IV

INVESTIGATION ON THE PROGNOSIS OF SYPHILIS WITH ESPECIAL REFERENCE TO RECIDIVATION IN THE BRAIN AND MARROW*

By JAMES STRANDBERG

DESPITE all statistics and all that has been written on the prognosis of syphilis our conception of this important question is as yet rather obscure. The causes hereof are manifold, but it is unnecessary to discuss them here. Likewise we need but hint that the pessimists concerning the value of the treatment are usually to be found among internists, neurologists, and psychiatrists, who see the majority of the later fatal recurrences of the disease. The increase of syphilitic vascular and nervous diseases of recent years, be it real or apparent, is a problem which has been illustrated from many quarters in dermatological literature. It has been attempted to prove by statistics that the modern treatment has changed the nature of the disease so that from being principally a skin disease it has now become more of a vascular and nervous disease. The treatment has even been charged with provoking nervous and vascular symptoms. The life insurance companies have produced extensive statistics which plainly point to an excess mortality in syphilitics; no sign that this has been changed for the better during the last decades has been observed. From the Scandinavian countries we have the oft-quoted statistics of Runeberg (1898), Bruhn-Fåhræus (1902), Tiselius (1904), and Lennmalm (1923); Bruusgaard's sensational account of the peculiar, untreated syphilis material from Norway which he published in 1928, will no doubt still be recalled. Boas, and likewise Lindstedt have put forward their views on the significance of syphilis in life insurance, and I have myself in a couple of papers referred to kindred problems and attempted a critical examination of them.

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The reason why I again take up this question for discussion is that I wish to bring forward new material which may perhaps be of a certain interest.

Since and including the year 1919 every case of syphilis in the infectious stage diagnosed by a physician has, under our Swedish "*lex veneris*," been compelled to undergo a prescribed treatment, and the patient can obtain this treatment free of charge at the expense of the State. The direct consequence of this has been that during the last seventeen years all cases of diagnosed syphilis in Sweden have been able to receive and usually also have received a vigorous specific treatment. Thus at St. Göran's Policlinic in Stockholm each case of fresh syphilis has been treated with at least 2 maximum combined series of Hg or Bi + salvarsan (each series of 10 Hg or Bi + 10 salvarsan of at least 6 gm. in all). Later the treatment has been continued for three years with about ten intermittent series of Hg or Bi, each such series of ten injections. If clinical or serological recidivation were ascertained during treatment, more salvarsan was usually added. According to this method many, indeed probably most, syphilidologists in Sweden will have treated their syphilitic patients. Some, however, have adopted the method indicated by Almkvist with so-called continuous treatment of syphilis, a method which is based on large doses of Hg, Bi and salvarsan (see *Svensk Läkartidningen*, 1926).

Hence, theoretically it should already now be possible to see whether a vigorous specific treatment of syphilis acted in one direction or the other with respect to the appearance and frequency of late recurrences. We have learnt by experience, however, that it is very difficult to follow and subject to post-examination a large material of syphilis from the time of the infection onward through several decades. The patients will easily be lost sight of and when all are not found again, the result of the investigation will be of diminished value, it may indeed even be deceptive. Bruusgaard's above-mentioned investigation shows what the loss may be in these attempted inquiries. Of 2,181 cases of syphilis treated during the years 1889-1910 he was only able to obtain information about 25 per cent.; of these 309 were alive and 164 deceased, *i.e.*, a total of 473.

Another method is to start from the late relapses and

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try to discover when these patients were infected, what treatment they have undergone, etc. In this case the difficulty lies mostly in procuring a large and well-observed material, about which the desired information can be obtained with a fair degree of certainty. However, I consider that I am able to produce a fairly good material, in respect of late nervous symptoms, namely, the material from the Malaria Department of St. Göran's Hospital. During the years 1927-34, 477 cases of late syphilitic cerebrospinal diseases have been under care there. Of these, however, the diagnosis has been doubtful in 16 cases. Hence they are not included in this account which therefore comprises 461 cases.

