THE POLIOMYELITIS EPIDEMIC OF 1937 IN DENMARK

EPIDEMIOLOGY AND CLINICAL STATISTICS

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(With 9 Figures in the Text)

I. EPIDEMIOLOGY

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In the *London Medical Gazette*, about a hundred years ago, Badham published a report on four cases of paralysis that most likely were instances of poliomyelitis. v. Heine, however, in 1840 was the first to assert that cases of acute paralysis in children constituted a disease *per se*, and Strümpell (1884) was the first to look upon infantile paralysis as a specific infectious disease.

In the last part of the nineteenth century a few small epidemics were reported from the Scandinavian countries also. Even as early as 1868, Bull described an epidemic in Odalen, Norway, and in 1890 Medin reported a series of epidemiological studies on poliomyelitis, and established the epidemic character of this disease. Following Wickmann's suggestion the disease was in the past called *Heine-Medin's disease* by many authors. No extensive epidemics of the disease were reported before 1900, and it is unlikely that extensive epidemics had occurred before that date.

For reasons, up to the present unexplained, the character of the disease has undergone a great change in the last four decades. In 1905 the first great epidemics occurred in the Scandinavian countries, and a few years later great epidemics occurred in America. A role in the spreading of these epidemics has been ascribed to the emigrants from the Scandinavian countries to the United States of America.

In Denmark there have been a number of epidemics, some of which have lasted for several seasons, others only for one season.

Although investigations on poliomyelitis have now been carried out for nearly a hundred years, the disease still presents many problems, epidemiological, clinical and therapeutical. Furthermore, even within a few years, the epidemics may vary in their clinical and epidemiological aspects. It is urgently necessary, therefore, not to neglect any opportunity for further study of this disease.

Recent extensive poliomyelitis epidemics in all the Scandinavian countries

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have placed the disease in the centre of the epidemiological problems of our time. In Denmark a great number of studies has contributed to elucidate the clinical aspects of the disease—in particular, the non-paralytic cases—as well as its epidemiology and its specific treatment by serum therapy.

The purpose of our investigations into the epidemic of 1937 has been partly to obtain a general statistical account of the more important epidemiological and clinical data of the disease during this epidemic, and partly to attempt a revaluation of convalescent-serum therapy.

The data include information about a little over 1100 patients. When we planned this investigation we realized that there were two principles we had to follow: (1) we had to obtain separate information about every one of the 1100 patients; (2) we had to limit ourselves to simple questions concerning the epidemiology, clinical features and therapy, so as to ensure the greatest possible certainty about the information relating to each case recorded in the various hospitals.

The questions were formulated on an index card as shown in Fig. 1.

HOSPITAL: Record No.:
Sex: Age: Clinical diagnosis:
Residence:
Date of admission:
Date of discharge:

Date of onset of disease:
Date of onset of meningitic stage:
If diphasic course: Date of onset of second phase:
Any paralysis present on admission?
Date of onset of paralysis:

CHARACTER OF PARALYSIS:
Permanent:
Transitory: Date of disappearance:
Doubtful:
Any respiratory paralysis? Death? Date:

Spinal fluid findings:		Serum treatment:	
Date:	Date:	iv.	im.
Cell count:		c.c.	c.c.
Albumin:		c.c.	c.c.
Globulin:		c.c.	c.c.

Fig. 1. Index card for individual patients, with questions about various data.

Before this card was posted to the various hospitals, its practical serviceability was tested on the case records of the Blegdam Hospital (epidemic hospital), Copenhagen. We went through about one-third of the case records

ourselves, and in this way gained a good idea of the serviceability of the index card. The cards were sent to the various hospitals and filled in by the hospital physicians from the case records.

We realized that the questions on the card would give rise to difficulties on some points, especially in the classification of the paralyses into permanent and transitory. In order to define precisely the information we wished to obtain, we enclosed with the cards an explanatory note in reference to paralyses which said: "In the classification of the undoubted paralyses into *permanent* and *transitory*, the prognosis is to be considered: especially whether the paralysis must be assumed to be likely to leave at least a remnant for the rest of life, or whether it has disappeared at the time of the discharge from the hospital or seemed likely to disappear entirely."

We have reason to think that this classification of the paralyses has been serviceable, as no particular difference was found in the distribution of the

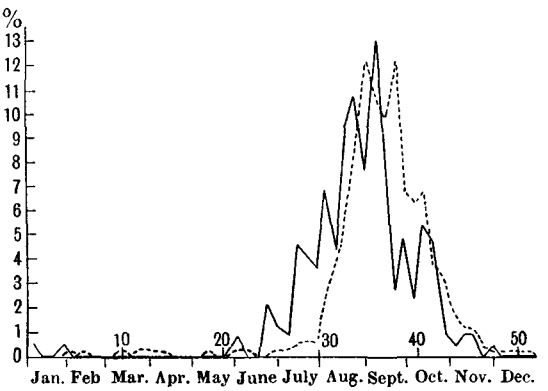

Fig. 2. Curve for poliomyelitis in the 1937 epidemic in Denmark.
Weekly curve for Copenhagen ——. Weekly curve for country districts - - - -.

cases in the two groups, permanent and transitory, between that third of the case records which we analysed ourselves and the remainder, which was analysed by our colleagues in the hospitals.

