THE WEIL-FELIX REACTION IN FEVERS OF UNCERTAIN ORIGIN.

By Major C. R. Christian,
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It is now a well-established fact that the Weil-Felix reaction is often positive in Indian "tick" typhus and it has been stated that the "O" agglutination in this reaction is completely specific and that a titre of 1:200, representing a definite rise, is diagnostic of this disease. The following two cases therefore become of interest.

Bareilly, United Province, is one of the endemic foci of Indian typhus and there had been several typical cases with positive Weil-Felix reactions and rash, etc., in 1932 and 1933. Following on these cases, Private R. was admitted to hospital on May 2, 1933, suffering from headache and vomiting. There was no definite rigor. The spleen was just palpable, but not tender. The eyes were somewhat injected. Temperature 102.8° F. and pulse 100. Examination otherwise negative. Previous history: patient had been in Bareilly just over three years. His medical history sheet showed admissions for malaria and syphilis. He had received a first and second inoculation with T.A.B. vaccine. He had had typhoid fever nine years previously. There was no history of typhus.

There was a continuous fever for nine days with a maximum of 104.4° F. on two occasions with corresponding pulse of 88 and 90. Blood films were negative to malaria daily during the first six days of fever. The tongue became covered with thick, greyish brown fur, and the patient was markedly constipated, requiring enemata, and repeated castor oil and liquid paraffin. Blood-cultures on fourth and seventh days were sterile. Urine cultures on fifth, seventh and tenth days were sterile. Chemical examination of the urine revealed nothing abnormal; no deposit. White blood cell count on fifth day gave 6,825; polymorphs 50 per cent, lymphocytes 42 per cent, large mononuclears 7 per cent. There was no trace of rash at any time, and the temperature remained normal after the tenth day, falling by lysis. Spleen was impalpable at end of the fever. There were no tender glands. Quinine was given from 11 p.m. on the fifth day, rather as a diagnostic test, but this was considered to be negative. No other signs or symptoms developed and the initial vomiting was not repeated. As there had previously been several of these vague P.U.O. cases in Bareilly giving a mildly positive Widal test (a rise of 200 or 300 per cent in one or other of the "H" agglutinins), but not feeling at all certain that they were cases of "enteric group," it was determined on this occasion to carry out Weil-Felix tests in addition to the Widals, as the Weil-Felix reaction is stated to be negative in true enteric group cases. The results are given as follows:—
Weil-Felix Reaction in Fevers of Uncertain Origin

<table>
<thead>
<tr>
<th>Day of Disease</th>
<th>4</th>
<th>7</th>
<th>11</th>
<th>13</th>
<th>19</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weil-Felix</strong></td>
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<tr>
<td>&quot;0&quot;</td>
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<td></td>
</tr>
<tr>
<td>X19</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>44</td>
<td>25</td>
</tr>
<tr>
<td>X2</td>
<td>32</td>
<td>19</td>
<td>170</td>
<td>367</td>
<td>282</td>
</tr>
<tr>
<td>XK</td>
<td>64</td>
<td>64</td>
<td>220</td>
<td>367</td>
<td>367</td>
</tr>
<tr>
<td><strong>Widal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T.</td>
<td>28</td>
<td>21</td>
<td>42</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>A.</td>
<td>28</td>
<td>16</td>
<td>48</td>
<td>48</td>
<td>35</td>
</tr>
<tr>
<td>B.</td>
<td>56</td>
<td>71</td>
<td>148</td>
<td>195</td>
<td>133</td>
</tr>
<tr>
<td>T. &quot;0&quot;</td>
<td>0</td>
<td>0</td>
<td>19</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

It must be remembered that the Widal test is often positive in cases of true typhus, whether louse-borne or tick-borne.

A second case of P.U.O. was investigated during this month. Private H. was admitted to hospital on May 6, 1933, suffering from headache, general pains and slight cough (no sputum). No vomiting or definite rigor. Spleen normal. Physical examination negative. Tongue clean. Urine normal (no albumin, deposit, etc.). Temperature 102.4° F., pulse 104. Previous history: He had been in Bareilly for one and a half years. No previous history of malaria, or of enteric group or typhus. T.A.B./2 inoculation, on March 18, and March 27, 1933.

