Effect of Anti-viral Substances on the Mouse Mammary Tumor Milk Agent in Vivo

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INTRODUCTION

The mouse mammary tumor milk agent, which has been shown to play a principal part in the genesis of some mouse mammary tumors (3), has the physical, chemical, and biological properties of a virus (1, 2, 7). The virus-like nature of the milk agent suggests that it may be inhibited by some of the recently discovered anti-viral substances.

Inactivation of the agent in vivo without injury to the mouse would permit a better understanding of the function of the milk agent in the production of mammary tumors and would help to determine whether or not the virus is necessary as a continuing cause of cancer.

Four viricidal compounds were tested for their effect on the milk agent. The compounds chosen were aureomycin,1 chloramphenicol, and streptomycin, which have been used successfully in experimental and clinical ricketsial and lymphogranuloma venereum infections (10-12, 14, 16), and sodium phenosulfazole (Darvisul) which has been reported (13), though not confirmed (5, 9, 15), as being effective against mouse poliomyelitis virus. In addition, it has been shown that chloramphenicol is effective in inactivating a gene-controlled substance, "Kappa," in Paramecium (4). This is of particular interest, since, as shown by Heston et al. (8), the concept of gene-cytoplasm relationship is strikingly applicable to the mammary tumor problem.

Data presented in Table 1 indicate the effect of these four antibiotics on the mouse mammary tumor milk agent in vivo.

MATERIALS AND METHODS

Two groups of animals were used: Group I, consisting of C3H female mice of the F15 and F16

1 Aureomycin and sodium phenosulfazole were kindly supplied by Lederle Laboratories Division of the American Cyanamid Co., Pearl River, N.Y., and chloramphenicol by Parke, Davis & Co., Detroit, Mich.


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In Group I, litter-mates were used as controls. In Group II, mice born at approximately the same time, though not necessarily litter-mates, were used as controls.

RESULTS AND DISCUSSION

None of the antibiotics tested produced statistically significant differences in the tumor incidence between treated and control mice. Control mice were maintained separately for each antibiotic. In the table, however, the controls are grouped, since they were nearly identical for all groups. Animals which died before 6 months of age were not included in the analysis. In the case of Group II, sodium phenosulfazole-treated animals, where only 11 out of 80 mice have developed tumors had they lived longer.

The difference of the mean is, therefore, 3.7 ± 1.22, where P < 0.01. This places the difference on the border line of significance. Since the streptomycin-treated and control mice in Group I show no significant difference in mean tumor age, the effect noted in Group II may represent a sampling error. Further study is perhaps indicated, however, since this may suggest an "activating effect" of streptomycin on the milk agent. A similar phenomenon has been previously noted on T. pallidum (6).

These results would indicate that the milk agent was not affected by aureomycin, chloramphenicol, or sodium phenosulfazole, when exposed to them in the manner described, and that streptomycin was without effect, except possibly in shortening the mean tumor age in C mice.

TABLE 1
THE EFFECT OF ANTI-VIRAL SUBSTANCES ON THE MAMMARY TUMOR INCIDENCE AND MEAN TUMOR AGE IN STRAIN C AND CSH MICE

<table>
<thead>
<tr>
<th>GROUP</th>
<th>ANTIBIOTIC TREATED</th>
<th>DOSAGE</th>
<th>No. of Mouse Strain CSH</th>
<th>Total</th>
<th>No. of Tumors</th>
<th>Per cent</th>
<th>Mean Age at Death Non-Tumorous (months)</th>
<th>Mean Age at Death Tumorous (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Aureomycin</td>
<td>2x0.5 mg.</td>
<td>7 mg.</td>
<td>20</td>
<td>20</td>
<td>100</td>
<td>18.5 ±1.22</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Streptomycin</td>
<td>2x3,000 units</td>
<td>42,000 units</td>
<td>20</td>
<td>19</td>
<td>100</td>
<td>18.2 ±1.09</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Sodium phenosulfazole</td>
<td>6x4.0 mg.</td>
<td>168 mg.</td>
<td>20</td>
<td>20</td>
<td>100</td>
<td>9.7 ±0.25</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td>71</td>
<td>71</td>
<td>100</td>
<td>10.0 ±1.50</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Aureomycin</td>
<td>2x0.5 mg.</td>
<td>7 mg.</td>
<td>51</td>
<td>17</td>
<td>55</td>
<td>14.7 ±2.05</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Streptomycin</td>
<td>2x3,000 units</td>
<td>42,000 units</td>
<td>22</td>
<td>15</td>
<td>47</td>
<td>18.3 ±2.05</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Sodium phenosulfazole</td>
<td>6x4.0 mg.</td>
<td>168 mg.</td>
<td>20</td>
<td>10</td>
<td>50</td>
<td>11.0 ±1.50</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td>79</td>
<td>56</td>
<td>45</td>
<td>12.7 ±2.05</td>
<td></td>
</tr>
</tbody>
</table>

SUMMARY

The effect of several anti-viral agents was studied in CSH mice containing the mammary tumor milk agent and in strain C mice given the agent during the course of treatment.

Aureomycin, chloramphenicol, and sodium phenosulfazole (Darvisul), when used in maximum tolerated doses, did not affect the tumor-producing properties of the milk agent.

Streptomycin did not influence the incidence of mammary tumors in the strains studied, but the mean tumor age was lowered in C mice given the mammary tumor milk agent.

REFERENCES

3. BITTNER, J. J. Some Possible Effects of Nursing on the
Malmgren and Law—Anti-viral Substances and the Milk Agent


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