

STUDIES ON THE WEIL-FELIX SEROLOGICAL TEST FOR THE LABORATORY DIAGNOSIS OF TYPHUS FEVER.

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TOWARDS the close of 1918 and the beginning of 1919, during the typhus season in Syria, I had an opportunity of carrying out a number of blood tests on cases of acute typhus, from the point of view of the Weil-Felix reaction recently described in connexion with this disease.¹ The reaction, be it recalled, is an expression of the power often possessed, and developed during the disease, by the blood serum of the typhus patient, of specifically agglutinating *in vitro* a bacterial emulsion of *Bacillus proteus* X19. Although the studies with which this paper deals, make no pretence at being exhaustive—which they could scarcely be, considering the "field conditions" under which they were carried out—still, in the confirmation which they afford of the constancy of the reaction in the disease, a short account of them may prove instructive. The contribution is merely a pioneer one.

CLINICAL MATERIAL.

Forty-seven blood tests were in all performed on some fourteen cases (British, Indian and Turkish prisoners of war) of the disease; the tests ranging from the fourth to the thirty-fourth day of illness, and consequently covering the various stages of the disease from onset to convalescence.

To Captain William Forsyth, R.A.M.C., and to Captain K. B. Dickson, R.A.M.C., under whose clinical care these cases were, my best thanks are due, for placing them at my disposal for the benefit of this investigation.

TECHNIQUE.

Blood from the patient's thumb was collected in a Wright's blood tube, and on arrival at the laboratory was centrifuged to separate off the serum. The agglutination titre of the latter was then determined towards a ten to twelve thousand bacterial emulsion of *B. proteus* X19 in saline phenolated to 0.5 per cent. The slide method of macroscopic agglutination associated with the names of Alcock² and Garrow³ was employed, the results being read off after three minutes' rotation of the slide in the agglutination box.

EXPERIMENTAL FINDINGS.

The following table briefly summarizes the main features of the cases and the results of the blood tests performed.

¹ E. Weil and A. Felix: *Wien. klin. Woch.*, xxi (No. 2), 1916, 33 to 35.

² Broughton Alcock: *JOURNAL OF THE ROYAL ARMY MEDICAL CORPS*, xxx, 1918, 424-431.

³ R. P. Garrow: *Lancet*, i, 1917, 262; *JOURNAL OF THE ROYAL ARMY MEDICAL CORPS*, xxviii.

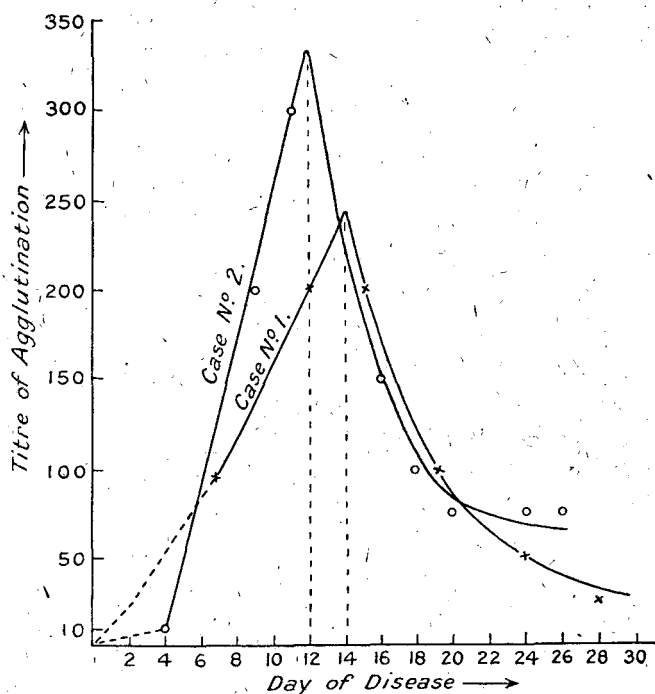
TABLE.

