

IS GENERAL PARESIS DEPENDENT UPON PREVIOUS TREATMENT WITH MERCURY?

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(With 4 Figures in the Text)

BEFORE dealing with this question it may be appropriate to present graphically the mortality of general paresis in Copenhagen in the period of 1866–1935 (see Fig. 1).

This period of 70 years is divided into 14 pentads, illustrating very plainly the increase in the yearly number of deaths, from eight deaths in the first pentad to fifty-five deaths in the eleventh pentad (1916–20). In other words, the yearly number of deaths increases to seven times the initial number, while the population of Copenhagen in these 55 years has increased only to three times its size at the beginning of this period.

The last three pentads, on the other hand, show a marked and rapid fall in general paresis. In the last pentad there were not even half as many deaths due to general paresis as were recorded in the pentad of 1916–20, although Copenhagen in these 15 years has been growing rapidly and steadily, its population being increased by nearly 25%.

The total number of deaths from general paresis in the 70-year period here concerned amounts to more than 2000.

The clinical picture of general paresis has been known for about 150 years, it is true, but its numerical importance was not particularly realized until about 1870. As pointed out at that time by Prof. Stenberg, general paresis then began to appear more frequently in certain places, especially in Paris and Copenhagen.

The classical studies of Jessen, Kjeldberg and Jespersen established with a high degree of certainty that general paresis was always preceded by infection with syphilis several years before. In particular, the excellent little dissertation by Jespersen established this fact, but Jespersen refuted decidedly the theory which was at that time advocated by various authors that previous treatment with mercury is a contributory factor in the development of general paresis. The chief argument advanced by Jespersen was that the poisoning of a patient at the age of 20 years could not possibly bring about the appearance of the disease from 20 to 40 years later.

Nowadays this argument does not seem particularly weighty. In recent years Aebly (1920) first advanced the view that the paralysis is directly

attributable to the antisymphilitic treatment with mercury, and this view has been corroborated later by the findings reported by various investigators. Among these, particular mention is to be made of the experiences reported from the Charité Hospital,¹ Berlin, that the length of the latent period is dependent upon the amount of mercury employed. These experiences hold good too when the patient material is divided into age classes.

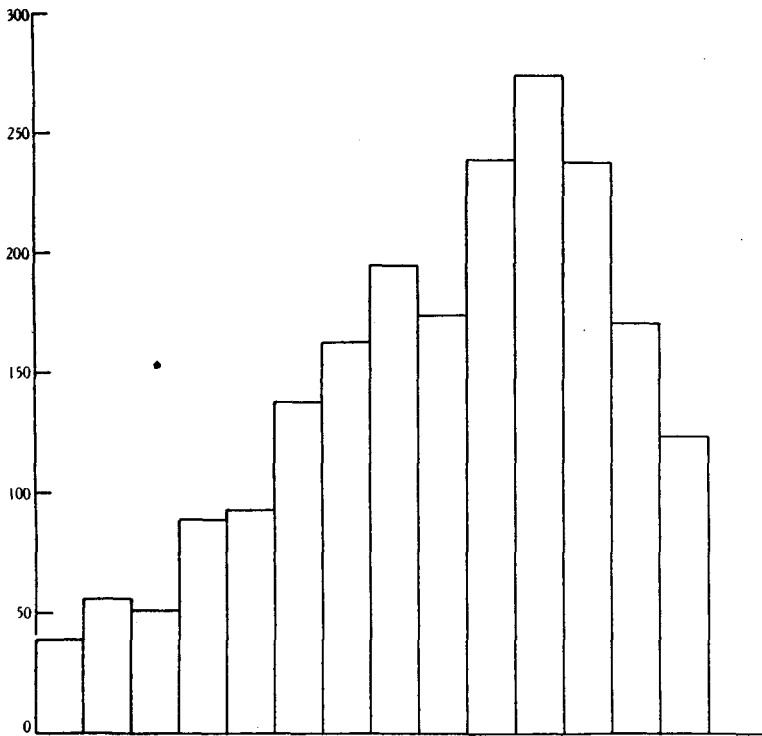


Fig. 1. Graphic presentation of the numbers of deaths of "general paresis" in Copenhagen during the period 1866-1935 (divided in pentads).