The curve of the epidemic. A curve, plotted for the percentage distribution of all the cases of poliomyelitis in each calender week, shows that the epidemic occurred at the usual time, namely in August, September and October, with its peak in September (Fig. 2). In Copenhagen the epidemic began about the 24th–25th week of the year, and rose rather abruptly to a maximum in the 35th–36th week (i.e. the 1st–2nd week of September). Afterwards it subsided rapidly. The epidemic may be said to have ceased in about the 43rd week. In the country districts the epidemic began about 5 weeks later, that is, about the 30th week of the year, and rose even more abruptly to a maximum, which extended over the 35th–38th weeks (i.e. the 1st–4th weeks of September). It stopped 2 weeks later than the epidemic in Copenhagen.

Distribution of the epidemic. The distribution of the poliomyelitis epidemic in 1937 has to be considered in relation to the epidemics in the preceding years and to that of the following year. Fig. 3 shows that while in 1933 the epidemic was limited to a single focus, in 1934, when epidemic cases were very numerous, dense epidemic foci appeared in extensive districts. In 1935 no new foci were formed, but the "tail" of the epidemic of 1934 continued. In 1936, although large parts of the country had not yet been attacked, only about seventy cases being reported throughout the year, the disease did not occur in epidemic form.

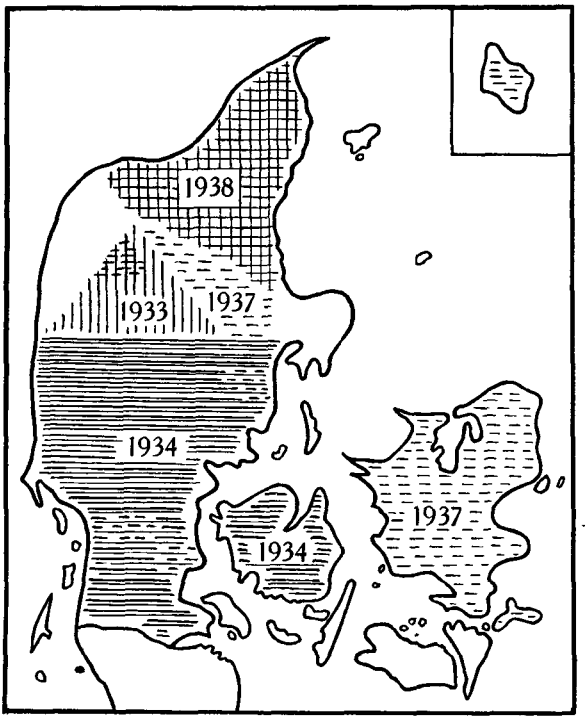

Fig. 3. Schematic presentation of the occurrence of poliomyelitis in Denmark in the period 1933–8.

In 1937 the disease again occurred in the form of an epidemic, diffused over a large district, but there were also a few small foci and many cases occurred in the old epidemic regions. A feature of particular interest was the epidemic occurrence of the disease in the district in which it had appeared in 1933; a closer location of the cases in 1937 showed, however, that though the same counties were affected as in 1933 the cases occurred in different localities.

In Greater Copenhagen and Copenhagen County a total of 223 cases was reported, and here the disease had an epidemic character; in the city, however, the cases were scattered without any predilection for particular districts (H. C. A. Lassen 1939).

Finally, in 1938 a new epidemic (about 560 cases) appeared, involving especially some districts in North Jutland that had escaped previously.

Surveying the distribution of the disease in Denmark in this 6-year period, one cannot help wondering at the apparently quite accidental manner in which it seemed to move about from year to year. It is the prevailing opinion that the disease, at least in the first days, is very contagious. It seems rather strange, then, that in Denmark, a small, densely peopled, country with rapid traffic all over, the disease fails to cover the entire country in one season which lasts for about 3–4 months.

The mode of transmission of poliomyelitis and the conditions of immunity among the people in general are still unsolved problems. As to the *way of transmission*, two hypotheses have been advanced: (1) transmission by droplet infection through contact with patients and healthy carriers, the nose and throat being the portals of entry; (2) transmission through water and articles of food with the intestinal tract as the portal of entry. The latter hypothesis was advocated especially by Kling and his collaborators. As to the *conditions of immunity*, there can be no doubt that a specific immunity really exists; but some investigators (Jungeblut and Engel) assume that, in addition, certain physiological factors, possibly endocrine, play a role in the establishment of immunity.

Our studies throw no direct light on these problems. We wish, however, to emphasize that investigations of this kind carried on through a greater number of years may possibly bring us nearer to their solution. Up to the present time experimental investigations have given little help.

Number of cases. About 1200 cases were notified in 1937, of which 599 had paralysis and 133 died. A comparison between these figures and the figures for 1934 is given in Table 1.

Table 1. *Comparison between the poliomyelitis epidemics in* 1934 *and* 1937

	1934	1937
Total no. of cases	*ca.* 4500	*ca.* 1200
No. of paralytic cases	*ca.* 650 = 14%	599 = 50%
No. of deaths	107 = 2·4%	133 = 11%
Deaths in proportion to no. of paralytic cases	16·5%	22%

In 1934 about 4500 cases were notified, of which about 650 had paralysis and 107 died. The question may therefore be asked: Was the epidemic of 1937 less extensive but more malignant than that of 1934? The question cannot be answered because though 3000 less non-paralytic cases were notified in 1937 it may be assumed that in 1934 not all mild cases were notified since we know from general practitioners and medical officers that in 1937 a great number of mild cases were not notified or sent to hospital.

