Joseph E. McDade and Charles L. Wiseman, Jr. Studies of proposed extrahuman reservoirs of epidemic typhus. The results of studies in Africa during the 1950's and 1960's (6-11, 24-27) indicated that man might not be the sole reservoir of epidemic typhus rickettsiae. The hypothesis that domestic animals and their ticks constitute a second cycle of epidemic typhus infection (25) emanated from studies in Ethiopia in which Reiss-Gutfreund found typhus antibodies in the sera of Ethiopian livestock (25), and reportedly isolated epidemic typhus rickettsiae from Ethiopian ticks (21, 24-27). Following these initial reports, other investigators began looking for typhus antibodies in the sera of domestic and wild animals or for typhus rickettsiae in ticks with variable...
degrees of success (1, 5, 12, 13, 14, 15, 17, 22, 23, 29), while on the other hand, those attempting to experimentally reproduce the proposed extrahuman cycle (3, 18, 19, 28) were generally unsuccessful. We recently conducted studies in one suspected focus of extrahuman typhus infection (Egypt), hoping to determine reasons for these apparently contradictory findings.

Our initial experimental approach was to screen Ethiopian and Egyptian domestic animal sera for typhus antibodies. Ethiopian livestock sera, collected between 1968 and 1971, were obtained from the serum bank of the Research Detachment of the U.S. Naval Medical Research Unit, No. 3 at Addis Ababa, Ethiopia, and Egyptian animal sera collected both from abattoirs and rural areas of Egypt during 1971 and 1972. Both collections were tested by standardized complement-fixation (CF) tests (20) with typhus antigens.

The survey of Ethiopian sera (Table 1) indicated that Ethiopian cows probably do not constitute a major reservoir of typhus rickettsiae as some suspected (27), since not a single animal among 768 bovines tested was confirmed positive for typhus antibodies. Our survey of other Ethiopian livestock was limited, and thus we cannot make definite conclusions about the occurrence of typhus antibodies in other Ethiopian animals.

The results of our serologic studies in Egypt were similar (Table 2). We tested 1,933 Egyptian animal sera and found 66 presumptive positives at titers ranging from 1:4 to 1:32. All but nine were negative in tests with specific antigens. The nine sera gave uninterpretable patterns in CF tests since all were slightly anticomplementary, and each serum reacted to about the same low titer with both epidemic and murine typhus-specific antigens. Thus, of nearly 2,000 Egyptian animal sera and more than 800 Ethiopian livestock serum samples, we did not find a single confirmable positive for either epidemic or murine typhus by CF tests.

We were surprised to find that all but one of the 683 Egyptian donkey sera were anticomplementary (AC) in complement-fixation tests (Table 2), in marked contrast to previous reports (13, 14, 15) in which as many as 70 per cent of donkeys reportedly were positive for typhus antibodies. We tried selectively to remove the AC substance by treating donkey sera with CO2 as described by Imam (16), but we were unsuccessful since reactivity against typhus antigens was removed at the same rate as anticomplementary activity.

We purified the anticomplementary factor from donkey serum by: removing beta-lipoprotein by precipitation with dextran sulfate (30), recovering globulins by three cycles of ammonium sulfate precipitation, and fractionating the globulins by Sephadex G-200 chromatography. All anticomplementary activity was found in the macroglobulin fraction, which contained one immunoelectrophoretically indentifiable component. The

<table>
<thead>
<tr>
<th>Type of serum</th>
<th>No. Tested</th>
<th>No. presumptively positive</th>
<th>No. Negative</th>
<th>No. anticomplementary</th>
<th>No. Confirmed Positives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine</td>
<td>768</td>
<td>10</td>
<td>608</td>
<td>150</td>
<td>0</td>
</tr>
<tr>
<td>Equine</td>
<td>26</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Ovine</td>
<td>44</td>
<td>5</td>
<td>21</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Caprine</td>
<td>8</td>
<td>0</td>
<td>7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Porcine</td>
<td>15</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Totals</td>
<td>861</td>
<td>19</td>
<td>660</td>
<td>182</td>
<td>0</td>
</tr>
</tbody>
</table>
isolated factor reacted only with specific anti-
equine IgM antiserum in gel-diffusion tests, and thus we conclude that the anticomple-
mentary substance in donkey serum is IgM. By immuno- 
electrophoretic and gel-diffusion 
tests we were also able to show that the only 
donkey serum that was not anticomple-
mentary contained greatly reduced amounts of 
IgM, which explained why it lacked AC 
activity and also confirmed the identity of the 
AC factor as IgM.