In a previous paper (Heiberg, 1934), attention has been called to a conspicuous difference in the frequency of general paresis among syphilitics in Oslo and in Copenhagen towards the end of the last century as a point of some significance in support of this view, as treatment with mercury in those years was employed in Oslo only in exceptional cases, while it was a routine treatment in Copenhagen. To this may now be added the findings recorded graphically in Fig. 2, covering the proportion between the number of reported syphilitics and deaths from general paresis in Copenhagen during a period of more than 50 years (see Fig. 2 and Table I).

¹ *Monatschrift für Psychiatrie und Neurologie*, **83**, 245, 1932.

Table I. *Numbers of reported cases of syphilis and deaths from general paresis in Copenhagen (grouped in correlated pentads)*

Years	Reported cases of syphilis	Deaths from general paresis 15 years later
1866-1870	4,523	89
1871-1875	3,996	93
1876-1880	4,026	138
1881-1885	6,473	163
1886-1890	7,024	195
1891-1895	5,289	174
1896-1900	6,737	239
1901-1905	7,689	274
1906-1910	9,127	238
1911-1915	10,095	171
1916-1920	12,368	124
1921-1925	8,790	—
1926-1930	6,406	—
1931-1935	1 597	—

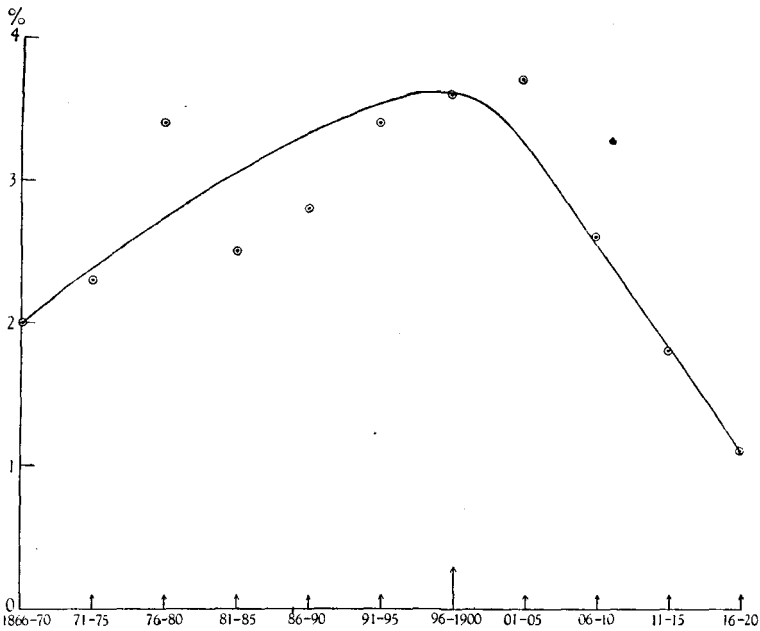


Fig. 2. Mortality of general paresis among syphilitics reported 15 years before.

The curve is plotted in this way: the number of deaths from general paresis is correlated with the number of syphilitics reported to the Department of Health 15 years before. Thus the number of paralytic deaths in the pentad of 1881-5 is correlated with the number of syphilitic cases reported by physicians in the pentad of 1866-70, and the same way of calculation is applied to the following 10 pentads. It will be noticed that the frequency of paralytic death in this material increases from 2% in the first pentad to 3.5% at the beginning of this century, and then it falls continuously through the following 3 pentads, making about 1% at 1920. Presumably there is no reason to believe that this

fall will stop. The entire period of 55 years comprises about 80,000 syphilitics and about 2000 paralytics.¹

The working hypothesis which explains best the form of this curve (Fig. 2), with its gradual rise followed by a rather abrupt fall, apparently headed for the zero level, is the hypothesis about the causal significance of the mercury therapy to the development of general paresis. About 1870 the use of mercurial ointment for intermittent and protracted treatment became more common in Copenhagen, and later this was the prevailing form of treatment through a considerable length of time. Since 1924, however, mercurial ointment has been replaced almost entirely by other remedies.

In the yearly report from the St Hans Hospital (mental disease) for 1932, Dr Bisgaard points out that the first admission of paralytics in that year included only thirty-eight men, while the number of reported syphilitics in Copenhagen 12-13 years before was still about 2500 per year. If the considerations here advanced be correct, it will take but a few years until instances of general paresis in the St Hans Hospital become very rare.

It is in keeping with an investigation reported by Hansen *et al.* (1900) that the interval of time between the two columns of figures here is set at 15 years. It may be, however, that this interval is rather short for the latter part of the curve (see Lomholt, 1936), presumably in part on account of the negative correlation between the intensity of the mercurial treatment and the length of the latent period.

