The Effect of Prior Injections of Tissue Antiserums on the Survival of Cancer Homoiografts in Mice*

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It had been previously noted (2) that prior injections of lyophilized normal and cancerous mouse tissues resulted either in break-down of host resistance, as evidenced by positive takes of tumor grafts, or in enhanced host resistance, evidenced by the failure of tumor takes. Whether enhancement or inhibition occurred was related to the dose of lyophilized tissue injected (1).

In investigations dealing with wound healing, it was found that the process of healing could be accelerated or retarded by dose gradation of tissue antiserum injections, administered immediately after wounding (8, 4).

The investigations reported here are directed to the question of whether the observed experimental alterations in normal tissue growth (wound healing) and cancerous tissue growth (tumor homoiografts) are under the control of common host mechanisms. To this end, a study was made of the effects of prior injections of tissue antiserums on the growth of cancer homoiografts in mice.

MATERIALS AND METHODS

The host strain of mice used was C57 black/6Ks. These were divided equally according to sex and were 2–3 months old at the start of the experiments. The transplantable tumors used were Sarcoma I and 15091a, both indigenous to the inbred A strain of mice. Sarcoma I is composed of dense sheets of spindle-shaped polyhedral cells. Tumor 15091a is an anaplastic carcinoma, predominantly spindle-celled. Both tumors grow rapidly in 100 per cent of strain A mice. Occasionally, they grow progressively in a C57 black mouse (about 1 in 300).

Antiserums to tissues from strain A mice were produced in rabbits and in C57 black/6Ks mice.

Received for publication September 26, 1951.
### TABLE 1

**PROTOCOL OF INJECTIONS OF ANTISERUMS INTO C57 BLACK/6KS MICE***

<table>
<thead>
<tr>
<th>Mouse group no.</th>
<th>Type of substance injected</th>
<th>Amount per injection (mg. dry wt.)</th>
<th>Total amt. (mg.)</th>
<th>Tumor graft</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Experiment 1:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Rabbit immune serum‡</td>
<td>10</td>
<td>50</td>
<td>Tumor 15091a</td>
</tr>
<tr>
<td>2</td>
<td>Rabbit normal serum†</td>
<td>10</td>
<td>50</td>
<td>&quot;</td>
</tr>
<tr>
<td>3</td>
<td>Distilled water</td>
<td>(0.5 ml.)</td>
<td>(2.5 ml.)</td>
<td>&quot;</td>
</tr>
<tr>
<td>4</td>
<td>Uninjected</td>
<td></td>
<td></td>
<td>&quot;</td>
</tr>
<tr>
<td>5</td>
<td>Lyophilized tumor 15091a</td>
<td>10</td>
<td>50</td>
<td>&quot;</td>
</tr>
<tr>
<td>6</td>
<td>Rabbit immune serum‡</td>
<td>20</td>
<td>100</td>
<td>Sarcoma I</td>
</tr>
<tr>
<td>7</td>
<td>Rabbit normal serum†</td>
<td>20</td>
<td>100</td>
<td>&quot;</td>
</tr>
<tr>
<td>8</td>
<td>Lyophilized Sarcoma I</td>
<td>5</td>
<td>25</td>
<td>&quot;</td>
</tr>
<tr>
<td><strong>Experiment 2:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Mouse immune serum‡</td>
<td>10</td>
<td>50</td>
<td>Sarcoma I</td>
</tr>
<tr>
<td>2</td>
<td>Mouse normal serum†</td>
<td>20</td>
<td>100</td>
<td>&quot;</td>
</tr>
<tr>
<td>3</td>
<td>Uninjected</td>
<td></td>
<td></td>
<td>&quot;</td>
</tr>
</tbody>
</table>

* Live tumor was inoculated subcutaneously 1 week after the last injection of antiserum. The tumor graft used is shown in the last column.

† Volume for each injection 0.5 ml.; 5 injections over 2-week period.

‡ Immune serum was produced in rabbits or mice, as indicated, to mixed-tissue antigens of strain A mouse spleen, kidney, and tumor 15091a. Normal serum from same rabbits or mice before they were immunized.

