, highly exaggerated knee and ankle reflexes, a positive Babinski sign, but no speech or macular defect or intention tremor. His father and eldest sister presented the same symptoms.

Cases of multiple sclerosis in uncle and nephew have been described by Reynolds (1904) and by Curschman (1920).

In many cases some nervous defect, such as weakness of gait, tremors, paralysis agitans and progressive paralysis has been described in one of the parents of the patient.

But the commonest condition of recurrence of the disease in the family is that of two or more affected persons in the same fraternity (Figs. 3 and 4).

In conclusion, I venture the suggestion that whatever may eventually prove to be the endogenous cause of multiple sclerosis, the factor of heredity cannot be left out of consideration. Just as tumors inoculated into a mouse will or will not grow, according to the racial constitution of the mouse; and just as *Bacillus tuberculosis* that inhabits the body of all of us does or does not flourish there, depending on the constitution and condition of the person, so probably there are internal conditions that inhibit and others that facilitate the development of this disease or the endogenous factors on which it depends. Therefore the manifestations or symptoms of the disease vary in different persons, and they are sometimes very similar in closely related people because the hereditary factors of the constitution in which they operate are similar.

It seems most probable that the geographic, ethnologic and familial distributions shown by multiple sclerosis depend in part on one or more hereditary factors.

Carnegie Institution of Washington, Department of Genetics.