The amount of mercury that was given only a few years ago in the intermittent treatment distributed over a number of years is illustrated very well by the following abstract of the case history of a male patient recorded by a Copenhagen specialist of high repute. The antisymphilitic treatment was instituted shortly after the infection was contracted, and it was continued through 9 years. Mercurial inunction was employed in seances (80-50-60-60-35-60-50), making a total of 395 inunctions. Most likely, each inunction consisted of 3 g. of mercurial ointment (33%). His wife went through a similar intermittent and protracted treatment.

Whether the modern methods of fever therapy (malaria, "sulfosin") for the treatment of general paralysis has had any influence at all upon the figures here recorded is difficult to decide. Thus, in 1923 and 1924, nearly 100 male paralytics in one department of the St Hans Hospital were given malaria therapy, and fifteen of these patients were discharged as cured; in the 4 years from 1928 to 1931 also 100 paralytics were given malaria therapy in the same department of the hospital, and only one was discharged as cured.²

There is something else that makes me doubtful about the life-saving effect of the malaria therapy, namely, the proportion between the number of

¹ A working table with the figures recorded from year to year until 1930 is given in *Acta psychiatrica et neurologica*, 7, 190, 1932, and the figures for the last 5 years (1931-5) are given in the annual report from the City Board of Health, Copenhagen.

² Yearly reports from the St Hans Hospital 1923-35.

deaths from general paresis and the number of deaths from tabes dorsalis in the period here concerned. On the whole, tabes dorsalis takes a course parallel to that of general paresis: at first a slow rise in the frequency of tabes, reaching its maximum in the pentad of 1911-15, and then a more rapid fall (see Fig. 3).

Throughout these 55 years there has been a rather constant proportion, 1 : 4, between the numbers of deaths from the two diseases (see Table II).

Table II. *Proportion between the numbers of deaths from tabes dorsalis and the corresponding number of deaths from general paresis*

Years	Deaths from general paresis	Deaths from tabes dorsalis	Tabetic deaths as percentage of paretic deaths
1881-1885	89	17	
1886-1890	93	36	29
1891-1895	138	36	
1896-1900	163	43	26
1901-1905	195	39	24
1906-1910	174	50	
1911-1915	239	68	25
1916-1920	279	60	
1921-1925	238	54	22
1926-1930	171	35	
1931-1935	124	32	26
1881-1935	1903	470	25

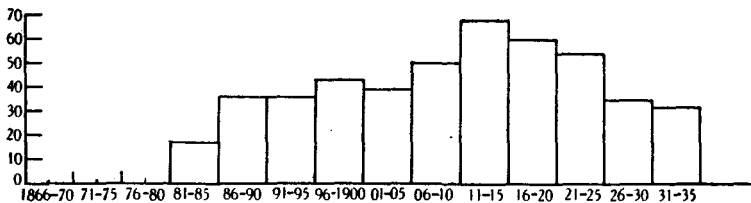


Fig. 3. Graphic presentation of the numbers of deaths of tabes dorsalis in Copenhagen during the period 1881-1935 (divided in pentads).

While the number of inhabitants of Copenhagen has doubled from 1883 to 1913, the number of tabetic deaths has quadrupled in this period; and from 1913 to 1933 the population of Copenhagen increased by one-third, while the number of tabetic deaths fell to one-half of the previous maximum.

If we choose to believe in the life-saving effect of malaria therapy on a fairly large scale, this hypothesis can explain at any rate only the 2-3 last steps in the fall of the curve. On the other hand, the working hypothesis as to the causal effect of mercurial therapy in the development of general paresis explains readily both the rise and the fall of the curve, besides being in concordance with other observations.

It was Fournier, an international leader in his field of medicine, who in the 'sixties introduced and advocated strongly the protracted intermittent treatment with mercurial ointment. In this way he avoided the acute mercurial poisoning which at that time was rightly dreaded. Now, however, the question is whether Fournier in susceptible persons replaced the acute mercurial

poisoning with a chronic intoxication. Originally Fournier recommended intermittent mercurial therapy for a couple of years, later for 3–5 years, but before he had finished he had gone on to recommend intermittent mercurial treatment for up to 10 years—in order to avoid the development of general paresis. As illustrated by the two case histories cited above, physicians in other countries also followed Fournier's advice to keep on with the treatment energetically. This therapy was given to syphilitics with clinical symptoms, and also to syphilitics who presented no symptom whatever.