The material may perhaps be considered too small to warrant general conclusions. It is, however, practically as large as that of Bruusgaard. Lennmalm's investigation does not comprise nearly as many cases. For it is based on the death-rate statistics of the life insurance company Thule during the fifty-year period 1873-1922. Syphilis is there given as the cause of death in 327 cases. Of 550 deceased insurees who were diagnosed as syphilitic on effecting the insurance, only 97, or 17.63 per cent., had died of syphilitic infections.

In Lennmalm's, as in other investigations based on life insurance, material first-hand information as to infection, diagnosis, treatment and the course of the disease is extremely scant, if present at all. As correctly pointed out by Rosenthal such statistic material, when large, may be of value in calculating average life-span and similar particulars, but for the estimation of the curability of syphilis it is without importance. As far as the material here to be discussed is concerned, the records of the cases are at any rate extremely accurate and full, and the diagnoses are based on detailed clinical observations with examination of the blood and cerebrospinal fluid in each case. The information in the records in respect of earlier treatment has, when necessary, been supplemented through written or oral inquiry of the physicians who have previously treated the patients. Thanks to their great helpfulness these particulars are now fairly complete. I am greatly indebted to Dr. Malcolm Tottie for his valuable help in collecting and co-ordinating this information.

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The whole of the material has been divided into four sections according to the clinical diagnoses.

A. Syphilis cerebrospinalis .	132	cases.
B. Tabes dorsalis . . .	75	„
C. Tabo-paralysis . . .	43	„
D. Dementia paralytica .	211	„
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Total . . .	461	„
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All these cases have then, according to the history given concerning treatment been again divided as follows :—

Group I.—Cases never treated before.

Group II.—Not treated until the late symptoms appeared.

Group III.—Cases treated insufficiently from the beginning.

Group IV.—Cases well treated from the beginning of the disease.

There was no difficulty in distinguishing Groups I. and II. With respect to Groups III. and IV. it should be noted that the designations “insufficiently” and “well” treated cases are quite subjective. In Group III. are included such cases as have only been subjected to short or irregular treatment with Hg or Bi alone, or perhaps one or two injections of salvarsan. In several cases the treatment was so deficient (*e.g.*, “inunction with Hg for a month,” “an Hg-bag cure,” “some Hg injections”) that it can almost be regarded as if none had been given. This often applies to persons who have purposely avoided treatment, or owing to journeys have been unable to

A. SYPHILIS CEREBROSPINALIS

	Number of cases.	Time of infection unknown.	Time of infection known.		Latent period of late symptoms. Years.
			Number of cases.	Per cent. of group.	
Group I. .	21	18	3	14·3	16·7
Group II. .	53	50	3	5·7	8·7
Group III. .	45	0	45	100	17·0
Group IV. .	13	0	13	100	10·0
	132	68	64	48·5	13·1

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B. TABES DORSALIS

	Number of cases.	Time of infection unknown.	Time of infection known.		Latent period of late symptoms. Years.
			Number of cases.	Per cent. of group.	
Group I. .	11	10	1	9.1	18
Group II. .	27	17	10	37.0	17
Group III. .	34	0	34	100	17.7
Group IV. .	3	0	3	100	7.6
	75	27	48	64.0	15.1

C. TABO-PARALYSIS

	Number of cases.	Time of infection unknown.	Time of infection known.		Latent period of late symptoms. Years.
			Number of cases.	Per cent. of group.	
Group I. .	9	8	1	11.1	18
Group II. .	12	10	2	16.7	11.5
Group III. .	21	0	21	100	18.1
Group IV. .	1	0	1	100	12
	43	18	25	58.1	14.9

D. DEMENTIA PARALYTICA

	Number of cases.	Time of infection unknown.	Time of infection known.		Latent period of late symptoms. Years.
			Number of cases.	Per cent. of group.	
Group I. .	64	59	5	7.8	13.8
Group II. .	60	50	10	16.7	14.3
Group III. .	85	0	85	100	16.2
Group IV. .	2	0	2	100	13.5
	211	109	102	48.3	14.4

carry it through. Group III. also includes some older cases, where the infection and treatment date from the time of and before the enactment of the law in 1919. With respect to Group IV. a summary will be given in the sequel including information as to treatment. First we will, however, take a look at the different sections (A, B, C and D).

