STUDY OF THE CEREBROSPINAL FLUID IN THE DIFFERENT PERIODS OF SYPHILIS.

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Lumbar puncture has been practised systematically since the year 1912 upon all the syphilitics treated in the service of Prof. Dind at Lausanne. The number of patients punctured is large enough to make it interesting to note the facts ascertained. A previous study upon it was published in 1915 by Dr. Isenegger, who has given the results of 173 lumbar punctures. Today we have at our disposal observations upon 354 patients, all syphilitic, and as many have been punctured before and after treatment we have the results of more than 500 examinations of the fluid.

Dr. Isenegger has established that the normal lymphocytosis is on the average 2.4 per cubic mm., basing this upon the lumbar puncture of a certain number of non-syphilitic patients who may also be considered nervously sound (lupus, chancroid, balanitis simple, etc.). Although some authors—Marcel Bloch and Vernes in particular—estimate that a normal cerebrospinal fluid does not contain more than 1 lymphocyte per cubic millimeter, we believe that a much higher figure can be found in individuals perfectly healthy and we consider lymphocytosis as pathologically increased only when it exceeds 5.

The measurement of the pressure of the fluid does not give us in syphilis any very useful indications. It does not seem to be parallel either with the lymphocytosis or with the albumin content of the fluid, and its increase, especially frequent in nervous lues, is interesting to note without our being able to attach to it actually any great importance.

We will now review rapidly the indications which lumbar puncture at the different stages of syphilis have given us, from the point of view equally of the lymphocytosis, the albumin content and the Wassermann reaction.

1. *Primary Syphilis*.—This deals with hard chancres with no secondary manifestations. There were in all 76 cases, all punctured before beginning treatment. In 24 patients the puncture was made at a time when the Wassermann reaction in the blood was still nega-

tive. The average lymphocytosis in these cases was only 2.4; it was increased—that is greater than five—only twice (8 per cent.). Of the 52 punctures made when the blood Wassermann was already positive, the average lymphocytosis was 6.1 it was increased in 35 per cent. of the cases. We observed once a pleocytosis rising to 34.

Wassermann reaction in the fluid was tested for 59 times; 58 times it was negative and only once positive with a patient whose blood was equally positive and who presented a lymphocytosis of 9.

The albumin, precipitated by nitric acid and measured approximately by means of the scale of Bloch, remained generally within normal limits, 0.20 or 0.30 per thousand. We found it plainly increased (0.70 per cent.) in only two instances. In one of these cases the lymphocytosis was 1 and in the other 8; there was therefore no parallelism between content of albumin in the fluid and the number of lymphocytes. Nonne's reaction, disclosing the presence of globulins, is, so to speak, always negative at the beginning of the luetic infection.

2. *Roseola* (with or without persistence of chancre).—We had 84 cases of this. These were also patients punctured before treatment.

The Wassermann was positive in the blood 84 times, that is every time.

The average lymphocytosis was 8.2 per cubic mm.; it was increased in 40 per cent. of the cases.

The Wassermann reaction was tested for in the fluid 71 times; 10 times it was positive (14 per cent., and for these 10 cases the average lymphocytosis was 17.1. In the 61 fluids in which the Wassermann reaction was negative the lymphocytosis had an average of only 5.6. There exists a parallelism between the two phenomena in the sense that, when the reaction of fixation of complement is positive in a fluid, that fluid presents most often a lymphocytosis clearly augmented.

The greatest pleocytosis was 67, observed in a fluid in which the Wassermann was positive.

The albumin was increased in 45 per cent. of the cases; this is an average of 0.06 per cent. As a rule if the albumin is abundant there is also augmentation in the number of lymphocytes. The Wassermann in the fluid may be positive with a normal quantity of albumin.

3. *Mucous plaques* (without exanthematous lesions).—Twenty-five patients punctured. They all presented only mucous plaques and not large condylomata nor remains of roseola. The blood

Wassermann was positive 24 times, that would be in 96 per cent. of the cases. The lymphocytosis was increased 8 times (32 per cent. of the fluids); this was an average of 5, therefore inferior to the degree attained in the roseola. The fluid Wassermann was positive only once (4 per cent.); in this case the lymphocytosis was 4. Increase of albumin was observed in 30 per cent. Of the cases; it averaged 0.5 per cent.

