healed and the Wassermann became negative. However, none of the three control rabbits relapsed during a similar period of observation.

(c) Lymph node transfers. Lymph node transfers from three of the five treated rabbits were positive in two instances and negative in 1 case. Transfers from the three control animals were all positive. Mercuric salicylate, therefore,
FIG. 1. Cat, ether; brain and medulla destroyed. Artificial respiration. Carotid blood pressure. Time in ten seconds. Duration of ephedrine action twenty-three minutes, of adrenalin action 4 minutes. Note the longer action of ephedrine in these doses and compare with figure 3.

FIG. 2. Same as figure 1. Carotid blood pressure. Time in ten seconds. Adrenalin and ephedrine after 7 mgm. ergotamine. Note reversal of both; note also the rise followed by fall of blood pressure on increasing the dose of ephedrine (approximately five-fold).
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In the case of the pulse rate the maximum action was taken as an increase in rate of 140 per minute and as 320.

The observed and calculated figures show a good agreement in the case of the changes in rate, and a moderate agreement in the case of the changes in blood pressure.

My figures for the rise of blood pressure in cats, which are shown in figure 5 also show a graded response over more than a thousand-fold range of dosage and the observed figures agree fairly well with the curve, which was drawn to the formula

\[ V_{100} \times x = \text{calculated figure} \]

<table>
<thead>
<tr>
<th>Dosage of adrenaline in mgm. per kgm. X 10^6</th>
<th>0.75</th>
<th>2.0</th>
<th>5.0</th>
<th>15</th>
<th>33</th>
<th>75</th>
<th>150</th>
<th>330</th>
<th>660</th>
<th>1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of observations</td>
<td>5</td>
<td>13</td>
<td>11</td>
<td>8</td>
<td>8</td>
<td>10</td>
<td>8</td>
<td>8</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Rise in blood pressure in mm. Hg:</td>
<td>5.6</td>
<td>3.7</td>
<td>10.4</td>
<td>18</td>
<td>28</td>
<td>47</td>
<td>78</td>
<td>129</td>
<td>157</td>
<td>169</td>
</tr>
<tr>
<td>Calculated figure</td>
<td>0.5</td>
<td>1.4</td>
<td>3.5</td>
<td>10</td>
<td>20</td>
<td>42</td>
<td>97</td>
<td>110</td>
<td>149</td>
<td>167</td>
</tr>
<tr>
<td>Increase in pulse rate in beats per minute:</td>
<td>0.6</td>
<td>0.54</td>
<td>4.1</td>
<td>5</td>
<td>14</td>
<td>25</td>
<td>43</td>
<td>67</td>
<td>78</td>
<td>97</td>
</tr>
<tr>
<td>Calculated figure</td>
<td>0.3</td>
<td>0.9</td>
<td>2.2</td>
<td>6.4</td>
<td>12.6</td>
<td>27</td>
<td>62</td>
<td>70</td>
<td>95</td>
<td>107</td>
</tr>
</tbody>
</table>

It is obviously dangerous to lay too much stress on an approximate agreement between a formula and averages of figures which show extensive individual variation.

The formula I have given does, however, provide an explanation for the fact that the intact animal shows a graded response over a remarkably extensive range of doses of adrenaline and it also explains the general shape of the curve obtained when the action is plotted against the dosage.

The agreement shown in Molinelli's figures between the observed and calculated variations in heart rate can be explained on the assumption that the laws governing the reaction between adrenaline and the pacemaker of the heart are the same as those at ASPET Journals on November 11, 2022 jpet.aspetjournals.org Downloaded from ASPET Journals on November 11, 2022 jpet.aspetjournals.org Downloaded from
entirely analogous to those reported by Greenbaum and Harkins (4), who found arsphenamine prophylactically effective at 30 mgm. per kilogram and neoarsphenamine at 45 mgm. per kilogram, when administered twenty-four hours after intratesticular inoculation of the rabbit with the Treponema pallidum. The arsphenamines are likewise excellent sterilizing agents in the actively syphilitic rabbit. On the other hand, the remaining compounds studied showed poor prophylactic powers as well as practically negative sterilizing properties in active syphilis. Therefore, the determination of the prophylactic power of a compound in experimental rabbit syphilis provides a fairly accurate conception of the sterilizing ability of the drug in the active disease. Furthermore, the result is obtained much more quickly than with the lymph node transfer method. The procedure of the determination of prophylactic ability should consequently be considered an addition to the technique employed in the therapeutic study of compounds in experimental rabbit syphilis. This method considerably shortens the time required in indicating the spirocheticidal action of the drug without, however, indicating its property of healing active luetic lesions.

SUMMARY

1. In experimental rabbit syphilis, there is a parallelism between the prophylactic and sterilizing powers of the organic arsenical and mercurial compounds studied.

2. The determination of the prophylactic power of a compound in experimental rabbit syphilis consumes but three months as compared with the minimum of eight months required for gauging the sterilizing power of a drug in this disease by the lymph node transfer method.

3. Because of the parallelism between the prophylactic and sterilizing powers of a compound and the promptness with which the prophylactic power can be ascertained, such a determination should become a part of the accepted technique employed in the evaluation of the therapeutic efficacy of a drug in the treatment of experimental rabbit syphilis.