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Starting from these tables we will first consider whether the treatment may have any bearing on the onset of late syphilitic nervous symptoms. Groups I. and II. will be taken together here since no specific therapy was applied to the cases of Group II. until the nervous symptoms had already been diagnosed.

	Groups I. and II.	Group III.	Group IV.	Total.
Syphilis cerebrospinalis .	74	45	13	132
Tabes dorsalis. . .	38	34	3	75
Tabo-paralysis . . .	21	21	1	43
Dementia paralytica .	124	85	2	211
Total . . .	257	185	19	461
Percentage of total . .	55.75	40.13	4.12	

That the infection of more than half of all the individuals who contracted syphilis in Sweden during the last decades should have remained undiscovered until late nervous symptoms appeared, and that only about 4 per cent. of the cases with recent syphilis during the same period of time should have obtained thorough treatment is not likely. There is the very greatest probability that this is far from being the case. In our aforementioned *lex veneris* the tracing of the sources of infection enters as an important element in the fight against the venereal diseases. This contributes to the discovery of more cases of syphilis than before, hence it can safely be asserted that the cases of *syphilis ignota* have now in Sweden been reduced as far as is possible. Probably the number of undiscovered early cases of syphilis is considerably lower than that of the cases of early syphilis treated *lege artis*. Under these circumstances the investigation shows that the specific treatment has not here provoked nervous symptoms but on the contrary has been capable of preventing such.

Out of 461 cases of syphilis in the central nervous system only 4.12 per cent. have undergone vigorous treatment from the beginning of the infection. If we consider alone cases of the so-called syphilis parenchy-

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matosa (tabes, tabo-paralysis, dementia paralytica), which, incidentally, are generally the least susceptible to the usual anti-syphilitic treatment and where the prognosis is as a rule less favourable than in syphilis cerebrospinalis, these constitute 329 cases. Of these only 6, or 1.63 per cent. have been well treated from the beginning.

The predominant number of cases in Group I., however, are syphilis cerebrospinalis. This diagnosis comprises a particularly variable *facies morbi* with a medley of symptoms. Sometimes they are mild and easily overlooked, in other cases they set in suddenly, become very severe and quickly lead to death. Between these extremes there occur countless variations. Cerebrospinal syphilis sets in at different times, thus occasionally during the secondary stage, already some months after infection, but also much later, at any period of life. Even though basal meningites are perhaps more often seen during the secondary stage than later during the tertiary stage, an oft-quoted old pronouncement by Mauriac as to the *facies morbi* of cerebrospinal syphilis still applies: "qu'elles sont precoces ou tardives, qu'elles appartiennent à la phase secondaire, ils ont toujours la même physionomie generales et la même gravité."

On examining the case histories in Group IV. one is struck by the fact that instances are there often met with in which the infection, despite the most thorough treatment with salvarsan, Bi and Hg, has progressed and developed into a neurosyphilis. It would almost seem as if a number of cases were predestined for this, and the cause of this malignity is extremely enigmatical. In order, if possible, to reduce the number of such cases and further to cut short their progress we must not weary in our care where the treatment and observation of the patients is concerned. The examination of the cerebrospinal fluid is especially an important aid in checking the results of treatment. If these do not seem satisfactory in some respect or other, if, *e.g.*, there is stubborn positive W.R. in blood, changes of the cerebrospinal fluid, vague nervous symptoms, etc., there should be no delay in instituting a malaria treatment. Unfortunately it is seen only too often that such a treatment is begun so late, that in the most favourable cases it can only bring about a defective healing.