There was fever for nine days, which was remittent and actually touched normal (98° F.) once on the morning of the seventh day, but did not again become normal until the tenth day, after which there was no relapse. Highest temperature 104.8° F., with corresponding pulse of 88. As with Private R. the pulse remained slow throughout considering the temperature. The bowels were always regular and the tongue developed only a slight fur. Spleen remained normal. Six blood films taken during the first five days were negative to malaria. Quinine, however, was given three times daily from midday of the third day, but there was definitely no response (in this and the previous case quinine hydrochloride in solution 10 grains t.d.s. was used and repeated urine tests for quinine were always strongly positive). No trace of rash at any time. Eyes not injected. No tender glands. Urine examined daily was normal; no deposit; no urobilin. Physical examination remained negative throughout and no fresh symptoms developed. Blood-cultures on sixth and ninth days were sterile. Urine cultures sterile on eighth and ninth days. Repeated stool cultures after the eighth day, but no "E" group found. Total white blood cells 8,150 on ninth day. Widal and Weil-Felix reactions were as follows:—

<table>
<thead>
<tr>
<th>Day of Disease</th>
<th>6</th>
<th>19</th>
<th>13</th>
<th>17</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weil-Felix</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;0&quot;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X19</td>
<td>22</td>
<td>44</td>
<td>44</td>
<td>32</td>
</tr>
<tr>
<td>X2</td>
<td>19</td>
<td>170</td>
<td>170</td>
<td>170</td>
</tr>
<tr>
<td>XK</td>
<td>38</td>
<td>282</td>
<td>282</td>
<td>192</td>
</tr>
<tr>
<td><strong>Widal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T.</td>
<td>48</td>
<td>375</td>
<td>187</td>
<td>110</td>
</tr>
<tr>
<td>A.</td>
<td>63</td>
<td>37</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>B.</td>
<td>143</td>
<td>66</td>
<td>72</td>
<td>85</td>
</tr>
<tr>
<td>T. &quot;0&quot;</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
The Widal T., A. and B. figures in these cases represent standard agglutinin units and the Weil-Felix and T. "O" figures were calculated by the reduction table from the actual results of the tests to represent that degree of dilution of the patient's serum which would have produced standard agglutination of the suspensions used. The Weil-Felix suspensions used were of the concentrated "O" type, one drop only being added to each tube.

From these results the question arises: Have these P.U.O. cases any relationship to tropical typhus and do they represent an intermediate degree between the masked or symptomless typhus ("typhus inapparente" of Nicolle and Lebailly) which occurs occasionally in guinea-pigs and other animals, and the typical severe typhus which occurs in man?

Both cases mentioned were mild. In this connexion it is believed that still milder and undiagnosed cases may occur among the children in an endemic area, and these patients might constitute the reservoir of the disease. This is rendered more probable by the fact that the virus is known to persist in the blood for some time after the end of the fever. The marked and selective rise in the Widal figures would appear to be something more than a merely febrile increase and may indicate antigenic relationship between the enteric group and typhus. The standard agglutinating "T.," "A." and "B." sera however gave entirely negative Weil-Felix results. No true cases of enteric group were available for Weil-Felix tests.

For comparison with the above the following cases occurring in Bareilly are briefly mentioned:

(1) Mrs. S., was admitted to hospital late in 1932. A typical case of tropical typhus with marked petechial rash, injected conjunctive, etc. Fever about two weeks' duration. Two blood cultures sterile. White blood cells 8,000, polymorphs. 60 per cent. Kingsbury and Muktesar "O" suspensions gave a maximum titre of 1:175 in the Weil-Felix reaction.

(2) Private D., was admitted to hospital on March 16, 1933. A case of severe typical typhus with petechial rash, injected conjunctive, etc. No previous history of typhus or enteric group. T.A.B. inoculations April 17 and 27, 1931, and February 2 and 12, 1932.

Initial symptoms were headache, general pains and shivering. Thereafter the case was characterized by marked constipation, raw red tongue, definite lethargy, occasional delirium, insomnia followed by somnolence, and moderate bronchitis. Continuous fever seventeen days. Pulse varied from 94 to 126, and occasional attacks of severe tachycardia necessitating stimulants occurred. Temperature varied from 100° to 104° F.

The following were the investigations. Repeated blood films taken daily were negative to malaria. Therapeutic test of quinine had no effect (urine on being tested gave quinine +). General examination of urine normal; no deposit. Blood cultures sterile on fourth and sixth days. White blood cell count on fourth day 14,200 (polymorphs. 76 per cent) and
fifteenth day 12,450. Repeated stool cultures were negative to "E" group. Urine cultures sterile. Wassermann test was then negative on the fourteenth day. Sputum negative to T.B. As there were several mild relapses of fever (99° to 100° F.) the chest was X-rayed with negative result. Weil-Felix and Widal tests:

