PARKINSON'S DISEASE

A CLINICAL STUDY OF ONE HUNDRED AND FORTY-SIX CASES *

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In this study only those cases were included in which the diagnosis was thought to be certain. Postencephalitic cases were not considered. For estimation of age and sex incidence 146 cases were used; for clinical studies, 140. The advantages of these records for source material as compared with hospital records are their uniformity, since they have all been under the direction of one person and written by a small number of historians (each has averaged about four years), and their brevity which, since only the more significant data are recorded, is in favor of greater accuracy. Their disadvantages are their occasional incompleteness and the limitation to positive data and to private cases. The restriction of statements to positive findings is compensated for by the fact that conclusions drawn from the recorded facts are minimal and therefore conservative. That age and sex distribution among private and dispensary cases runs along the same curve has been shown by Erb.¹ As numerous studies of the same subject have been previously recorded, only points of contrast and of special interest will be noted.

AGE DISTRIBUTION

By decades, the 146 cases fall into the usual sequence. Figure 1 shows the well established order of frequency. Of this group 80 per cent. are between 40 and 70 and 55 per cent. above 50 years of age at the onset of the disease. The age incidence reported by different authors is strikingly uniform. Figure 2 represents percentage distribution for the cases of Souques,² Dana,³ and Patrick. The discrepancies appear only at the ends of the scale where cases are few and slight differences in number make comparatively large percentage differences.

When it is remembered that these curves are for groups of from 100 to 150 cases, each group representing a different part of Europe or America, their similarity is significant. It indicates that paralysis

* Read before the Chicago Neurological Society. The cases are from the private records of one of us (H. T. P.).

1. Erb, Wilhelm, in Church: Diseases of the Nervous System, in Modern Clinical Medicine, 1908.

2. Souques, A.: *Rev. neurol.* **28**:552, 1921.

3. Dana, Charles L.: *Nervous Diseases*, New York, William Wood & Co., 1919.

Fig. 1.—Percentage of distribution according to age at the onset of the disease in 146 cases of paralysis agitans.

Fig. 2.—Percentage of distribution of paralysis agitans by age in decades. Souques' 125 cases are indicated by the dash and dot line, Dana's 127 cases by the dash line and Patrick's 146 cases by the continuous line.

agitans is a definite entity. Moreover, it adds weight to conclusions derived from the study of any one series, since they probably would hold for the others.

Age distribution in the sexes is practically the same. A small difference may be partly accounted for by the smaller number of cases in our female series (58), hence a greater element of chance (Figs. 3 and 4).

The age incidence of paralysis agitans taken regardless of the general population of each decade has limited value. It is obvious that one case in a group of ten shows relatively a much greater frequency value than five cases in a group of 100; and it follows that one case in a person in the seventies, a decade in which only 2 per cent. of the population are represented, is relatively more than three times as frequent as one case in a person in the fifties, a decade in which 7 per cent. of the

RELATIVE FREQUENCY VALUES

Age	No. of Cases	Percentage Distribution by Decade, Native Population, 1910.		Frequency Values
20-30	5	17.7		1.8
31-40	20	13.1		10.5
41-50	41	9.2		30.7
51-60	49	6.9		49.0
61-70	27	4.4		42.3
71-80	4	2.1		13.1
	<hr/> 146			<hr/> 147.4

population are represented. Taking the number of cases in the fifties as a basis for comparison, the values in Figure 1 have been interpreted in terms of relative frequency values in the table. The percentage distribution of the native population by decades, on the basis of which frequency values are derived, is also shown in this table, which indicates that this disease is relatively more frequent in the sixties than in the forties, more frequent in the seventies than in the thirties, and rare in the twenties. It is relatively two and a half times as frequent in persons over 50 as in persons under 50. This is in favor of the theory that the disease is a degenerative process.

SEX

The ratio of males to females in this series is as 3 to 2. A preponderance of males over females has been found by most workers studying large series. Erb's ratio like that of Gowers⁴ was 2 to 1 in

4. Gowers: Diseases of the Nervous System, 1893, Vol. 7, p. 637.

Fig. 3.—Percentages of distribution in males according to age (eighty-eight cases).