BRIEF HISTORY OF THE CASES IN GROUP IV.

Case 1.—A woman, born in 1897. Infected with syphilis in 1914 and treated by Dr. K. Marcus. Received regular treatment with salvarsan and Hg for three years. Not seen later until 1926. Was then admitted to the Malaria Department.

Diagnosis : syphilis cerebrospinalis.

Case 2.—A woman. Born in 1892. Infected with syphilis in 1919. Remains of sclerosis + mucous papules. W.R. positive. Treated later by Professor Almkvist.

1919 : 9 salvarsan + 39 Hg.
 1920 : 48 Hg ; W.R. negative at beginning of year.
 1921 : 18 Hg ; W.R. positive at beginning of year.
 1922 : 20 Hg ; W.R. positive at beginning of year.
 1923 : 10 „ + 10 Hg.
 1924 : 10 „ + 10 Hg.
 1925 : 15 Bi + 10 Hg ; W.R. negative at beginning of year.
 1926 : 40 Bi.
 1927 : 39 Bi. Admitted to the Malaria Department.
 Diagnosis : syphilis cerebrospinalis.

Case 3.—A man, born in 1898. Infected with syphilis in 1928. Extensive roseola. Treated regularly for years with salvarsan + Hg. In 1924 W.R. was found to be positive, was given 20 Bi. 1925 W.R. still positive, was given 10 salvarsan. In the autumn of 1926 continuous treatment started with salvarsan + Hg + Bi according to Almkvist. This treatment was terminated at the beginning of the year 1927. W.R. was then still positive. In November of the same year some nervous symptoms set in, general restlessness, etc. Gradually became subject to fits of vertigo and dizziness. Transient unconsciousness. Was admitted to the Malaria Department. Diagnosis : syphilis cerebrospinalis.

Case 4.—A man, born in 1900. Infected with syphilis in 1923. Sclerosis, W.R. positive. Twelve treatments with salvarsan and Hg, the last treatment terminated in November, 1927. W.R. taken five times during treatment, always negative, the last time in November, 1927.

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In February, 1928, acute retention of the urine. Saw a physician about it : urine collected. Continued difficulty in urination. Admitted to the Malaria Department. Diagnosis : syphilis cerebrospinalis.

Case 5.—A man, born in 1881. Infected with syphilis in 1914. Continuous treatment by Dr. Marcus with salvarsan and Hg. Last treatment in 1926. W.R. was then positive. Admitted to the Malaria Department in 1928. Diagnosis : syphilis cerebrospinalis.

Case 6.—A man, born in 1892. Infected with syphilis in 1919. 1919–21 under the care of Dr. S. Birger in Stockholm. Repeated treatments of salvarsan and Hg. Moved to the provinces and continued there with salvarsan + Hg + Bi during the years 1921–29. As W.R. remained positive he was admitted to the Malaria Department. Diagnosis : syphilis cerebrospinalis.

Case 7.—A man, born in 1889. Infected with syphilis in 1919. Sclerosis + roseola + W.R. positive. He received, till the end of November, 1922, 9 treatments with Hg in conjunction with salvarsan, altogether 32 injections usually of 0.9 g. salvarsan sodium (ns).

1923 : April W.R. indistinct.

May W.R. positive. Six salvarsan (5 g. ns).

1924 : January W.R. faintly positive, treatment with Bi + 3.15 g. ns.

March W.R. negative.

1926 : April W.R. positive, vague nervous symptoms, "creepy all over." Treatment with Bi + 5.4 g. ns.

June W.R. positive. Treatment with Bi + 6.3 g. ns.

Autumn W.R. negative.

1927 : Spring W.R. negative.

September W.R. faintly positive, fresh treatment after which W.R. was negative.

1929 : W.R. negative, since the summer constantly sluggish pupils. September W.R. positive in the cerebrospinal fluid. Treatment with Bi + 10 ns (8.25 g.).

