Mammary Tumors in Mice of Strains C3H and DBA/1 and Their F1 Hybrids*

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SUMMARY

Mice of strain C3H/HeHu, which have a 96.7 per cent incidence of tumors of the mammary glands at a mean age of 8.9 months, were crossed with mice of strain DBA/1 Hu, which have a lower incidence of mammary gland tumors (71.6 per cent) at an older mean age (13.4 months). The reciprocal hybrid females were force-bred and compared with normally bred females of the two parental strains. Tumor incidences were high in both hybrids, approximating that in strain C3H; but in tumor age, the hybrids were unlike, each resembling the maternal strain. Tumors developed at a faster rate in the two groups of mice nursed by strain C3H mothers than in the other two groups nursed by strain DBA/1 mothers. Since the source of the mammary tumor agent was the known variable, it was concluded that the agent from mice of strain C3H was more virulent than that from mice of strain DBA/1.

MATERIALS AND METHODS

Mice were of the two high mammary tumor strains, C3H/HeHu and DBA/1Hu (4). Crosses were made between the two strains, the hybrids with strain C3H mothers (C3H × DBA/1) and those with DBA/1 mothers (DBA/1 × C3H) being raised separately and saved for observation. All hybrids were born between October and June, were kept in the same room, and received the same food and care. They were mated with males of the low tumor strain BALB/c and force-bred by destroying the young soon after birth, thus allowing only short intervals of lactation to intervene between pregnancies. Each female had at least three litters in rapid succession, after which no records were kept, although force-breeding was continued throughout life. Mice were observed weekly for the presence of mammary gland tumors and were killed soon after these were noted. Other mice were killed when moribund; some died tumor-free. All tumors and suspicious nodules in the mammary gland areas were prepared for histological diagnosis. Adenocarcinomas were the only mammary gland tumors included in the tabulations, and no noncancerous mouse dying before the age of 140 days was included.

RESULTS AND DISCUSSION

Table 1 summarizes the observations on tumor incidence and tumor age (the age of the female female...
when the tumor was noted) for females of strains C3H and DBA/1 (normally bred) and their reciprocal F1 hybrids, (C3H × DBA/1) and (DBA/1 × C3H) (force-bred). Mammary tumors were found more frequently and at younger ages in mice of strain C3H than in those of strain DBA/1. In the former, tumors occurred in 96.7 per cent of the females at a mean age of 8.9 months, compared with an incidence of 71.6 per cent at 13.4 months in the latter.

Both groups of hybrids had a tumor incidence of over 90 per cent, approaching that of strain C3H. However, the reciprocal hybrids had their tumors at mean ages closely approximating those of their respective maternal parents; the mean tumor ages of 8.4 months in the (C3H × DBA/1) hybrid females and 12.1 months in the (DBA/1 × C3H) hybrid females were significantly different ("t" = 4.073, P = <0.01). The strain C3H females and the (C3H × DBA/1) hybrid females had all their tumors by the time they were 16 months old; in contrast, 18 per cent of the tumors of the (DBA/1 × C3H) hybrid females and 25 per cent of the tumors of strain DBA/1 females appeared after the mice had reached the age of 16 months. Comparison of the ages at which the different stocks of mice had a tumor incidence of 50 per cent showed two distinct groups: the (C3H × DBA/1) hybrids and the strain C3H females at 7.5 and 8 months, and the (DBA/1 × C3H) hybrids and strain DBA/1 females at 11.5 and 14 months.

Differences in rates of tumor development are shown in Chart 1, where the proportions of total tumors that had developed at bimonthly intervals between the ages of 6 and 26 months are compared. It will be noted that the curves for tumor development are grouped into those for females of strain C3H and (C3H × DBA/1) hybrids, which are almost identical, and those for females of strain DBA/1 and (DBA/1 × C3H) hybrids, which are much alike. It is clear that there were two rates

Differences in tumor development between females of strain C3H and DBA/1 can be attributed in part to their inherited susceptibilities and hormonal patterns, differences in tumor development between the reciprocal hybrid female mouse must be exclusively extrachromosomal. The hybrids were infected with mammary tumor agent from two sources, while all other extrachromosomal factors, such as reproductive performance, were as uniform as is possible with biologic material. It is possible that had the F1 hybrids been observed as virgins, differences in mammary tumor incidence would have resulted as in the reciprocal hybrids (virlgin) between strains C3H and RIII (7). Although force-breeding may have obliterated differences in tumor incidence in the reciprocal

TABLE 1
MAMMARY GLAND TUMORS IN FEMALES OF TWO HIGH-TUMOR STRAINS OF MICE
(NORMALLY BRED) AND THEIR RECIPROCAL F1 HYBRIDS (FORCE-BRED)

<table>
<thead>
<tr>
<th>Stock</th>
<th>No. Observed</th>
<th>No.</th>
<th>Per cent</th>
<th>Age (months)</th>
<th>Died without tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean</td>
<td>S.D.</td>
</tr>
<tr>
<td>(C3H × DBA/1)</td>
<td>39</td>
<td>37</td>
<td>94.9</td>
<td>8.4</td>
<td>1.99</td>
</tr>
<tr>
<td>C3H</td>
<td>92</td>
<td>89</td>
<td>90.7</td>
<td>8.9</td>
<td>2.28</td>
</tr>
<tr>
<td>(DBA/1 × C3H)</td>
<td>29</td>
<td>27</td>
<td>93.1</td>
<td>12.1</td>
<td>5.01</td>
</tr>
<tr>
<td>DBA/1</td>
<td>93</td>
<td>83</td>
<td>71.6</td>
<td>15.4</td>
<td>4.46</td>
</tr>
</tbody>
</table>

Chart 1.—Graphs comparing the percentage of total mammary tumors that had developed at ages between 6 and 26 months in the reciprocal hybrids and the parental stocks.
hybrids between strains CSH and DBA/1, the tumor ages and rates of development differed with the source of the milk ingested. The conclusion that the mammary tumor agent in the milk of strain CSH/HeHu mice is more virulent than that in the milk of strain DBA/1Hu mice appears to be valid on the basis of the data presented.

REFERENCES
Mammary Tumors in Mice of Strains C3H and DBA/1 and Their F$_1$ Hybrids

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