During the 1934 epidemic, as reported by Nissen (1935), there was a rise in the number of influenza and angina cases for the entire country in August

and September, a time at which the seasonal curve for these diseases is usually at a low level. In 1937 also the same phenomenon was observed. A thorough investigation of the districts where epidemic poliomyelitis occurred and of other districts where only sporadic or no cases occurred showed that the rise in the influenza and angina morbidity was confined to the districts first mentioned. There can be no doubt that numerous non-paralytic cases of poliomyelitis were concealed under the diagnoses of influenza and angina. This is a problem we are planning to investigate further.

That a comparatively far smaller number of non-paralytic cases were notified and hospitalized in 1937 than in 1934 is undoubtedly attributable to the circumstance that in 1937 the disease showed a lesser tendency to appear in large dense foci, in which, we know from experience, a state of panic may readily develop among both the people and the physicians. Probably a contributory factor is to be found in the fact that the general belief in the convalescent-serum therapy was not so prevalent in 1937 as in 1934, so that the basis for such an extensive hospitalization may be said to have been absent. On the whole, there is no reason to assume that the epidemic of 1937 was much less extensive than that of 1934. The incidence of paralysis shows a surprising similarity in the two epidemics. The case mortality, calculated in proportion to the number of cases of paralysis, was greater in 1937 than in 1934, which is in keeping with the general impression among the clinicians that the disease in 1937 appeared to be more malignant and to have a greater tendency to produce bulbar-pontine paralysis.

Sex distribution. It has been a general experience in epidemics all over the world that the rate of morbidity, the incidence of paralysis and the case mortality are greater amongst males than females. The sex distribution of cases in our material is given in Table 2.

Table 2. *Percentage of females notified in the epidemics of* 1934 *and* 1937

	1934 %	1937 %
Total no. of cases	46·1	41·1
Paralytic cases	42·2	45·2
Deaths	38·2	38·9
Total population	51·0%	

It will be noticed that the figures for the two epidemics are in close agreement. In the epidemic of 1934 there was a great preponderance of males in the age classes under 12 years; but in the older age classes the proportion was reversed. This sex distribution was not observed in the 1937 epidemic, in which the proportion was similar throughout the age classes.

The age distribution has always been an interesting problem. At its first epidemic occurrence in Denmark, in 1905, the aspect of the disease was quite in keeping with its name, infantile paralysis. Since then, the age distribution has undergone a considerable change. A curve (Fig. 4) plotted for the

percentage-age distribution of the total number of cases (1112) in the entire country in 1937 shows that the morbidity was greatest in the age groups under 7 years, which included about one-third of all cases. Many adults were attacked, 30% of all cases being over 15 years, and about 14% over 20 years.

Somewhat similar findings are observed also when the percentage-age distribution of cases suffering from paralysis (599, Fig. 5), is examined.

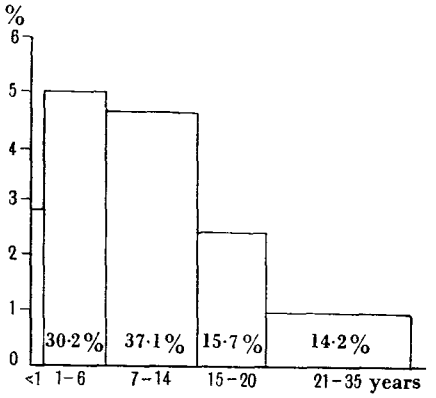

Fig. 4. Poliomyelitis in 1937. Percentage-age distribution in the entire country. Total number of cases: 1112.

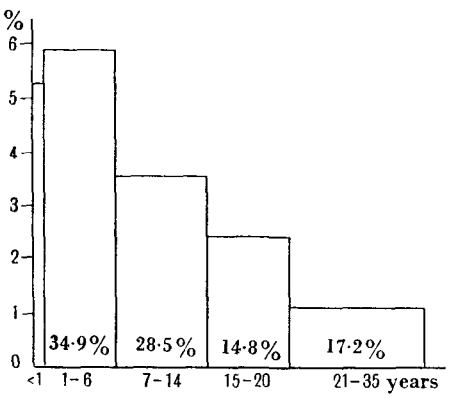

Fig. 5. Poliomyelitis in 1937. Percentage-age distribution of cases suffering from paralysis (599) in the entire country.

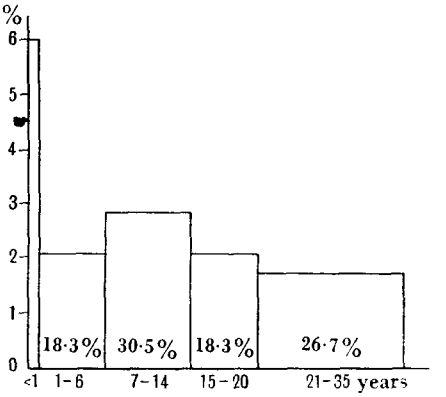

Fig. 6. Poliomyelitis in 1937. Percentage-age distribution of fatal cases (131) in the entire country.