1930 : January W.R. negative. Endolumbar injection 0.5 mg. ns. Admitted to the Malaria Department. Diagnosis : syphilis cerebrospinalis.

Case 8.—A man, born in 1873. Infected with syphilis

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in 1925. Secundaria, W.R. positive. Treated until the beginning of 1928 with 10 salvarsan + 7 series of Hg + 1 series of Bi. In 1928 further 4 salvarsan. In 1929 pain in the loins, tired and sometimes dizzy. The symptoms increased, and since W.R. was positive, he was admitted to the Malaria Department in 1931. Diagnosis: syphilis cerebrospinalis.

Case 9.—A man, born in 1898. Infected with syphilis in 1929. Primary sclerosis + W.R. positive. Two maximum series of salvarsan + Bi. W.R. 1930 negative. In 1932 he was admitted to the Malaria Department. Diagnosis: syphilis cerebrospinalis.

Case 10.—A man, born in 1877. Infected with syphilis in 1917. Sclerosis + roseola. Treatment for three years with a total of 12 Hg series, in addition 2 salvarsan in each series. In 1920, following immediately upon discontinuance of treatment, bilateral "trigeminus paralysis." Saw Professor Nonne at Hamburg, who performed a lumbar puncture. "A very little lues." Advised against salvarsan, prescribed inunctions, which advice the patient followed. In 1922 a physician diagnosed psoriasis plantaris. The patient was given Bi for three years until 1925. After 1928 various nervous symptoms: loss of taste, change of disposition, numbness of legs. In 1930 lumbar puncture, "some bad tests," amongst others W.R. in the cerebrospinal fluid positive. The nervous symptoms increased and the patient was admitted to the Malaria Department in 1931. The W.R. of the blood was never positive (not taken at the beginning of the first treatment in 1917). Diagnosis: syphilis cerebrospinalis.

Case 11.—A man, born in 1893. Infected with syphilis in Chile in 1926. Had then a distinct exanthema. Was at once given 2 Hg treatments (number of injections?). W.R. being strongly positive treatment with salvarsan and Bi was continued until 1931. Lumbar puncture at Berne in 1931 with negative findings. W.R. in blood then negative for two years. Admitted to the Malaria Department in 1932. Diagnosis: syphilis cerebrospinalis.

Case 12.—A woman, born in 1900. Infected with syphilis 1919. Sclerosis + extensive secundaria. Treated till 1923 with a total of 25 salvarsan + 103 Hg + 14 Bi. W.R. throughout positive. Stopped treatment and warnings had no effect. Treatment resumed in 1926

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and since continued till September, 1928. During this period she received a total of 98 salvarsan + 112 Bi + 10 Hg. Admitted to the Malaria Department in September, 1928. Diagnosis: syphilis cerebrospinalis.

Case 13.—A man, born in 1898. Infected with syphilis in Hamburg in 1921. Was there given 5 salvarsan and 8 Hg injections. Some months later in Stockholm 5 salvarsan + 7 Hg injections. In April, 1922, epileptiform fits. Lumbar puncture: W.R. negative, great increase of cells, 220 cells per cubic millimetre. W.R. in blood negative. As the patient contracted a severe stomatitis and evidently tolerated Hg badly, treatment was continued with salvarsan and Ki only. In April, altogether 6 salvarsan (of which 5 silver salvarsan). On October 1st, 1922, suddenly severe epileptiform fits (*status epilepticus*).—Salvarsan + Ki. In 1923, 7 salvarsan. Later the patient kept away and did not come back for treatment until April, 1928, when he complained of headache and giddiness. W.R. positive (stated that tests had been taken with negative result twice in the interval). Was now given 9 salvarsan and was subjectively well. Admitted to the Malaria Department in 1932. Diagnosis: syphilis cerebrospinalis. At times there appeared to have been excessive indulgence in alcohol.