Fig. 4.—Percentage of distribution in females, according to age (fifty-eight cases).

favor of males. Reverse findings are largely confined to smaller series in which chance factors are greater.⁵

TRAUMA

There was a history of trauma in twenty-two cases. In three of these patients the trauma was operative—a left mastoid operation, removal of a cervical rib, and fracture of the jaw during extraction of a molar tooth. Apparently there is a high correlation between the site of trauma and the site of the first symptom of the disease, the tremor or rigidity taking its lead from the traumatized part, regardless of the time interval between the injury and the onset of the disease. For example, a man aged 39 at the onset of the disease, gave a history of a fall from a colt at 12 or 13 years of age, landing on his right shoulder and suffering from pain in that shoulder for a year. The right hand was first involved by the tremor. A man, aged 56 at the onset of the disease, which started in his left arm, had had his left hand cut off thirty-five years before. On the other hand, within two months following a fall in which the left arm was sprained, a man aged 65 at the onset of his disease, had the initial tremor in the left hand. Cases of paralysis agitans following trauma and affecting the injured side within a day have been described. In nine of our cases the trauma was of one designated extremity; in seven this extremity was the first involved; in one the opposite limb showed the first sign of the disease, and in one the other limb on the same side.

That the predilection may be for a part injured by disease is shown by the correlation of the onset with a part affected by rheumatic arthritis or some other nontraumatic disease. Of eight patients in whom a single extremity was thus affected, in six the first symptom of paralysis agitans appeared in the same extremity. Possibly not in agreement was the case of a man aged 48 at the time of the onset, who had had a right hemiplegia during the last ten years, and in whom the disease started on the unaffected side. As in the cases of trauma, there is no relation between the time of disease in an extremity and the time of onset of the initial symptom. In the nonoperative trauma group there were sixteen males and three females. The three operative cases were in females. The close relation between the area traumatized and the distribution of the symptoms has been especially emphasized by Mendel⁵ and Oppenheim⁶ and is apparently a frequent observation. Of course trauma is not to be considered as a direct etiologic factor,⁷

5. Mendel, K.: *Die Paralysis Agitans*, Berlin, S. Karger, 1911. See Mendel's review of these and other lists.

6. Oppenheim, H.: *Text-Book of Nervous Diseases*, Ed. 5 2:1298, 1911.

7. Pearce, F. S.: Trauma as an Exciting Cause of Paralysis Agitans, *Phil. M. J.*, May 25, 1901, p. 1019.

but that it is a predisposing influence to the locus of onset of the disease, if it occurs, is borne out by these findings. Erb would add to the election of the traumatized part the factor of physical strain; he cites a case in which the part first affected in a painter was the left hand in which he held his palette.

To prove that trauma is an etiologic factor it would be necessary to show that the chances for getting the disease are greater in the traumatized part of the population. Such statistics are not at hand, nor does it seem likely that there is a less frequent history of trauma in the general population than in our lists (15 per cent.). This is no more significant than the predilection of rheumatic arthritis for a part receiving injury or bearing strain, or the predilection of syphilitic gummas for the frontal bones of Mohammedans, who in bowing to Allah repeatedly scrape their foreheads on cold marble.⁸

MENTAL SYMPTOMS

As described by most authors such symptoms are largely depressive reactions to the hopelessness of the disease. Wilson⁹ writes that the mental symptoms are "limited to a depression of mood, the natural outcome perhaps of an incurable disease, and to an irritability also explicable by the nature of the ailment; anything beyond these is to be ascribed either to a concomitant arteriosclerosis or to some incidental condition." As recorded in this series, mental symptoms are naturally grouped as they occur before or after the disease and in the following order:

Group 1. History of acute mental symptoms following "shock" at or before onset of the first symptom of the disease. There are six cases in this group—three in males and three in females. In four of these the symptoms occurred within a year before the onset of paralysis agitans. Symptoms under this heading were: marked grief following death of wife and in this state when paralysis agitans began; frightened by burglar and in bed one month with weakness and "nerves"; breakdown and in a sanatorium for three months; great emotional shock and strain. The ages of the patients at the onset of acute mental symptoms were: 31, 46, 20, 51, 45 and 66; and at the onset of paralysis agitans in the same order: 31, 47, 50, 51, 53 and 66.