4. *Large Condylomata*.—Thirty patients presented neither roseola nor mucous plaques. Blood Wassermann was positive in 100 per cent. of the cases. Lymphocytosis was increased in 27 per cent. of the cases with an average of 5.1. Fluid Wassermann was positive four times (13 per cent.). In one instance a negative Wassermann had become positive when a second puncture was made after a complete treatment with neosalvarsan.

The albumin content averaged 0.5 per cent., increased in 30 per cent. of the cases.

5. *Latent Syphilis*.—This treats of long-standing syphilis, 65 cases, already treated previously or of patients in whom the lues was incidentally discovered without their presenting active specific manifestations. In those of them in whom the blood Wassermann was positive (70 per cent.), the lymphocytosis, increased in 40 per cent. of the cases, showed an average of 8; for the patients in whom the blood Wassermann was negative the average was only 4.7 (increase in 30 per cent. of the cases).

Fluid Wassermann was positive 5 times in 64 examinations (7.8 per cent.). In one instance we found the Wassermann negative in the blood and positive in the fluid. This was in a long-standing syphilitic treated on several occasions. The albumin, increased in 35 per cent. of the cases showed an average of 0.6 per cent.

6. *Hereditary Lues*.—We had at hand only 6 observations. One small patient presented hydrocephalus with idiocy. His lymphocytosis was 67. If we exclude this special case, we have for the 5 others a normal lymphocytosis averaging 3.9. The blood Wassermann was positive in 100 per cent. of the cases, the fluid negative 6 times at the first puncture. In one instance it had become positive at a second puncture made after treatment the lymphocytosis remaining normal.

The quantity of albumin was not modified.

7. *Tertiary Syphilis* (gummata and ulcerations).—Forty-five patients were punctured. The blood Wassermann was positive for 77 per cent. of the cases. Lymphocytosis, increased in 37 per cent. of the cases, averaged 7.1. It was evidently the same whether the

blood Wassermann was positive or negative. The fluid Wassermann was positive 3 times (6.6 per cent.). Here also we found in one instance the Wassermann reaction positive in the fluid and negative in the blood. Increase in albumin was noted in 40 per cent. of the cases; it is most often parallel with the pleocytosis.

8. *Cerebral Syphilis and Meningomyelitis*.—Six cases. Blood Wassermann was positive 4 times (66 per cent.). There was marked pleocytosis in 100 per cent. of the cases. This averaged 51 lymphocytes per cubic mm., one case presenting an exceptional pleocytosis of 235, the 5 others giving an average of 15 lymphocytes. The fluid Wassermann was positive every time, even in the two cases where the blood reaction was negative. The quantity of albumin surpassed 0.6 per cent. only in the patient noted above who presented a lymphocytosis of 235; it reached in this case 1.5 per cent.

9. *Tabes*.—We punctured 13 patients. The blood Wassermann was positive 9 times (69 per cent.). The average lymphocytosis, which was 30, was increased in 11 instances (85 per cent.). It was still normal with the two patients presenting clear symptoms of tabes at the outset. Fluid Wassermann was positive 9 times at the beginning but after treatment by neosalvarsan or novarsenobenzol it became positive in the 13 patients (100 per cent.). Once, in a case of demonstrated tabes, the fluid Wassermann had become positive after treatment while remaining completely negative in the blood.

The average quantity of albumin is 0.6 per cent. Here its increase is generally proportional to the lymphocytosis.

10. *General Paresis*.—We were able to examine only 4 cases. Of course this means from the beginning of general paresis. So many of these patients having been diagnosed in the service and discharged successively into a special establishment.

The Wassermann reaction was positive all 4 times in the blood and the fluid (100 per cent.). The average lymphocytosis was 28; it was increased in every case.

The quantity of albumin, 0.8 per cent. on the average, was in each instance equally augmented. It attained a maximum of 1.5 per cent. in a case where the lymphocytosis was 12. On the other hand in another patient it was only 0.8 per cent. for a lymphocytosis of 51, which shows that the parallelism between the quantity of albumin and the number of lymphocytes is not by any means constant.