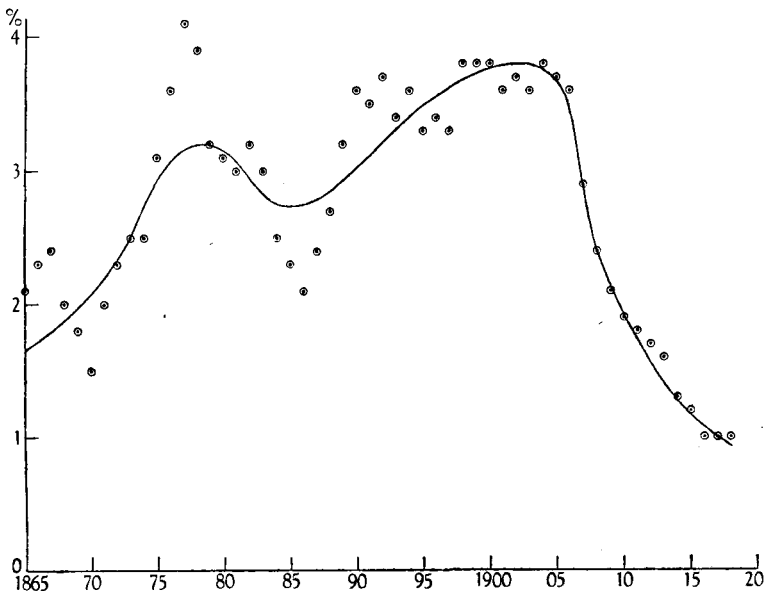


Fig. 4. Mortality of general paresis among syphilitics reported 16 years before. Material plotted in periods of 5 years, with sliding averages.

If the working hypothesis here advanced be correct, it is the leadership of Fournier that has brought about the curve presented in Fig. 2—a tragedy in the history of medicine. Fournier found himself that one out of every nine syphilitics in his private practice finally became paralytic. He found altogether 631 paralytics among 5749 syphilitics. On plotting the present findings in the 55-year period here concerned as triennial and sliding averages the resulting curve is on the whole, of course, of the same form as the curve in Fig. 2. In the 'eighties, however, there is a tendency to a decrease, probably owing to a change in the method of reporting of syphilitic cases to the health authorities (see Fig. 4 and Table III).

However this may be, this temporary decrease in the early 'eighties was pointed out in 1885 and 1886 by Dr Schleisner, Chief Medical Officer of Health, Copenhagen. In the latter year Schleisner says: "Most likely the marked increase in the incidence of constitutional syphilis is due to a change in the conception of the nature of a great many morbid conditions, resulting in a

Table III. *Percental frequency of death from general paresis among syphilitics reported in Copenhagen 15 years before*

Years	Percental frequency of death from general paresis calculated for the number of syphilitics reported 15 years before
1881-1885	2.0
1886-1890	2.3
1891-1895	3.4
1896-1900	2.5
1901-1905	2.8
1906-1910	3.3
1911-1915	3.5
1916-1920	3.6
1921-1925	2.6
1926-1930	1.7
1931-1935	1.0

more frequent employment of the designation 'constitutional syphilis' instead of 'ulcus venereum', rather than to an actual increase in the frequency of constitutional syphilis, and this applies in particular to cases reported from the hospitals."

Presumably Copenhagen is the only town in which a statistical account like the one here presented may be worked out, as this is the only large city where, for more than two generations, it has been the duty of the physicians to report the cases of syphilis to the health authorities. Naturally the number of syphilitics reported per year is not very accurate, but systematic errors will presumably be relatively alike from year to year. In earlier days, however, it happened far more often than now that a case of syphilis was reported more than once. If such repetitions could be eliminated from the statistical tables the level of the graphical account—the curve—would be changed, it is true, but not its form as presented here in particular. The slow rise of the curve followed by a more abrupt fall would only be accentuated even more strongly.

It is rather by chance that I now have realized the form of this curve. When last I was occupied with these figures, in 1930, the fall of the curve did not seem so pronounced as to ensure that it was not merely a temporary down-grade course. Now the fall seems so pronounced that one does not have to be visionary in order to predict that general paresis before long will be a very rare disease in Copenhagen.

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(MS. received for publication 21. I. 38.—Ed.)