Group 2. History of depression preceding onset; seven cases: three in males and four in females. Under this heading such cases as the following were included: (1) Depressed, crying spells, suicidal thoughts, quitting work on account of depression, gradual improvement with return of symptoms two years ago with first symptom of paralysis agitans; (2) periodic depression one to two years preceding; (3)

8. Lacapère and Laurent: *Paris méd.* 8:94, 1918.

9. Wilson, S. A. K.: *Diseases of the Central Nervous System*, Oxford Medicine, Vol. 6, Oxford, 1921.

depression four years preceding, attempted suicide by gas followed two days after the first attempt by the first symptom of paralysis agitans; (4) depression for ten years preceding onset with suicidal feelings.

Group 3. This is a less definite group. The patients were "very nervous," "highstrung," "worrisome," of a "nervous temperament," "easily upset" and "excited at least provocation." This group comprises twenty cases: thirteen in males and seven in females. In this group three patients showed fear—fear of something dreadful, a choking sensation with fear of death, fear of the shaking palsy. Three were patients with some form of apathy—apathetic, loss of interest; loss of ambition preceding the first symptom by six months; crying spells and careless of appearance. Generally these symptoms had preceded the paralysis agitans.

Mental symptoms during the course of the disease are recorded in twenty cases, but five of these are considered in the first group as occurring also before the onset. Of the fifteen remaining patients (seven males, eight females), depression or loss of interest is noted in ten (depressed only since onset of paralysis agitans, cries while examined; crying spells over condition for past nine months; depressed, careless of appearance and frequent crying past two months; nervous, depressed, insomnia, convinced is going to die, etc.). Worries and fears are noted in two cases; mental slowing-up, confusion, memory defects in three. In these three groups there are forty-eight cases, or 34 per cent. Even discounting Group 3 as being ambiguous, there remain twenty-eight, or 20 per cent., of whom definite mental symptoms are recorded. Especially noteworthy is the fact that mental symptoms are recorded more frequently as occurring before the onset of paralysis agitans than after, and as far as these records go, a depressive reaction is as frequent before the onset of the classical signs of the disease as after. There is no record of bonhomie as noted by Oppenheim⁶ and only one record of periods of excitement. Actual mental deterioration is not mentioned in these records. The percentages found by other writers are in fair agreement.

Heredity findings are as in other reports: "Neuropathic" heredity in about 25 per cent. and direct heredity in six cases, of which two are questionable. Of these, the mother, the father, and a brother, had paralysis agitans. In the two questionable cases, the father also had a marked tremor, and the father had "the same tremor." Insanity (not described), one; melancholia, one; epilepsy, four; and migraine, three, are noted in antecedents.

Menopause or menstrual disturbance occurred in only ten cases, not a significant number for a group of fifty-eight women—of these, six had mental symptoms.

The complications are similar to the list in Mendel's monograph: tabes, one; hemiplegia, two; trifacial neuralgia, two; hyperthyroidism, one; diabetes, one. Two brothers of the patient with tabes, aged 70 when first seen, had general paresis. One of the cases complicated with hemiplegia was that of a printer, aged 65 at the time of onset, with tremor in the right hand which later involved the left. About fourteen months after the initial tremor he had a right hemiplegia with disappearance of the tremor on the right. With gradual recovery of the use of the right arm the tremor returned. Such a case was first described by Parkinson—one of his six cases.