In the age distribution of the 131 fatal cases the adult age classes again dominate the picture to a marked degree (Fig. 6); 45% of the patients who died were over 15 years, 20% over 20 years.

The experience gained from numerous epidemics shows that the age distribution changes in the course of the epidemic, so that there is a rise in the number of adult patients during the last part of the epidemic. In 1937 this feature was found both in Copenhagen and in country districts (Table 3).

Table 3. *Poliomyelitis in* 1937. *Age distribution in the first and the last phases of the epidemic*

Age years	Copenhagen		Rest of the country	
	1–8 months %	9–12 months %	1–8 months %	9–12 months %
1	2·6	2·8	4·0	2·3
1–6	37·9	22·4	34·8	28·3
7–14	30·2	39·3	38·9	37·2
15–20	12·9	17·8	14·6	16·4
over 20	16·4	17·8	7·7	15·5
Total	116	107	247	642

It will be noticed that during the first part of the epidemic (calculated up to 1 September) the patients in the age class of 1–6 years were very numerous. In Copenhagen this age class included 38% of the cases, as compared to 22% in the last part of the epidemic, and in the country the corresponding figures were respectively about 35 and 28%. It is difficult to give any explanation of this shift in the age distribution during the epidemic. It has been attributed, but without sufficient evidence, to a rise in the virulence of the virus.

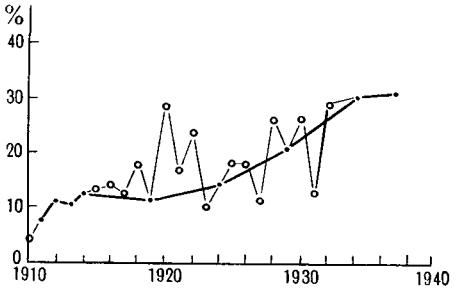

Fig. 7. Age distribution in epidemics covering the entire country in the period 1910–37. The numbers of cases of paralysis over 15 years plotted as percentages of total number of cases of paralysis. ——— connecting years with at least 100 cases of paralysis (epidemic years). o-o-o-o indicating years with at most 100 cases of paralysis (non-epidemic years).

Looking into the change in the age distribution of the cases in the epidemics that have occurred in Denmark since 1910, we find a gradual rise in the percentage for the age groups over 15 years (Fig. 7). In the intermediate non-epidemic years the percentage varies considerably, but the figures are very small. The same change in the age distribution is reported in other parts of the world, and there can hardly be any doubt that this difference between earlier and later epidemics is real and not due to changes in the diagnostic conception of the disease. It is difficult to imagine to what other diseases paralytic or fatal cases might have been attributed erroneously.

Serum treatment. The first attempt at a specific serum therapy in poliomyelitis was made by Netter in 1911, who used convalescent serum. The theoretical basis for this therapy was that he and other investigators had

demonstrated virus-neutralizing antibodies in the blood of poliomyelitis convalescents.

In 1917 Pettit reported the first cases in which the patients were treated with serum from immunized animals, monkeys and horses.

Since then, convalescent serum as well as animal-immune serum have been employed in many places all over the world. The only sure thing we know about these sera is that, when they are given before the animals are infected, or within the next 24 hr., they are able to prevent the appearance of the characteristic morbid phenomena in monkeys. Estimations of the effects of serum therapy in man have been most uncertain and various, and, in spite of numerous investigations, this question is far from settled.

During the epidemic of 1934 a majority of the cases—about 80%—were treated with convalescent serum. In estimating the effect of this serum therapy Claus Jensen (1935) in his reports fully realized the lack of non-serum treated patients as controls. It was necessary, therefore, to try to elucidate the problem in another way.

During and after this epidemic large amounts of convalescent serum were collected for the purpose of employing this therapy in a possible future epidemic as extensively as possible, in the form of uniform, large doses. Owing to technical accidents in drying and storing, large amounts of the serum were found to be unsuitable for our purpose. During the epidemic of 1937, however, the State Serum Institute had at its disposal a fair amount of serum (which had not been desiccated) taken from patients in 1934–5 and 1936, and also serum from a great many fresh cases in 1937. In 1937, however, serum therapy was not employed in the epidemic hospitals of Copenhagen. Outside Copenhagen no uniform principle was followed; in some places serum was given to all non-paralytic cases, in others it was given to selected cases. Thus, outside Copenhagen, 489 cases were treated with, and 400 without, serum. In the group of serum-treated cases the treatment was practically the same as that followed during the 1934 epidemic. As a rule serum was given early, in most cases immediately after admission to the hospital. No less than 88% of patients were given the treatment on the day of admission, and 10% on the following day. In most of these cases the serum was given intravenously, and the dosage corresponded to the average dosage in the 1934 epidemic (i.e. 20–40 c.c. for children, about 60 c.c. for adults). The extent to which serum treatment was given varied during the course of the epidemic. In the beginning less than one-half of the patients were given serum therapy and at the height nearly two-thirds. Then serum treatment became less frequent and, finally, as the epidemic was subsiding, the serum treatment was again employed more frequently. These variations in the employment of the serum therapy were not due to variations in the amount of serum available; they illustrate very well the uncertainty prevailing among the clinicians with regard to the value of the treatment.

