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The Luetin Test in Parasyphilis.

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DURING the spring of this year, my friend Lieutenant Crocket, R.A.M.C., obtained, through the kindness of Dr. Noguchi, a small supply of luetin, and with this he carried out a series of tests, to which he was anxious to add some observations on its use in mental cases. By permission of Dr. G. M. Robertson he was able to examine a series of cases in Morningside Asylum, and I was fortunate in being asked to co-operate with him. Owing to our small supply of luetin, the number of tests done was necessarily limited, and we intended carrying our observations further when Crocket was called away to duty. Only a short time ago the sad news of his death in action was received, and it is largely on this account that I venture to place on record so small a number of observations.

In 1911, Noguchi reported, in the *Journal of Experimental Medicine*, that he had succeeded in growing the *Treponema pallida in vitreo*, and, a few months later, he published his first article on the luetin test in the same journal. This test for syphilis is analogous to the intra-dermal tuberculin test of Mantoux and Moussu, and the technique is the same. Luetin consists of a sterile emulsion made from cultures of the

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Treponema pallida, and to obtain it the organism is grown on ascitic fluid agar for from six to fifty days under anaërobic conditions. The growths are then ground down in a mortar, and an emulsion is made by adding cultures of treponema in ascitic fluid. This emulsion, when sterilised, is ready for use. A dose of 0·07 c.c. is diluted with an equal amount of normal saline, and injected intra-dermally with a fine needle, and the local reaction observed.

When the reaction is negative, a small wheal appears in a few hours, and in twenty-four there is some induration, and a faint hyperæmic blush at the site of injection. This hyperæmia fades rapidly in a day or two, but the induration, which is usually about 3 mm. in diameter, may still be felt four or five days later as a minute nodule in the skin.

Three types of positive reaction have been described. First, an indurated papule surrounded by more or less erythema, and usually quite tender, appears in twenty-four hours, and tends to increase to the third or fourth day, when it may regress ; or it may pass into the second or pustular type of reaction, in which a small pustule forms at the site of injection, and after a few days becomes absorbed, leaving an indurated area which may persist for a considerable time. The pustule is usually small and remains dry, requiring no particular attention. None of our cases in which pustulation took place required any local dressing whatever. In some cases, however, much more marked local reactions have been reported. Wolfsohn, in his first series of cases, records two who complained of painful and tender arms, and one of these had enlargement of the axillary glands. He also mentions several cases in which hæmorrhagic pustules appeared, which were opened and exuded semi-fluid, grumous material. Benedek also records three cases in which on the fifth day the areola measured 3 to 5 cm. in diameter, and in which the pustules discharged a thick, brownish-yellow fluid on the eighth to the tenth days, after which involution began. A papule could be distinctly felt three weeks later, and the skin was discoloured.

The third type of reaction has been termed the torpid form. In it the reaction is delayed for anything from four to twenty-eight days after injection, and, when it does appear, usually takes the pustular form. This torpid form is most commonly seen in parasyphilitic and congenital cases, and was present in

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two of our cases, one a general paralytic in a state of remission which had lasted two years, and the other a boy of nine suffering from congenital general paralysis. Wolfsohn, out of 12 cases with cardio-vascular lesions, obtained a torpid reaction in six.

Constitutional disturbances are not common. None of our cases manifested any. Cohen reports 179 cases tested with no bad effects, while Boardman and Gorham record 52 with no constitutional disturbances, and Kilgore saw none in 120. When present the symptoms consist of malaise, tachycardia, abdominal pains, bone pains, slight nausea, and occasionally a little fever. These usually last only twenty-four to forty-eight hours. Wolfsohn records one case, a tabetic, who after injection had a fever of 103°, with severe abdominal pains and vomiting resembling crises.

Some doubts have been thrown on the value of the test in view of the fact that a similar reaction has been obtained with other substances than luetin. For example, if the luetin emulsion be injected into one arm, and a control emulsion made from the uninoculated culture media into the other, a reaction of almost equal intensity may appear in both arms. This is due to a special sensitiveness to trauma of the skin of syphilitic persons in the later stages of the disease, and has been termed by Neisser "Umstimmung." It is in itself characteristic of syphilis, but is a very inconstant phenomenon, and has little bearing on the luetin reaction.

Most observers are agreed that the test is of little value in primary and secondary untreated syphilis. If the test be looked on as an anaphylactic phenomenon, indicative of a state of hypersensitiveness to the specific proteins of the spirochætes, which state is induced by a period of cessation of the introduction of these specific proteins, then its failure in the primary and untreated secondary phases of the disease is easily understood. The disease is then so active that the patient cannot acquire the anaphylactic state necessary for the reaction. This also explains the fact that cases which, previous to treatment, gave a negative reaction, after treatment may give a positive one, and in this way the test may be used as a gauge for the efficacy of treatment. In tertiary, congenital, latent, and parasyphilitic cases the hypersensitiveness to the proteins of the spirochæte necessary to give a positive luetin reaction is to

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be expected, and it is in these cases that the test should prove of value, and this expectation has been confirmed by the clinical findings.

We were able to carry out the test in sixteen cases and to contrast it in each case with the Wassermann reaction. Out of these cases, twelve were general paralytics, and two cases of cerebro-spinal syphilis. Of the remaining two cases, one was a man who stated that he had contracted syphilis thirty-six years previously, and had received little or no treatment. In his case, both the luetin and Wassermann tests were quite negative, and, on further questioning him in the light of these results, we considered it most probable that his venereal infection was not syphilitic. The remaining case was one of some interest; the patient had suffered for some years from maniacal excitement, and the character of his mental symptoms, the absence of knee-jerks, and the presence of unequal and sluggish pupils, along with the development of early optic atrophy, had suggested the possibility of general paralysis and syphilitic infection. The Wassermann test first proved negative in the blood serum, but on applying the luetin test a markedly positive reaction was obtained. This led us to apply the Wassermann test to the serum and cerebro-spinal fluid once again, and, on this occasion, we found the reaction still negative in the serum, but faintly positive in the spinal fluid, five doses of complement being deviated. In this case, the luetin proved of very considerable assistance in confirming the diagnosis.