Case 14.—A man, born in 1889. Infected with syphilis in 1916. Repeated treatment with salvarsan and Hg for three years. W.R. negative in 1918. In 1920 cerebral hæmorrhage. W.R. strongly positive, paralysis of left leg. Regressed during treatment for seven to eight months. Until and in 1921 abundant salvarsan and Hg. After this repeated treatments, the last few years with Bi, until March, 1928. W.R. in cerebrospinal fluid then positive. The patient had a psychic breakdown and became irritable and violent. After 1923, occasionally shooting pains in the extremities. Admitted to the Malaria Department in 1928. Diagnosis: Tabes dorsalis.

Case 15.—A man, born in 1888. Infected with syphilis in 1911. Sclerosis of the lips. According to information received from Professor Antoni, the patient had undergone abundant treatment from the beginning, first with salvarsan in series, later intermittently with much Hg and Bi until 1930, when he was admitted to the Malaria Department. Diagnosis: tabes dorsalis.

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Case 16.—A man, born in 1900. Infected with syphilis in 1918 or 1919. First treated at the Holterman Hospital at Göteborg and later continued with regular treatment at the polyclinic of the hospital for three years. Repeated blood samples taken later on were always negative. In 1931 sudden neuralgic pain and lancinating pains in the legs. Admitted to the Malaria Department. Diagnosis: *tabes dorsalis*.

Case 17.—A man, born in 1897. Infected with syphilis in 1920. Sclerosis + sclerotic adenitis. Treatment instituted at once and continued for four years. Every year 15 salvarsan and 2 to 3 series of Hg or Bi of 7 injections each, *i.e.*, in all 60 salvarsan and about 60 Hg or Bi injections. Annual blood samples negative until 1931, when the reaction became positive. Was then given salvarsan + Hg continually for a year. Admitted to the Malaria Department in 1922. Diagnosis: *tabo-paralysis + ethylismus chronicus*.

Case 18.—A man, born in 1881. Syphilis recens in 1912. Treated immediately with Hg and salvarsan, 10 treatments in each series. Treatment continued at short intervals for four years. During the years 1926–33 periodical Bi-series. Thus the patient has received much salvarsan as well as Hg and Bi. It has not been possible to ascertain the exact number of injections. Admitted to the Malaria Department. Diagnosis: *Dementia paralytica*.

Case 19.—A woman, born in 1894. Abortion in the fifth month of 1916. Had then a "blister" in the vulva. W.R. strongly positive. Went to the polyclinic in 1927. Remains of papules in vulva. W.R. strongly positive.

1927 :	10 salvarsan +	10 Bi.
1928 :	18 „ +	29 Bi.
1929 :		10 Bi.
1930 :	10 „ +	10 Bi.
1932 :	7 „ +	10 Bi.

W.R. was negative at the test in 1929, the other years positive. The patient evaded treatment in 1931. Towards the close of 1933 she began to stutter and showed a peculiar behaviour. Admitted to the Malaria Department in 1934. Diagnosis: *dementia paralytica*.

It has been pointed out as a disadvantage attaching to the treatment in respect of the outset of neurosyphilis,

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that the latent period between the infection and the neuro-recidivation is shorter in treated than in untreated cases. Let us see how matters stand in our material.

According to the case histories the latent period was :—

Unknown in . 222 cases, *i.e.*, in 48·2 per cent.

Known in . 239 cases, *i.e.*, in 51·8 per cent.

Total . 461 cases

The length of the latent period in the different groups will appear from the table below.

	Number of cases.	Per cent. of all cases.	Cases with known latent period.	Per cent. of each group.	Average latent period. Years.
Group I. .	105	22·8	10	9·5	16·6
Group II. .	158	33·0	35	23·0	12·9
	257	55·8	45	17·5	14·75
Group III. .	185	40·1	185	100	17·3
Group IV. .	19	4·1	19	100	10·8

This table, then, shows that
 45 cases not treated from the beginning have a latent period of 14·75 years.
 185 cases treated from the beginning, but insufficiently, have a latent period of 17·3 years.
 19 cases well treated from the beginning have a latent period of 10·8 years.