The fact that in this epidemic there was a large group of non-serum

treated cases and another group of serum-treated cases, and that the two groups happened to be of about the same size, made it reasonable *a priori* to assume that these groups might give some valuable information as to the effect of the convalescent serum. Indeed, as already mentioned, this was one of the principal aims of our investigation. Dr Rasch and I have worked up this material together, trying to combine the medical requirements with the statistical.

The statistical studies on this material are presented in Part II.

The course of the disease. We had not planned in this investigation to gather detailed data on the course of the disease. Still, the data collected allow of a rough grouping of the cases according to the character of the paralysis and the outcome of the disease (Table 4).

Table 4. *Poliomyelitis in* 1937. *Absolute distribution of cases according to the course of the disease*

	Copenhagen		Provincial districts		Entire country	
	No.	%	No.	%	No.	%
Deaths	42	18·8	89	10·0	131	11·8
Permanent paralysis	107	48·0	175	19·6	282	25·4
Transitory paralysis	43	19·3	125	14·1	168	15·1
Doubtful paralysis	4	1·8	14	1·5	18	1·6
No paralysis	27	*12·0*	486	*54·5*	513	46·1
Total	223		889		1112	

Table 4 illustrates very well the enormous preponderance of non-paralytic cases in the country districts in both sexes and in all the age groups.

The question now arises as to the cause of this difference in the distribution.

(1) It might be a real difference of an immunological nature caused by the environment.

(2) Or, conceivably, it might be an artificial difference due to differences in diagnosis, in hospitalization or in notification of cases.

Such differences showed themselves in the places attacked in the epidemic of 1937. The account given of the influenza and angina outbreak bears on this point.

(3) Finally, the difference might signify an effect of the serum therapy, for serum was employed in the country but not in Copenhagen. If the serum had any effect, it should be shown in a lower percentage of cases of paralysis in the district where it was employed.

SUMMARY

The poliomyelitis epidemic of 1937 in Denmark was investigated by means of information obtained about each individual case.

It occurred in the usual season, culminating in September. The districts involved were limited largely to Zealand, including Copenhagen. It is of particular interest that the disease occurred also in rural districts that were the sites of similar epidemics in 1933 and 1934.

It is noted as a peculiar fact that poliomyelitis seems to be unable to invade the whole of Denmark within one season.

The 1937 epidemic comprised 1200 notified cases, of whom 599 developed paralysis and 113 died. Everything suggests that the number of non-paralytic cases was far greater than the number of cases notified. Influenza and angina were notified with striking frequency in the districts where poliomyelitis prevailed.

The morbidity, frequency of paralysis and mortality were greater among males than among females.

A change in the age distribution during the past 35 years is pointed out. In 1937, 30% of the patients were over 15 years, and about 14% over 20 years; of those who died 45% were over 15 years, 20% over 20 years.

Convalescent serum was not employed in Copenhagen, but in the provinces 489 patients were treated with, and 400 without, serum. The principles of the treatment were the same as in 1934. Serum was given early in the disease, as a rule intravenously.

II. CLINICAL STATISTICS

BY G. RASCH

IN Part I three possible explanations of the difference in the results of treatment with convalescent serum between Copenhagen and the provincial districts have been suggested. The one which most urgently calls for consideration is whether the difference may be due to the more general employment of serum treatment in the provincial districts.

In order to investigate this problem it is necessary to compare the serum-treated and the non-serum-treated cases. Possibly, however, the disease, regardless of the serum treatment, differs widely in its manifestations in Copenhagen and in the provincial districts, and therefore this comparison should be restricted to the provincial cases.

At a first glance the result seems quite plain. Of the 400 patients treated without serum 60% had paralysis, whereas of the 489 treated with serum only 33% had paralysis.

This result is in agreement with Claus Jensen's view based on the 1934 epidemic in Denmark, that early serum treatment reduces considerably the risk of paralysis.

In spite of Claus Jensen's work several prominent clinicians distrusted serum treatment, pointing out, amongst other things, that he had failed to keep the Copenhagen and the provincial data distinct. This objection does not apply to our material, but it should be remembered that many instances are on record in which some subdivision of material has completely altered the conclusions. Therefore we cannot be content with the mere statement we have just made without a careful analysis.

Subdivision of the material according to sex and age did not alter the picture, and further several additional detailed studies on diphasic cases and monophasic cases with a long pre-meningitic stage seemed to exclude the possibility of the result being accidental.

To conclude, however, from this result that the serum treatment actually protected the patients from paralysis is not entirely justified. Had it been a strictly scientific experiment on uniformly infected animals there would have been no doubt. But this was a clinical experiment and in each case some physician decided whether serum was to be employed or not. The question therefore arises, What has been the effect of the selection of patients for serum treatment? Might not the more favourable results in the serum-treated patients have been due entirely to the accident that cases with a favourable prognosis were more numerous amongst the serum-treated than amongst the non-serum-treated?

A weak point may be called attention to at once; in cases in which paralysis had appeared before treatment, serum therapy could at the most be used only to mitigate the paralysis. With the limited belief in the efficiency of the

serum treatment which prevailed in 1937, it is difficult to suggest how frequently serum was given in such cases.

