Sleeping sickness alters sleeping times in mice

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The demonstration of central nervous system involvement in mice infected with Trypanosoma brucei has encouraged the use of this animal model of late-stage African trypanosomiasis (Jennings et al., 1977, 1979; Murray & Jennings, 1983). We have used this model within our laboratory for studying prospective trypanocides and here describe the results of a preliminary examination of the effect of the disease on two simple indicators of the status of drug metabolism, pentobarbitone sleeping time and the duration of zoxazolamine-induced paralysis.

Female mice, CFLP strain with body weight 30-35 g, were inoculated intraperitoneally with 10⁵ trypanosomes of strain TRUC 34000, obtained originally from Dr. R. W. F. Lepage, University of Cambridge. Control mice were infected with the same volume of isotonic saline. At 5, 10, 15 and 20 days after inoculation, pentobarbitone-induced sleeping time and zoxazolamine-induced paralysis time were each measured for groups of five infected mice and five control mice. Sodium pentobarbitone solution (6 mg/ml) was prepared for intraperitoneal injection by dilution of Sagatal (May and Baker, Dagenham, Essex, U.K.) and administered at a dose level of 60 mg/kg. Zoxazolamine was dissolved in the minimum quantity of 1 M-HCl and diluted to 10 mg/ml for intraperitoneal injection at a dose level of 100 mg/kg. Sleeping time and paralysis time ceased when an animal could assume normal posture twice within 10 s. Mice examined 20 days after infection were subsequently killed by exposure to diethyl ether and the livers removed and weighed.

During 20 days after inoculation with T. brucei, sleeping times and duration of paralysis were each longer in infected mice than in control animals. The differences between infected and control mice were more obvious at 5 days and 10 days after infection, although some mice dosed with pentobarbitone at 15 days or 20 days after inoculation failed to regain consciousness. The duration of sleeping time or paralysis is given for individual animals in Table 1 and shows variation within as well as between treatment groups. In mice examined 20 days after infection, a liver weight equivalent to a mean of 8.7 ± 0.7% (s.d.) of body weight was recorded; for control mice, liver weight corresponded to 5.5 ± 0.3% (s.d.) of body weight. There was no significant difference in body weights [infected mice, 41 ± 3 g (s.d.); control mice, 39 ± 3 g (s.d.)].

The changes in zoxazolamine-induced paralysis time and in phenobarbitone hypnosis reported here possibly reflect altered rates of hydroxylation of aromatic and aliphatic compounds within the liver. Changes in hepatic mixed-function oxidase activity have previously been reported for laboratory rodents acutely infected with trypanosomiasis (Shertzer et al., 1981; Emerole et al., 1983). Shertzer et al. (1982) demonstrated hepatic microsomal alterations during chronic trypanosomiasis in the field vole, Microtus montanus, where a chronic infection has been evaluated as a model for human trypanosomiasis (Seed & Hall, 1980).


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Table 1. Pentobarbitone-induced sleeping time and zoxazolamine-induced paralysis in mice during infection with T. brucei

<table>
<thead>
<tr>
<th>Day no.</th>
<th>Pentobarbitone sleeping time (min)</th>
<th>Zoxazolamine paralysis time (min)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Infected</td>
</tr>
<tr>
<td>5</td>
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<td>20</td>
<td>45, 50, 54, 60, 68</td>
<td>57, 63, 74, 80, *</td>
</tr>
</tbody>
</table>

*Animal did not recover consciousness.