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, possesses a low order of sterilizing power in experimental rabbit syphilis.

ORGANIC MERCURIAL COMPOUNDS IN SYPHILIS

FIG. 1. THE HEALING POWER OF MERCURIC SALICYLATE IN EXPERIMENTAL RABBIT SYPHILIS

II. FLUMERIN

I. Healing power. The tolerated dose of flumerin administered intravenously to rabbits is 30 mgm. per kilogram (1). Five actively syphilitic rabbits were each given four weekly intravenous injections of flumerin. The first and fourth doses were 7.5
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).

38 F. H. CURTIS

CONTENTS

XVIII. Mercury Diuresis. By Kenneth J. Melville and Raymond L. Stehle. 209
XIX. A Study of the Fate and Toxicity of Bromine and Chlorine Containing Anesthetics. By G. H. W. Lucas. 223

NUMBER 3, NOVEMBER, 1928

XX. The Peripheral Vasomotor Mechanism in Experimental Shock. By Maurice I. Smith. 239
XXI. Studies in Serum Calcium. II. Experimental Tuberculosis—Intrapertoneal Inoculation. By J. C. Hoyle. 259
XXII. The Renal Blood-Flow of the Bird. By O. S. Gibba. 277
XXIII. A New Method of Measuring Blood Flow. By O. S. Gibba. 293
XXIV. The Stimulating Effect of Alcohol and the Depressing Effect of Anesthetics on Sugar Utilization Directly Determined. By W. E. Burge and D. J. Verda. 299
XXV. The Renal Excretion of Chlorides and Water. By A. R. Fee. 305
XXVI. Studies in Serum Calcium. III. Experimental Tuberculosis—Subcutaneous Inoculation. By J. C. Hoyle. 317
XXVII. Thermal Conductivity Methods of Gas Analysis in the Study of Pharmacological Problems. By P. D. Lamson and B. H. Robbins. 325

NUMBER 4, DECEMBER, 1928

XXVIII. Studies in the Pharmacology of Bismuth Salts. V. Tissue Distribution of Bismuth. By Clifford S. Leonard. 333
XXIX. Studies in the Pharmacology of Bismuth Salts. VI. The Permeability of the Placenta to Bismuth. By Clifford S. Leonard and Robert B. Love. 347
XXXI. Clinical and Experimental Studies on Phototherapy in Pernicious Anemia. By David I. Macht and William T. Anderson, Jr. 365
XXXIII. The Pharmacodynamics and Value of Bismuth Subnitrate in Hypertension. By Edward J. Stieglitz. 407
XXXIV. Iso-amyl-ethyl-barbituric Acid (Amytal) as a Laboratory Anesthetic for Cats. By Michael G. Mulinos. 425
XXXV. The Salicylates. XVII. The Alleged Inefficiency of the Phosphoric Acid-Distillation Method of Estimating Salicylic and Salicylic Acids. By Charles C. Johnson. 437
XXXVI. Index. 445
ILLUSTRATIONS

Action of adrenaline on isometric response of carotid strip (Fig. 1) ........ 2
—— of adrenaline on isometric responses of several carotid strips (Fig. 2) . 3
—— of adrenaline on isotonic contraction of carotid strips (Fig. 3) ... 5
Effect of perfusion with adrenaline on outflow and radius of frog's aorta (Fig. 4) ........................................ 7
Action of adrenaline injections on blood pressure of cat (weight 2 kgrm.) (Fig. 5) .................................................. 9
Healing power of mercuric salicylate in experimental rabbit syphilis (Fig. 1) . 25
—— of flumerin in experimental rabbit syphilis (Fig. 2) ............. 26
—— of the sodium salt of 1-mercuri-bis-3-nitro-naphthalene-8-carboxylic acid (drug 93) in experimental rabbit syphilis (Fig. 3) .. 27
Electromotive action of drugs as a cause of their toxicity (Fig. 1) .......... 31
Reversal by ergotamine of the effect of ephedrine on the blood pressure (Figs. 1 and 2) ........................................ 38
—— by ergotamine of the effect of ephedrine on the blood pressure (Figs. 3 and 4) ............................................. 39
Studies on the toxicitv of various lead compounds given intravenously (Figs 1 to 6) .............................................. 102
Curve showing the average rate of decrease in the response to the respiratory impulses of the intact diaphragmatic muscle, in six dogs, due to the peripheral action of Nicotin. (Dose, 15 mgm. per kilogram) (Fig. 1) .... 119
Records showing the effect of experimental procedures on the contractions which persisted in the excised diaphragmatic muscle after peripheral paralysis due to nicotin had occurred elsewhere in the animal (Fig. 2) ... 125
Simultaneous records of the contractions of the intact right side and excised left side of the diaphragm, and the blood pressure, in a dog (11 kgrm.) that received 15 mgm. of nicotin per kilogram intravenously (Fig. 3) ... 126
Experiment. February 21, 1928. Dog. Paraldehyde anesthesia (Fig. 1) ... 139
——. February 23, 1928. Dog. Paraldehyde anesthesia (Fig. 2) ........ 140
——. February 23, 1928. Dog. Paraldehyde anesthesia (Fig. 3) ....... 141
Reaction of the liver of a dog to 1.2 cc. epinephrine per liter. July 29, 1924 (Fig. 1) ...................................................... 163
Action of epinephrine (1:500,000) upon the liver of a rabbit. May 24, 1924 (Fig. 2) .......................................................... 163
—— of barium chloride, 0.4 per cent upon the liver of a cat. May 17, 1924 (Fig. 3) ............................................................ 164
—— of barium chloride, 0.4 per cent upon the liver of a rabbit. May 23, 1924 (Fig. 4) ............................................................ 164
Velocity of fatality culex quinquefasciatus (Fig. 1) ...................... 180
Hyperglycemic action of epinephrine and of ergotamine (Fig. 1) ......... 199
Combined hyperglycemic action of epinephrine and ergotamine (Fig. 2) ... 200
CONCENTRATION AND ACTION OF ADRENALINE

320. 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

\[ V = 100 \times \frac{1}{X} \]

<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>
</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>
</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>
</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>149</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>
</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>
</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 another place.
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.