Patients who were admitted with paralysis have therefore to be omitted from consideration. On the other hand, when the patients, paralysed on admission, are omitted from the serum-treated group, a group with a particularly good prognosis remains, and then the problem is, Is it possible to obtain control groups of untreated cases in whom at the time corresponding to the institution of the serum therapy the prognosis was as good as in the serum-treated?

This seems to be the case, for serum therapy was instituted in 430 of the 489 serum-treated cases on the day of admission and in 48 on the next day. In the serum-treated cases, therefore, "paralysis at the institution of treatment" was practically synonymous with "paralysis on admission". The comparison with the non-serum-treated patients therefore may be based on those who had no paralysis on admission to the hospital.

Table 5. *Provincial districts. Patients admitted without paralysis. Percentage occurrence of paralysis in patients treated with and without serum*

Serum	No. of cases	Subsequent paralysis (%)
+	409	18·1
−	200	19·0
Total	609	18·4

From Table 5 it is seen that of the 609 patients admitted without paralysis 409 were given serum, of whom 18·1% developed paralysis, and 200 were not given serum, of whom 19·0% developed paralysis. These patients therefore furnish no evidence that the serum treatment reduced the percentage of paralysis.

The question may be asked, however, Does the serum treatment mitigate the paralysis? Table 6 shows that among those who developed paralysis after admission the mortality was lowest in the serum-treated group, but the difference, 8·6%, with the small numbers available (74 and 38) is not sufficient to afford any conclusive evidence.

Table 6. *Provincial districts. Course of the disease in paralytics treated with and without serum*

Nature of paralysis	Patients admitted without paralysis		Patients admitted with paralysis	
	+ Serum	− Serum	+ Serum	− Serum
Transitory %	37·8	39·5	26·6	29·8
Permanent %	39·2	29·0	43·0	52·0
Died %	23·0	31·6	30·4	18·2
No. of cases	74	38	79	198

An attempt may be made to estimate the effect of serum treatment on patients admitted with paralysis. The difference in mortality was 12·2%, in favour of those not treated. Although this difference is statistically significant

it should not be interpreted as due to a noxious effect of the serum for it is probable that when serum was given to patients who already had paralysis—and this happened in nearly 30% of the cases—it was often in serious cases in whom no remedy must be left untried. Accordingly, it is only reasonable to assume that the serum-treated patients with paralysis included relatively more cases with a poor prognosis than did the untreated group.

From these data it is impossible therefore to demonstrate that the serum therapy had any effect.

In this connexion I cannot help questioning a conclusion arrived at by Claus Jensen in regard to the epidemic in 1934, namely, that unquestionably the effect of serum treatment was favourable. He based this conclusion on records showing that in over 2000 cases in whom serum treatment was commenced within 3 days after the onset of the meningitic stage the percentage of paralysis was only 5·4, while in a little over 600 cases in whom the serum treatment was commenced later the percentage of paralysis was 17·6. The difference is too great to be accidental, and it is necessary to inquire which patients were given serum shortly after the appearance of the meningitic stage, and which later on.

Table 7. *Percentage of paralysis in relation to the day of serum treatment in* 2992 *cases*

Time of onset of the meningitic stage before serum treatment	Serum-treated cases			
		Cases with paralysis		
	No.	No.		%
Less than 1 day	802	33		4·1
1 day	913 } 2367	50 } 127		5·5 } 5·36
2 days	652	44		6·7
3 days	283	48		17·0
4 days	125	15		12·0
5 days	78 } 625	11 } 110		14·1 } 17·6
6 days	50	9		18·0
More than 6 days	89	27		30·3
Total	2992	237		7·9

As it seems impossible to answer this question on the data presented, the effect of the serum treatment in the 1934 epidemic remains unsettled.

The apparent negative result of the treatment in 1937 must not, however, be taken summarily as a reason for giving up serum therapy. It has happened before that a serum therapy has been started with doses which were too small and later has proved serviceable with larger doses. Thus Fibiger in 1895–6 used only about 2000 units in his treatment of diphtheria, while now 200,000 units is a dosage commonly employed. Furthermore, such a means as horse serum therapy (Pettit) is as yet almost untried in this country.

One thing, however, is clear. The serum treatment has to be changed radically if it is to serve a therapeutic purpose.

Some other aspects of the disease are now considered without distinguishing between patients treated with and without serum.

The first question to be considered is whether there is any difference in the course of the disease in males and females in different age groups living in Copenhagen or in provincial districts.

In the provincial districts the percentage of paralysis is only half as high as in Copenhagen, but both in Copenhagen and in the country districts the percentage of paralysis is a little higher in females than for males. In the country this sex difference amounts to 2·6 × the mean error; so statistically it is unquestionable. The percentages of paralysis in the different age groups are rather different in Copenhagen from those in the provincial districts. In Copenhagen these percentages keep nearly at the same level in all age groups,

Table 8. *Percentage of paralysis in males and females in Copenhagen and in provincial districts*

	Copenhagen %	Provincial districts %
Males	83·1	40·0
Females	90·9	48·9

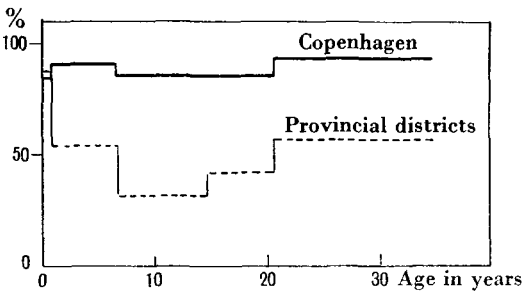

Fig. 8. Percentage of paralysis in relation to age.

about 80%, while in the provincial districts the percentage of paralysis reaches a minimum in the age class of 7–14 years (patients less than 1 year of age are extremely few, but they fit very well in the general picture).