If these figures are accepted unconditionally, the result will be highly peculiar. The outlook would be worst for the well-treated patients (shortest latent period), considerably better for untreated patients, and best of all for insufficiently treated patients.

Here it should be pointed out that the latent period is only known for half the number of cases, for which reason the figures are very low. We cannot exclude the possibility that the result would be quite different if the latent period were known in every case. There are particularly few well-treated cases in our material. Furthermore, it is difficult to fix a time for the onset of the late relapses especially, as is often the case, when

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they are insidious. Therefore, the latent period is not infrequently calculated more or less approximately. In Case 7, for example, where the patient was infected in 1919, a number of vague nervous symptoms appeared as early as 1926, which, however, disappeared after continued treatment with salvarsan and Bi. Not until 1930 was this case diagnosed as syphilis cerebrospinalis. Had repeated spinal punctures been performed during the treatment, this diagnosis would probably have been made much earlier. That the latent period is often given as being longer in untreated than in well-treated cases may be explained to a certain degree by the fact that the latter are usually under careful control and the symptoms observed earlier than in the untreated cases who do not see a doctor until the symptoms are more pronounced. Hence the value of the information regarding the latent periods and their relation to the treatment is very problematic. The literature contains many contradictory reports on this question. Unfortunately, it cannot be denied that there are cases which do not react satisfactorily despite consistent and intensive treatment with salvarsan and Bi or Hg shortly after infection. Still, in our material, their number seems to be relatively small. However, late symptoms and a short latent period between the infection and recidivation should not be unconditionally interpreted as a direct result of the treatment, as this relationship has not been proved.

The result of this investigation must not be too generalised. The material is too scant and, furthermore, we have only taken into consideration the late symptoms in the nervous system. So much may, however, be said that it has lent support to an optimistic view of the value of the treatment, even when the object is to prevent the gravest consequences of the disease.

Nihilism and distrust must not discourage us ; on the contrary, each advance should incite us to further efforts in our endeavour to improve the prognosis of syphilis.

DISCUSSION

BOAS said that of 35 cases of dementia paralytica from the Frederiksberg Hospital only one was really well treated.

LOMHOLT: Dr. Strandberg's investigation must be

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welcomed with gratitude. As far as I know, it is the first time such a collective view has been presented, and fortunately it has given a clear, positive answer. Cases of syphilis which have been well treated from the beginning are only to a very slight degree threatened with the danger of late outbreaks in the central nervous system. This closes a long-lasting, very confusing discussion, and all talk of the risk of diverting the natural course of the syphilitic infection by suddenly stopping it must now come to an end.

Only a couple of practical questions at last. How and where is the limit drawn between well-treated and insufficiently treated cases?

What indications are given for the institution of a malaria treatment? I have for many years as far as possible followed the rule of giving malaria to all syphilitic patients who when spinal puncture is performed, usually a year after the termination of the current treatment, show a distinct pleocytosis ($> 14/3$), and with very encouraging results.

STRANDBERG (in reply): In reply to Dr. Lomholt's first question I should like to say that of course there are a number of cases in which it has been difficult to decide whether the treatment has been "insufficient" or "good," that is to say, whether they should be placed in Group III. or IV. When the patients had had a fairly regular three-yearly treatment, even though the salvarsan treatment had been deficient, they were placed in Group IV. The treatment given to the well-treated cases in which nerve symptoms developed will appear from the case histories.

My reply to the second question is, that at St. Göran's Hospital we have been very liberal with malaria treatment. We have been anxious to get neurosyphilis under malaria treatment as early as possible. Even cases exhibiting no symptoms of neurosyphilis, but in which other symptoms, for instance, obstinate positive W.R. in the blood, seemed to indicate that the current treatment had not been satisfactory, were as far as possible treated with malaria.