§ Immune serum produced in C57 black/6Ks mice.

### TABLE 2

**THE EFFECT OF PRIOR INJECTIONS OF RABBIT AND MOUSE IMMUNE SERUMS AGAINST STRAIN A MOUSE TISSUES ON THE GROWTH OF HOMOIOGRAFTS OF TUMOR 15091a AND SARCOMA I IN C57 BLACK/6KS MICE***

<table>
<thead>
<tr>
<th>Substance injected</th>
<th>Total amt. per mouse (mg. dry wt.)</th>
<th>Tumor graft used</th>
<th>C57 black/6Ks hosts dying with tumors†</th>
<th>Growth of graft‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Experiment 1:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Immune serum from:
- Rabbit No. 2‡ No. 3§
- Normal serum from:
  - Rabbit No. 2
  - No. 3
- Lyophilized 15091a
- Distilled water

Immune serum from:
- Rabbit No. 1‡ No. 3§
- Normal serum from:
  - Rabbit No. 1
  - No. 3
- Lyophilized Sarcoma I
- Control (nothing)

**Experiment 2:**

C57 black/6Ks immune serum‡
- 50 Sarcoma I
- 100 Sarcoma I

C57 black/6Ks normal serum
- 50
- 100

Lyophilized Sarcoma I
- 50

Control (nothing)

* Live tumor was inoculated subcutaneously 1 week after the last injection. Tumors were simultaneously grafted in strain A mice as tumor viability controls; 100 per cent died with tumors.

† Numerators indicate numbers dying with tumors; denominators the total animals in the group.

‡ + indicates growth of tumor, followed by complete regression; — indicates no growth of the graft. Number in parentheses gives number of + animals.

§ The hemagglutinin titers of the immune serums were: rabbit No. 1, 1:5120; rabbit No. 2, 1:128; rabbit No. 3, 1:512; mouse immune serum, 1:256.

† The size of these tumors before regression was comparable to those found in the strain A control animals at death.
thereafter. Negative animals were kept for a minimum of 2 months before being classified as “no-take.” Animals with tumors were followed until death.

RESULTS

Table 1 gives the experimental protocol. The findings are given in Table 2.

The data presented in Table 2 clearly show that prior injections of immune antiserums to strain A mouse tissues, whether produced in rabbits or mice, led to partial or complete breakdown of resistance to the tumor homoiografts in a significant number of the C57 black/6Ks hosts. This is shown by the several cases of successful "takes," leading to death of the host, and the large size to which the grafts grew before regressing in a number of the experimental animals. Growth was particularly marked in the animals that had been injected with the immune serum produced in mice. In the control hosts the grafts grew not at all, or grew slightly and regressed rapidly.

The data also indicate that there may be a relationship between the relative strengths of the rabbit antiserums (as indicated by their hemagglutinin titers) and the magnitudes of their effect, as measured by the altered reactions of the hosts to the homoiografts. The decreasing order of effectiveness of the three rabbit immune sera is the same as the relative order of their hemagglutinin titers.

It is of interest that the mouse immune serum, with a relatively low hemagglutinin titer, had a much more marked effect than the rabbit sera. The reason for this is not known.

In the case of the mouse antiserum, the magnitude of the effect appears to parallel the amount injected, in terms of dry weight. If we consider that the hemagglutinin titer is a measure of the amount of antiserum present, then these findings are in accord with the larger effect noted with the higher titer rabbit antiserums.

The effects of the antiserums on host-graft relationships parallel our previously reported results on the effects of lyophilized mouse tissues on tumor homoiografts (2).

SUMMARY

Antiserums were produced in rabbits and C57 black/6Ks mice to mixed antigens of spleen, kidney, and tumor from strain A mice. Prior injections of the antiserums into C57 black/6Ks mice led to marked growth, and some takes, of two strain A tumors. These tumors normally regress in nearly 100 per cent of C57 black/6Ks mice.

REFERENCES

4. ———. Studies in Cellular Growth. II. Effect of Anti-splenic Tissue Serum on Large Experimentally Produced Wounds in Guinea-Pigs. Ibid., pp. 313–16.
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