To what extent these statistical differences are due to differences in the course of the disease and to different degrees of hospitalization is not evident.

Hospitalization was carried out to a relatively greater extent in some provincial districts than in Copenhagen, and, perhaps, males were hospitalized rather more than females. Possibly, in the provincial districts schoolchildren were hospitalized more frequently than younger children and adults. If so, the very pronounced minimum for the age class of 7–14 years may be to some extent an artificial product.

The differences in hospitalization seem to preclude a satisfactory discussion of the course of the disease in general, and it is better to consider cases which suffered from paralysis.

Sex. Table 9 leaves no doubt that, at any rate in Copenhagen, the course of the disease was alike in males and females. In the provincial districts the mortality appears to have been rather lower among the females.

Table 9. *Course of the disease in patients suffering from paralysis. Sex distribution*

Nature of paralysis	Copenhagen		Provincial districts	
	Males	Females	Males	Females
Transitory %	23·0	21·5	29·3	35·4
Permanent %	55·8	55·6	43·7	46·4
Died %	21·2	22·8	26·9	18·2
Total	113	79	208	181

Copenhagen and the provincial districts. Taking the two sexes together (Table 10), the mortality in Copenhagen and in the provincial districts was the same. On the other hand, in Copenhagen, about 10% more cases suffered from permanent paralysis than in the provincial districts; if the percentage is calculated on survivors with permanent paralysis the difference was 13·1%, a figure which seems unlikely to be accidental. It must be remembered, however, that to some extent the terms transitory and permanent depend on the prognosis in each case, and this depends partly on the possibility of orthopaedic after-treatment. Such treatment is more easily obtainable and is therefore utilized to a greater extent in Copenhagen. Furthermore, the material from Copenhagen has been collected by one person, Dr Juel Henningsen, whose personal judgment naturally has put its stamp on the findings, and his judgment may possibly have been a little more pessimistic than that of the notifying physicians in the provincial districts. This view suggests that any new data ought to be collected as far as possible by one person.

Table 10. *Course of the disease in patients suffering from paralysis. Copenhagen—Provincial districts*

Nature of paralysis	Copenhagen	Provincial districts	All Denmark
Transitory %	22·4	31·6	28·9
Permanent %	55·7	45·5	48·5
Died %	21·9	22·9	22·5
Total	192	389	581

In discussing previous epidemics it has been asserted that there was a difference in the course of the disease in Copenhagen and in provincial districts, and it is of interest to ascertain whether the disease took a more rapid course in Copenhagen than in these districts. Table 11, which gives the distribution of the cases of paralysis according to the duration of the pre-paralytic stage as calculated from the onset of the disease, shows that there was no demonstrable difference.

Table 11. *Percentage distribution of cases of paralysis arranged according to the duration of the pre-paralytic stage*

Days	Copenhagen	Provincial districts	All Denmark
0	8·2	8·8	8·6
1	10·4	12·9	12·1
2	21·8	15·7	17·7
3	15·8	17·3	16·8
4	11·5	11·3	11·4
5–9	22·4	26·0	24·9
≥10	9·8	8·0	8·6
Total	183	388	571

On the whole it seems justifiable to say that in this epidemic the main difference between Copenhagen and the provincial districts was in the extent of hospitalization.

Age. As no material difference was noticed in the effects of the disease either on the sexes or between Copenhagen and the provincial districts, the influence of age on those who suffered from paralysis may be disregarded.

Table 12. *Course of the disease in patients of different age groups suffering from paralysis*

	Age in years				
Nature of paralysis	<1	1–6	7–14	15–20	21–35
Transitory %	25·9	39·4	26·8	25·6	21·6
Permanent %	44·4	48·5	49·4	46·6	44·1
Died %	29·6	12·1	23·8	27·9	34·3
Total	27	198	168	86	102

The percentage of permanent paralysis kept remarkably steady, which is rather surprising in view of the fact that the mortality, as shown in Fig. 9, varied greatly with the age.

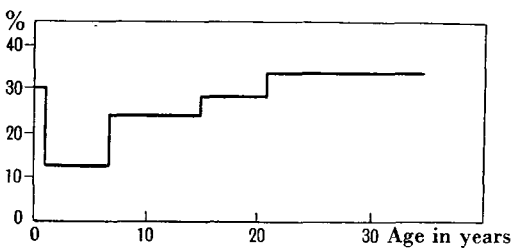

Fig. 9. Mortality among patients suffering from paralysis. All Denmark.

The death-rate was high for infants (30%); in children under school age it was as low as 12%; in schoolchildren it rose to 24%; after this it increased gradually, being 28% in the age group of 15–20 years, and 34% in adults.

The percentage increase of paralysis in the provincial districts with age (reckoning from the school age) was therefore probably not due merely to lesser hospitalization of adults with relatively mild attacks, but to a more serious course in adults than in children.