Besides the unusual cases included under "complications," the following may be mentioned: hemiparalysis agitans, fifteen cases. These were cases usually seen early in the disease in which the tremor at the time of the examination was limited to one side, with however the typical gait, attitude and facies. In three of these cases the duration was one year or less; in eight, from one to two years; in three from two to three years. In one case the disease was of eight years' duration, and with minimal rigidity. In only four of these cases was the rigidity severe.

Unusual in this as contrasted with other series is the number (five) of patients with one-sided facial involvement.¹⁰ In one of these cases the diagnosis was in doubt for a long time.¹¹ These cases of one-sided facial involvement occurred in the hemiparalysis agitans group and represent a fairly complete unilateral involvement including the face. No reference to such a series could be found in the literature.

Intention tremor was found in eighteen, or about 13 per cent. of all cases, indicating that the typical tremor is not invariable, a point already made with sufficient emphasis in the literature. Absence of tremor (paralysis agitans sine agitatione) is recorded in only five cases, in contrast with Erb's 20 per cent. The latter, however, included also cases with minimal tremor, a group not considered in this list. In these cases the duration was in order: seven months, two years, three years, five years and six years. Cases without rigidity (sine rigiditate) are thought to be the rarest of all types; not one was found in Erb's group of 183 cases. This condition was recorded in two patients in our series, one in a woman aged 46, who for one year and three months had shown the typical attitude of face and body. This was preceded by severe constant pain in the right arm which disappeared when the typical attitude began. The second case was that of a man, aged 51, who had had typical tremor of the left hand and arm for eighteen months with tremor in both legs for six months. Not the slightest rigidity was determined in either case.

10. Patrick, Hugh T.: An Unusual Case of Paralysis Agitans, *Arch. Neurol. & Psychiat.*, *Proc. Chicago Neurol. Soc.*, this issue, p. 790.

11. Patrick, Hugh T.: *J. Nerv. & Ment. Dis.* **30**:469, 1903.

Three cases are classified in the "bulbar" group. One patient had slight difficulty in swallowing, one had choking spells at night and the third had marked difficulty in swallowing food. In these three cases the disease had made some progress before the "bulbar" symptoms commenced.

The focal distribution is represented in Figure 5. The extremities involved at the time of the last examination with the order of progress are indicated by numbers. For each type the number of cases seen is in the lower right hand corner in Roman numerals.

Fig. 5.—Focal distribution showing extremities involved at time of last examination with the order of progress are indicated by numbers. For each type the number of cases seen is in the lower right hand corner in Roman numerals.

SUMMARY

One hundred and forty-six private cases of "classical" paralysis agitans were used for studies in age and sex distribution; 140 for clinical studies. Frequency by decades was found to be greatest in the fifties and next in the forties; 80 per cent. of the patients were between 40 and 70 and 55 per cent. over 50 years of age. These find-

ings agree with other statistics. Considered in relation to the age incidence of the general population, the vast majority of patients are over 50 when the disease begins, and the onset is relatively more frequent in the seventies than in the thirties. The ratio of males to females was 3 to 2. Trauma occurred in twenty-two cases, and in these as in the histories of infected parts it was shown that the symptoms of paralysis agitans tend to start in a traumatized or diseased part. Since in this series there was a history of trauma in only 15 per cent. of all cases, it cannot be concluded that trauma is predisposing in any sense except as to the site of the initial symptom.

A large number of mental symptoms were shown by forty-eight patients, or in 34 per cent. of the cases. In contrast with the findings in other studies, mental symptoms were found to occur as frequently before as after the onset of the disease. These symptoms were largely in the form of depressive reaction.

Menstrual disturbances were found to be of no special significance. Heredity findings were not significant except in the form of "neuropathic heredity" in about 25 per cent. of the cases. Direct heredity of the disease was traced in six cases. The complications were: tabes, one; hemiplegia, two; trifacial neuralgia, two; hyperthyroidism, one, and diabetes, one. Fifteen patients had hemiparalysis agitans; eighteen cases were accompanied by intention tremor; five patients had one-sided facial involvement; four had paralysis agitans sine agitatione, two paralysis agitans sine rigiditate, and three had "bulbar symptoms."