<table>
<thead>
<tr>
<th>Day of Disease</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>25</th>
<th>59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weil-Felix: &quot;O&quot;</td>
<td>17</td>
<td>17</td>
<td>145</td>
<td>170</td>
<td>192</td>
<td>85</td>
<td>64</td>
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<tr>
<td>X19</td>
<td>17</td>
<td>17</td>
<td>145</td>
<td>170</td>
<td>192</td>
<td>85</td>
<td>64</td>
</tr>
<tr>
<td>X 2</td>
<td>64</td>
<td>64</td>
<td>282</td>
<td>282</td>
<td>282</td>
<td>170</td>
<td>141</td>
</tr>
<tr>
<td>XK</td>
<td>73</td>
<td>183</td>
<td>192</td>
<td>322</td>
<td>322</td>
<td>250</td>
<td>44</td>
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<tr>
<td>Widal:</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>T.</td>
<td>71</td>
<td>71</td>
<td>71</td>
<td>63</td>
<td>80</td>
<td>75</td>
<td>43</td>
</tr>
<tr>
<td>A.</td>
<td>19</td>
<td>38</td>
<td>48</td>
<td>64</td>
<td>64</td>
<td>64</td>
<td>35</td>
</tr>
<tr>
<td>B.</td>
<td>36</td>
<td>72</td>
<td>333</td>
<td>717</td>
<td>427</td>
<td>286</td>
<td>33</td>
</tr>
<tr>
<td>T. &quot;O&quot;</td>
<td>69</td>
<td>84</td>
<td>96</td>
<td>110</td>
<td>74</td>
<td>73</td>
<td>17</td>
</tr>
</tbody>
</table>

A guinea-pig was injected intraperitoneally on the sixth day of fever with 6 cubic centimetres of the patient's blood, with negative result as regards fever or symptoms. On the twenty-second day after injection this guinea-pig's serum was tested for the Weil-Felix reaction, and also two control animals, with the following results:

<table>
<thead>
<tr>
<th>Experimental guinea-pig</th>
<th>X19</th>
<th>X2</th>
<th>XK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control 1</td>
<td>0</td>
<td>17</td>
<td>73</td>
</tr>
<tr>
<td>Control 2</td>
<td>0</td>
<td>0</td>
<td>38</td>
</tr>
<tr>
<td>Control 2</td>
<td>0</td>
<td>28</td>
<td>37</td>
</tr>
</tbody>
</table>

All three gave a completely negative Widal.

It will be noticed that this definite case of tropical typhus gave lower Weil-Felix figures than Private R. and not much higher than Private H.; also that a rise in Widal "B" figures occurred here and with Private R.

(3) Sepoy S. S. Admitted to hospital on April 9, 1933. Typical typhus with petechial rash, injected conjunctivae, tender and just palpable glands in the neck, axillary and inguinal regions. No previous history of typhus or enteric group. T.A.B./2 inoculation on September 13 to 23, 1932.

Initial symptoms were shivering and frontal headache, with temperature 103°-4° F. on second day. Thereafter continuous fever 100° to 101° F. until the fifth day followed by intermittent fever 98° to 100° F. from sixth until thirteenth day. Physical examination otherwise negative. The case was generally mild.

Investigations: Repeated blood films were negative to malaria. White blood cells, second day 12,000; ninth day 6,875; seventeenth day 7,187. Blood culture sterile tenth day; urine cultures sterile during convalescence. Serum tests as follows:
This case of typhus shows lower Weil-Felix results than Private R. or H. and gives a Widal rise of "T" similar to Private H. (Note.—In the cases of Privates R., H. and D. and Sepoy S. S. the same bottles of Weil-Felix "0" suspension were used and the technique was exactly the same in each case.)

(4) Sepoy R. S. Previous history—nothing relevant. T.A.B./2 inoculation February 16 to 26, 1933. Onset of fever May 26, 1934. A case of tropical typhus with petechial rash, eyes somewhat injected. Twenty-three days continuous fever, temperature 101°F to 103°F, pulse 80 to 88, definite insomnia and constipation. Tongue moderately furred at first but became clean as the fever progressed. Mild bronchitis. Physical examination otherwise negative.

White blood cells 4,320 on the fifth day (polymorphs. 71 per cent); two blood cultures during fever were sterile and one contaminated (staphylococci). Blood films were negative to malaria; no T.B. found in sputum; stool cultures negative to "E" group. Blood serum was sent to the laboratory at about four-day intervals with the following results:

<table>
<thead>
<tr>
<th>No. of Test</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
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<tbody>
<tr>
<td><strong>Weil-Felix</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>&quot;O&quot;</td>
<td></td>
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<td></td>
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<tr>
<td>X19</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
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<tr>
<td>X2</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>XK</td>
<td>-</td>
<td>-</td>
<td>3,500</td>
<td>10,000</td>
</tr>
<tr>
<td><strong>Widal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A.</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B.</td>
<td>30</td>
<td>32</td>
<td>45</td>
<td>80</td>
</tr>
<tr>
<td>T. &quot;O&quot;</td>
<td>17</td>
<td>20</td>
<td>20</td>
<td>0</td>
</tr>
</tbody>
</table>

The concentrated "0" XK suspension was used here as in the other cases (except Mrs. S.) and the technique was exactly the same. It will be seen, therefore, that in typhus the Weil-Felix results vary greatly.

My thanks are due to Major E. A. Sutton, M.C., R.A.M.C., Officer Commanding British Military Hospital, Bareilly, for kind permission to forward the notes of the British cases.