Some light may be thrown also on the question, whether the character of the disease had undergone any change in the course of the epidemic. Table 13 shows that the percentage of paralysis was higher in the latter part of the epidemic than in the first. This applied to Copenhagen as well as to the provincial districts; and in the latter the difference is statistically significant, as it amounts to 3·4 × the mean error. The prognosis for patients with paralysis, however, underwent no change in the course of the epidemic, so that it seems worth considering whether the apparently increasing severity of the disease in the course of the epidemic might not have been due entirely to a change in the tendency to hospitalization.

Table 13. *Course of the disease in the early and later part of the epidemic*

	Copenhagen		Provincial districts	
	1–35 weeks %	36–52 weeks %	1–35 weeks %	36–52 weeks %
Paralysis percentage	9·7	13·5	48·7	60·4
Transitory paralysis	24·3	18·7	32·5	31·8
Permanent paralysis	55·4	57·5	46·0	44·2
Died	20·7	23·7	21·5	23·9

Little evidence likely to be of value in prognosis has been obtained in these investigations.

In our attempts to estimate the course of the disease on the basis of the frequency of paralysis, the influence of the hospitalization has been a drawback throughout. In order to get around this difficulty we have tried to utilize the spinal fluid examinations.

Table 14. *Paralysis percentages in relation to the cell count in the spinal fluid*

Day of examination after onset of illness	Provincial districts Cell counts				Copenhagen Cell counts			
	≦30/3 %	30–300/3 %	>300/3 %	Total %	≦30/3 %	30–300/3 %	>300/3 %	Total %
0–2	8·9	29·5	50·0	24·8	45·4	66·7	87·0	71·8
3–6	29·7	75·0	65·3	58·9	83·3	94·5	93·1	92·2
≧7	40·0	77·1	95·0	70·0	60·0	86·2	93·3	83·3
Total	15·8	56·0	59·1	39·5	66·5	87·0	91·0	87·5
Not examined				84·2				89·2

In Table 14 the cell counts are grouped according to the day of examination after the onset of illness. It is evident that the higher the cell count at a given point of time the worse is the prognosis, except cell counts below 30/3 which indicate an increasingly worse prognosis the later they are found. It can be seen that cell counts at any point of time are far higher in Copenhagen than in the provincial districts. This is surprising in view of the fact that with the other criteria of the course of the disease we have not been able to demonstrate any particular difference between Copenhagen and these districts. The

explanation is probably to be looked for, at any rate in part, in the large group of non-examined patients in the districts, where the percentage of paralysis was exceedingly high (84%). In order fully to establish the significance of cell counts lumbar punctures will have to be carried out far more systematically so that the form of the cell-count curves may be compared with other indications of the course of the disease.

When discussing the value of the serum therapy the difference between the patients admitted to hospital with paralysis and without paralysis was pointed out. It seems clear that the former group was made up largely of patients with very short pre-paralytic stages. Table 15 shows that the prognosis is decidedly worse in cases with a short pre-paralytic stage than in those with a longer. The former had a mortality higher by 10% and a higher incidence of permanent paralysis. They had also a considerably lower incidence of transitory paralysis than patients in whom paralysis did not appear till 4 days or later after the onset of illness. This feature is common to Copenhagen and the provincial districts.

Table 15. *Cases of paralysis. Course of the disease and duration of the pre-paralytic stage reckoned from the onset of illness*

Nature of paralysis	Duration of the pre-paralytic stage	
	0–3 days	≷4 days
Transitory %	20·0	39·8
Permanent %	52·7	43·4
Died %	27·3	16·8
Total	315	256

Table 16. *Course of the disease in paralytics with respiratory paralysis*

	Patients with paralysis	Respiratory paralysis in such patients %	Cases with respiratory paralysis	Case mortality %
Copenhagen	196	18·2	35	77·1
Provincial districts	403	20·1	81	90·1
All Denmark	599	19·4	116	86·2

As will be seen from Table 16, about 20% of the paralysed patients both in Copenhagen and the provincial districts suffered from respiratory paralysis. Of the 35 patients with respiratory paralysis in Copenhagen 77% died, while of the 81 in the provincial districts 90% died. The difference of 13% is not sufficient, however, to prove that the energetic employment of a respirator in Copenhagen had a decisive value.

Summary

In the poliomyelitis epidemic of 1937 in Denmark there was no demonstrable effect from treatment with convalescent serum. There must therefore be some radical change in the method if serum treatment is to be of any value.

The disease was most serious in infants and adults.

No difference was demonstrated in the course of the disease in males and females.

In the provincial districts hospitalization of relatively mild cases was employed more extensively than in Copenhagen, but the course of the disease seems to have been similar.

Paralysis was apparently more frequent in the latter part of the epidemic, but, as in the cases with paralysis the disease took the usual course, a change in the frequency of hospitalization seems to be a plausible explanation.

Examinations of the cerebrospinal fluid did not throw much light on the prognosis, presumably because they were carried out too unsystematically.

In patients with a brief pre-paralytic stage ($\leqq$3 days) the prognosis was poor.

Of 35 cases with respiratory paralysis in Copenhagen 77 %, and of 81 cases in the provincial districts 90 %, terminated fatally. The difference is insufficient to furnish statistical evidence of the value of a respirator in Copenhagen.

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