Cases of General Paralysis.

Of the series of cases of general paralysis, 9, or 75 *per cent.*, gave a positive luetin reaction. On making a table of these results, and comparing them with those of the Wassermann reaction, one finds that the positive cases may be divided into two groups—those giving the papular or slight type of reaction, and those giving the pustular or marked type. In the first group there are four cases, and in the second five. If the degree of the luetin reaction be compared with strength of the Wassermann reaction, that is, with the number of doses of complement deviated, an interesting co-ordination is brought out. In the cases giving a "slight" luetin reaction, the extent of deviation of complement was also slight, ten doses or under,

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while in the cases giving a marked reaction the extent of deviation of complement was also marked, ten doses or over.

Positive Cases of General Paralysis.

Case.	Luetin.	Wassermann.* Blood Serum.	C.S.F.
1	slight	0	7
2	„	10	10
3	„ (torpid)	6	1
4	„	5	10
5	marked	12	12
6	„	12	12
7	„ (torpid)	15	15
8	„	10	10
9	„	15	15

I am not aware that there is any series of cases in which any connection between the degree of the two tests has been noted, and it is, of course, not permissible to draw any conclusion from such a short series of cases as this. As the positive Wassermann is indicative of the presence of metabolic substances produced by present or recent activity of the spirochæte, while the luetin is indicative of a state of hypersensitiveness to the specific proteins, there is no very apparent reason why there should be any correlation between the degrees of the two reactions. A more extended series of observations on this point would be of considerable interest.

Negative Cases of General Paralysis.

Case.	Luetin.	Wassermann. Serum.	C.S.F.
1	Negative	30	30
2	„	15	10
3	„	7	3

In the first two negative cases, it will be seen that the Wassermann reaction was strong, and in both the disease was progressing steadily, and the physical symptoms particularly were marked. In the third case, the patient had been in a state

* The figures in this column indicate the number of doses of complement deviated.

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of acute excitement for a year, but had very few physical signs of the disease. The Wassermann reaction in his case was slight, and he was exactly the type of case in which a positive luetin might have been expected, and would have been of diagnostic help. The further progress of this case, however, has been such as to render the diagnosis of general paralysis very doubtful, and a Wassermann reaction recently performed proved entirely negative. The percentage of positive reactions in this series of cases coincides fairly well with that of Benedek, who in a much larger series (81 cases) of general paralytics obtained a positive luetin in 80·4 *per cent.*

Cases of Cerebro-spinal Syphilis.

The test was applied to two cases of cerebro-spinal syphilis, and was positive in both. In both, the reaction was a well-marked one, and this is of some interest, as Benedek noted, in the three cases which he tested, a reaction which was so well marked in comparison to those which he obtained in his cases of general paralysis as to lead him to suggest that the type of reaction might be of aid in distinguishing the two conditions:

		Wassermann.	
Case.	Luetin.	Serum.	C.S.F.
1	Marked	2	1
2	„	Partial	Partial.

Both these cases gave very slight deviation of complement with alcoholic extract, but with lecethin and cholesterin were definitely positive. Both had been under treatment by potassium iodide and mercury with very beneficial results, as the number of cells in the cerebro-spinal fluid had fallen in a period of sixteen months from, in the first case 555 to 4 per c.mm., and the second from 520 to 7·3 per c.mm.

If the case with optic atrophy, which has already been described, be included in the series, we found that out of fifteen cases of parasyphilis, twelve gave a positive luetin reaction, that is, 80 *per cent.* This figure agrees well with the average results of other observers. If the series of parasyphilitic cases recorded by Kilgore, Wolfsohn, Benedek, and Boardman be added together, it is found that, out of a total of 121 cases, 95, or 78·5 *per cent.*, gave a positive luetin reaction.

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The results obtained with the Wassermann reaction especially in general paralysis are more constant. Dr. Robertson, in his *Morrison Lectures* for 1913, states that the reaction in general paralysis is positive in 99 *per cent* of cases in the blood serum, and in 94 *per cent.* in the cerebro-spinal fluid.

In conclusion, the luetin reaction is a valuable addition to our diagnostic tests for syphilis. It is easily carried out by the clinician, is absolutely specific for the disease, and is occasionally positive in cases in which the Wassermann is negative. In comparing the value of the two tests, Much states that when it is a question of ascertaining if the patient has ever been infected with syphilis, the luetin is the more instructive, but when it is desired to know if the disease is still active, the Wassermann is the more helpful. These facts warrant its receiving much more attention than has hitherto been the case in this country.

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Remarks on the Intracranial Injection of Salvarsanised Serum.

By G. H. MONRAD-KROHN, M.B., M.R.C.P.Lond., M.R.C.S.Eng., Assistant Medical Officer, London County Asylum, Bexley, Kent.

IN the *Lancet*, July 4th, 1914, I have briefly described the method of what I called "subdural injection."

In a very interesting article in the *Journal of Mental Science*, October, 1914, by Mapother and Beaton, dealing with the intrathecal treatment of general paralysis, the authors criticise the different methods of intracranial injection. As regards the subdural injection, they state that it appears "to have no

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