In more recent studies, we attempted to 
isoitate rickettsiae from various Egyptian 
ticks, but we were not successful. Ticks from 

Table 3. Summary of survey of Egyptian livestock 
ticks for rickettsiae.

<table>
<thead>
<tr>
<th>Kind of tick</th>
<th>Males</th>
<th>Females</th>
<th>Nymphs</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Hyalomma dromedari</em></td>
<td>46</td>
<td>187</td>
<td></td>
<td>Camels</td>
</tr>
<tr>
<td><em>H. anatolicum excavatum</em></td>
<td>12</td>
<td>33</td>
<td></td>
<td>Camels</td>
</tr>
<tr>
<td><em>H. anatolicum excavatum</em> subsp.</td>
<td>25</td>
<td>45</td>
<td></td>
<td>Cows</td>
</tr>
<tr>
<td><em>H. impeltatum</em></td>
<td>1</td>
<td></td>
<td></td>
<td>Camels</td>
</tr>
<tr>
<td><em>Hyalomma sp.</em></td>
<td>138</td>
<td>221</td>
<td></td>
<td>Camels</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td>63</td>
<td></td>
<td>Buffalos</td>
</tr>
<tr>
<td></td>
<td>69</td>
<td>41</td>
<td></td>
<td>Cows</td>
</tr>
<tr>
<td><em>Boophilus annulatus</em></td>
<td>16</td>
<td>80</td>
<td></td>
<td>Cows</td>
</tr>
<tr>
<td><em>Boophilus sp.</em></td>
<td>8</td>
<td></td>
<td></td>
<td>Buffalos</td>
</tr>
<tr>
<td><em>Rhipacephalus s. sanguines</em></td>
<td>130</td>
<td>152</td>
<td></td>
<td>Dogs</td>
</tr>
<tr>
<td><em>Ornithodoros erraticus</em></td>
<td>55</td>
<td>50</td>
<td>55</td>
<td>Rat (Arvicanthus) burrow</td>
</tr>
<tr>
<td><em>O. savigny</em></td>
<td>100</td>
<td>145</td>
<td>100</td>
<td>Sheep grazing ground</td>
</tr>
<tr>
<td>Totals</td>
<td>629</td>
<td>1,028</td>
<td>155</td>
<td></td>
</tr>
</tbody>
</table>

* No rickettsiae discovered in ticks surveyed.
The negative results of our serologic survey of Egyptian and Ethiopian animal sera, together with the negative findings of our search for rickettsiae in Egyptian ticks, lend little support to the hypothesis that domestic animals in Africa are involved in an extrahuman cycle of typhus infection. Our finding that all Egyptian donkey sera are anticomplementary in CF tests indicates that earlier reports of typhus antibodies in Egyptian donkey sera may have been experimental artifacts, and we suggest that most of the serologic evidence for an extrahuman cycle of typhus in Egypt should be reevaluated.

REFERENCES


To emphasize this concept I quote Zuckerman (83), who refers to the classical isolation of a Borrelia from a wild Panamanian monkey (14) and its passage to mice, rats, guinea pigs, other monkeys, and man: “Here then is a disease without very definite boundaries in the mammalian world.” No species name was ever given to the Borrelia involved. A more recent reference to the possible evolution of the epidemic louse-borne form of Borrelia (34) (“The parasite presumably changes its antigenic composition during this hypothetical evolution: its name changes from B. crocidurae to B. duttoni and finally to B. recurrentis in the louse-borne form”) is a gentler way of putting the point.

The real question posed by the title of this contribution is: Can any of the borreliae found in wild hosts and vectors convert to the devastating form transmitted by human lice? Conversely, could that epidemic form return “underground” to the wild reservoirs?

The answer is difficult since much fundamental work was carried out before this century or in its early days and involves translation. Thus, the reader who takes this thesis seriously should read it in conjunction with that of Felsenfeld (27) and his contribution to this Symposium (28).

Progress in achieving an understanding of the probable dynamic nature of the problem stems from the elusive characteristics of the strains of borreliae causing endemic relapsing fever both in man and in their vectors. This spirochete can lurk undetected...