No. of case	Name	Nationality	Date of blood specimen	Whether rash present, or absent	Day of illness (patient's statement)	Result of the agglutination test, for the following dilutions of the patient's serum							Date the patient's temperature fell to normal
						$\frac{1}{2}$	$\frac{1}{10}$	$\frac{1}{50}$	$\frac{1}{100}$	$\frac{1}{200}$	$\frac{1}{400}$	Saliva continued	
1	S. ...	British	1.1.19	Present	7	++	++	++	+	-	-	-	5.1.19
			5.1.19		12	++	++	++	++	-	-	-	
			8.1.19		15	++	++	++	++	-	-	-	
			12.1.19		19	++	++	++	++	(+)	-	-	
			17.1.19		24	++	++	+	-	-	-	-	
			21.1.19		28	++	++	(+)	-	-	-	-	
2	R. ...	British	27.1.19	Present	34	++	++	(+)	-	-	-	-	12.1.19
			5.1.19		4	++	+	-	-	-	-	-	
			8.1.19		7	++	++	++	+	(+)	-	-	
			10.1.19		9	++	++	++	++	++	-	-	
			12.1.19		11	++	++	++	++	++	(+)	-	
			17.1.19		16	++	++	++	++	++	(+)	-	
			19.1.19		18	++	++	++	++	++	(+)	-	
			21.1.19		20	++	++	++	++	(+)	-	-	
			25.1.19		24	++	++	++	++	(+)	-	-	
			27.1.19		26	++	++	++	++	(+)	-	-	
3	H. ...	British	8.1.19	Present	7	-	-	-	-	-	-	-	17.1.19
			10.1.19		9	-	-	-	-	-	-	-	
			12.1.19		11	-	-	-	-	-	-	-	
			17.1.19		16	++	-	-	-	-	-	-	
			19.1.19		18	++	+	-	-	-	-	-	
			22.1.19		21	+	-	-	-	-	-	-	
4	Capt. B.	British	9.1.19	Absent	4	+	-	-	-	-	-	-	...
			10.1.19	Present	5	++	+	-	-	-	-	-	
			12.1.19	8	++	++	-	-	-	-	-		
5	S. R. ...	Turkish P. of W.	10.1.19	Present	5	++	++	-	-	-	-	-	19.1.19
			15.1.19		10	++	++	(+)	-	-	-	-	
			23.1.19		14	++	++	-	-	-	-	-	
6	M. A. ...	Turkish P. of W.	10.1.19	Present	4	++	++	-	-	-	-	-	19.1.19
			15.1.19		9	++	(+)	-	-	-	-	-	
			23.1.19		17	++	-	-	-	-	-	-	
7	A. S. ...	Turkish P. of W.	10.1.19	Present	4	++	++	-	-	-	-	-	21.1.19
			15.1.19		9	++	++	++	++	-	-	-	
			23.1.19		17	++	++	+	-	-	-	-	
8	M. ...	British	23.1.19	Present	5	++	+	-	-	-	-	-	...
			25.1.19		7	++	++	(+)	-	-	-	-	
			27.1.19		9	++	++	+	-	-	-	-	
9	O.M.A.	Turkish P. of W.	10.1.19	Present	10	++	++	++	+	(+)	-	-	15.1.19
			23.1.19		23	++	++	(+)	-	-	-	-	
10	Y. S. ...	Turkish P. of W.	10.1.19	Fading	12	++	++	+	(+)	-	-	-	21.1.19
			23.1.19		25	++	+	-	-	-	-	-	
11	M. H.	Turkish P. of W.	10.1.19	Present	5	++	++	(+)	-	-	-	-	22.1.19
			23.1.19		18	++	++	-	-	-	-	-	
12	K. S. ...	Indian	11.1.19	Present	9	++	++	++	+	-	-	-	11.1.19
13	R. R. ...	Indian	12.1.19	Present	9	++	+	-	-	-	-	-	...
14	Y. M. ...	Turkish P. of W.	15.1.19	Present 4 days	6	++	++	+	-	-	-	-	...

++ = agglutination very marked.
 + = " distinct to naked eye.
 (+) = " feeble, requiring hand lens to be certain.
 - = " negative.

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The above table (columns 6 and 7) shows that these cases all, with the exception of Case 3, gave a markedly positive reaction from the first days of the disease; and that the strength of the reaction varied from day to day. Some idea of the nature of this variation is revealed by the accompanying diagram, which is a graphical representation of the findings for Cases 1 and 2.



These curves show that the Weil-Felix reaction in typhus fever steadily increases during the first fortnight to attain its maximum about the twelfth to fourteenth day of the disease-period, when, in the uncomplicated case, the temperature as a rule falls by crisis—to decrease rapidly thereafter during the period of convalescence. This finding indicates, other things being equal, wherein as a test the Weil-Felix reaction may render conspicuous service to the physician. It points to the conclusion that in an early case of doubtful pyrexia, which shows a positive Weil-Felix reaction steadily rising in the twenty-four hours, there is strong presumptive evidence of typhus fever.

Consider now Case 3, which appeared to us at first in the light of an exception (see tests of January 8, 10, and 12) to the test; there being no doubt clinically as to the diagnosis of typhus. This man's Weil-Felix reaction was persistently negative throughout the first fortnight, to become positive about the sixteenth day of the disease—when it was first observed—

his blood having then acquired the power to agglutinate markedly *B. proteus* X19 in a serum dilution of $\frac{1}{2}$, but not beyond. On the sixteenth day his temperature fell by crisis. A blood test forty-eight hours later revealed that the titre of agglutination, although still low, had increased slightly, being again well marked in the $\frac{1}{2}$ dilution and feebly so in the $\frac{1}{10}$ dilution. Thereafter in his case, as for the others, this feebly positive Weil-Felix reaction—which might well have been missed, on the method employed, had it not been studied persistently and that in very low dilutions—its maximum having been reached, fell gradually off.

Of the fourteen cases, then, of typhus tested by us: thirteen (or ninety-three per cent) showed well-marked Weil-Felix reactions, and one (or seven per cent) gave such a feeble reaction that it might well have passed unperceived and been returned as negative. The percentage figures here have little value; the number of cases examined being so small.

The significance of positive Weil-Felix reactions, other than the practical one that they may be utilized as a laboratory method for the diagnosis of typhus, is unknown.¹ As to that of such feebly positive reactions as the one above described—for no truly negative Weil-Felix reaction has been met with in any case of typhus examined by me—it may be that such reactions are to be correlated with the curious phenomenon, recently described by Nicolle and Lebailly,² of “inapparent infection.” In the latter phenomenon, observed so far only in laboratory animals and that in connexion with experimental typhus, a guinea-pig occasionally shows no temperature reaction, following inoculation with the virus of typhus; and yet its blood, at the time when the control animals show well-marked fever, is found to be virulent, especially for the African monkey. Rats, again, do not ordinarily react by even an elevation of temperature to the virus of typhus; but their blood is virulent about the twelfth day.

These, then, are some at least of the interesting problems connected with this disease which it is for future investigation to solve.

¹ C. Craig and H. Fairley (*Lancet*, September 28, 1918, p. 386) view the Weil-Felix phenomenon in the light of a group agglutination; the virus of typhus being probably an organism allied to *B. proteus* X19, but resistant to cultivation on ordinary media.

² Ch. Nicolle and Ch. Lebailly. *Comptes rendus*, 1919, clxviii, p. 800.