The results may be tabularized as follows:

	Average Lymphocytosis	Lymphocytosis Increased In	Wass. Fluid Positive	Blood Wass. Positive
Hard chancre (Wa. +)....	6,1	35%	1,6%	} 68%
Hard chancre (Wa. -)....	2,4	8%	0 %	
Roseola.....	8,2	40%	14 %	100%
Mucous plaques.....	5,0	32%	4 %	96%
Large condylomata.....	5,1	27%	13 %	100%
Latent lues (Wa. +).....	8,0	40%	8,8%	} 70%
Latent lues (Wa. -).....	4,7	30%	5%	
Hereditary lues.....	3,9	0%	0%	} 100%
			16,6%	
Tertiary lues.....	7,1	37%	6,6%	77%
Meningeal lues.....	51,0	100%	100 %	66%
Tabes.....	30,1	85%	69% after neo,	} 69%
			100%	
General peresis.....	28,0	100%	100 %	100%

Influence of Treatment.—By the treatment with neosalvarsan or with novarsenobenzol one obtains as a rule a modification of the liquid in the sense of an amelioration, at least as concerns the pleocytosis. The 80 per cent. of patients presenting at the outset a clear exaggeration of lymphocytosis have been notably and very rapidly benefited by the treatment. This is particularly the case for the pleocytoses of the primary and secondary periods.

We have been able to note in tabes most frequently a marked diminution in the number of lymphocytes. Following an intensive treatment with novarsenobenzol one tabetic passed from 51 leucocytes to 12, another from 56 to 20, a third from 30 to 2 and a fourth from 16 to 3. This rapid transformation of the lymphocytosis was not on the other hand accompanied by an equivalent diminution of the quantity of albumin. This remains most often at its high figure or it is even often shown to be increased upon a second or third puncture. There is therefore frequently disassociation between the two phenomena.

As for the Wassermann reaction in the fluid, we have proved in many an instance that it becomes positive under the influence of treatment when it is negative at the first examination. Following an injection of neosalvarsan (biologic reactivation) it can even become positive in the fluid while remaining negative in the blood. There is here the ascertaining of an interesting fact which, for this alone, shows of what utility a lumbar puncture may be when it has to do with fixing the etiology of a case of tabes. The syphilitic infection would be in danger of being contested if one were content with investigating the complement fixation in the blood serum alone.

We have unfortunately only very few observations upon patients treated solely by mercuric preparations and we are not able to say

whether, from the point of view of the diminution of the lymphocytosis, mercury gives results as satisfactory as salvarsan. A comparatively interesting study might be made between the action of the two specifics. Some researches have actually been made in this sense at Lausanne under the direction of Prof. Dind and some cases of pleocytosis submitted to mercurial treatment (cyanide), which we have been able to follow, seemed to us to be modified much more slowly than the average of cases treated slowly by neosalvarsan.

Conclusion.—Our observations permit us to confirm fully that which our master had already pointed out in 1914, that is, how frequent and early is the extension of the syphilitic infection into the meninges, since in the 35 per cent. by the cases of hard chancre the number of leucocytes was already increased at a time when the cutaneous or mucous manifestations were still totally absent or at least could not be demonstrated by our means of investigation.

It is the lymphocytosis which at first betrays the modifications in the fluid, when the quantity of albumin is still normal and when the generalization of the infection has not yet been demonstrated by the Wassermann reaction.

In the exanthematous stage 14 per cent. of the fluids gave a complement fixation. This figure is met with again much the same (13 per cent.) in the cases of large condylomata when, among the patients showing mucous plaques, the fluid Wassermann was positive only once in 25 cases. This curious difference is not easily explained. Are there anatomico-histological conditions favoring the passage in the fluid of bodies capable of becoming fixed in the antigen especially among the carriers of the condylomata or indeed do the condylomata result in a more abundant formation of these bodies? The modifications of the fluid seem at least to be in accord with the reactions of the skin and we may ask if we have not here a question of the phenomenon of *allergia*. This conclusion would support the idea which Prof. Dind has been one of the first to defend, that *allergia* is an essentially cutaneous phenomenon. The condylomata, cutaneous lesions, would provoke a violent reaction of the organism when the lesions of the mucous membrane alone would not excite the individual to defense in the same degree.

As soon as the syphilis localizes itself in the central nervous system, the cerebrospinal fluid constantly presents important modifications and it is of great value in investigation for fixing the diagnosis or for controlling the course of treatment. The Wassermann reaction should be specially made in these cases for it is rela-

tively frequent that it is positive in the fluid and negative in the blood.

This little study will make evident, we hope, the utility of practising lumbar puncture upon syphilitics. The operation presents besides no danger. In many hundred cases of punctures we have had no serious accident to record. The patients rarely complain of vertigo or headache but it is absolutely necessary that those who have undergone puncture should lie flat without a pillow for 24 hours. The quantity of fluid withdrawn should be as little as possible. Five cubic centimeters are enough for the enumeration of lymphocytes in the cell of Nageotte, the measurement of albumin and the Wassermann reaction.

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