Spontaneous Primary Hepatomas in Mice of Strain C3H

II. The Influence of Breeding on Their Incidence

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Spontaneous primary tumors of the liver were observed in stock laboratory mice as early as 1908 (6). More recently these have been described in the inbred mice of strains CBA (4, 7), C3H (1, 3), C57 (5), and in a subline of C3H (2).

In most of these reports it has been shown that the neoplasms affect preponderantly the males, although Strong, Smith, and Gardner (7) reported that the tumors in the CBA strain were equally divided between the two sexes. Gorer (4), working with CBA mice over 14 months of age, reported an incidence of 48 per cent in males as compared to 7.8 per cent in females. Andervont (1) found that in strain C3H mice more than one year of age 22.5 per cent of the males developed spontaneous liver tumors as compared to 11.7 per cent of the females, the majority of which were nonbreeding. In C3H mice over one year of age we (3) found the neoplasms in 53.33 per cent of breeding males as compared to none in females, the majority of which were breeding. Little, Murray, and Cloudman (5), in observations on strain C57, found 3 epithelial liver tumors in male mice, as compared to 2 in breeding females and none in nonbreeding females. In a subline of strain C3H mice over one year of age, Andervont and McEleney (2) reported primary liver tumors in 26.87 per cent of the males, as compared to 9.95 per cent of the females.

The purpose of this paper is to report further studies on hepatomas in strain C3H mice, particularly in regard to the influence of breeding on the incidence of these growths.

MATERIALS AND METHODS

The parent animals of the mice used in these experiments were obtained from the Jackson Memorial Laboratory, at Bar Harbor, Maine. The methods of breeding and caring for the mice were the same as those outlined in a previous report (3).

One hundred and thirty-three untreated mice over 12 months of age, of which 76 were males and 57 females, were subjected to postmortem examination for this study. Sixty of the males and 47 of the females were breeding, 16 of the males and 10 of the females nonbreeding.

Most of the animals were killed with chloroform when they appeared ill. The remainder died spontaneously and were examined as soon as possible after death. The presence of a liver tumor was determined by gross and microscopic examination in each instance.

RESULTS

Sixteen (27 per cent) of the 60 untreated breeding males developed hepatomas at the average age of 15.5 months, the age range being from 13.4 to 21.9 months. The age average of the 44 animals that did not develop liver tumors was 15.7 months. The average age of all 60 breeding males was 15.6 months (Table I).

Table I: Incidence of Hepatomas in Untreated Breeding and Nonbreeding Male and Female C3H Mice

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>With tumors</td>
<td>Without tumors</td>
</tr>
<tr>
<td></td>
<td>No. of mice</td>
<td>Age range and av. age, mos.</td>
</tr>
<tr>
<td>BREEDING</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With tumors</td>
<td>16</td>
<td>13.4–21.9</td>
</tr>
<tr>
<td>(27%)</td>
<td>Av. 15.5</td>
<td>(73%)</td>
</tr>
<tr>
<td>Without tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6%)</td>
<td>Av. 14.5</td>
<td>(94%)</td>
</tr>
<tr>
<td>With tumors</td>
<td>9</td>
<td>12.2–19.8</td>
</tr>
<tr>
<td>(90%)</td>
<td>Av. 14.4</td>
<td></td>
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<tr>
<td>Without tumors</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>16</td>
<td>13.4–21.9</td>
</tr>
<tr>
<td></td>
<td>Av. 15.5</td>
<td>(73%)</td>
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</table>
One (6 per cent) of the 16 untreated nonbreeding males developed a hepatoma at the age of 14.5 months. The average age of the 15 animals that did not was 17.5 months, the age range being from 12.3 to 20.7 months. The average age of all 16 nonbreeding males was 17.3 months (Table I).

No hepatomas were observed among the 47 untreated breeding females. The average age of the animals in this group was 14.0 months and the age range was from 12.0 to 18.8 months (Table I).

One (10 per cent) of the untreated nonbreeding females developed a hepatoma at the age of 15.8 months. The average age of the 9 animals that did not develop tumors was 14.2 months, the age range being from 12.2 to 19.8 months. The average age of all 10 nonbreeding females was 14.4 months (Table I).

**COMMENT**

In a previous report (3) we pointed out that spontaneous liver tumors develop more frequently in male than in female mice of strain C3H. These observations, however, were made almost exclusively on breeding mice, and we suggested that it would be necessary to study nonbreeding animals before the sex distribution of liver tumors could be determined. In the present studies the incidence of hepatomas was observed in breeding and nonbreeding animals of both sexes, an observation which, to our knowledge, has not previously been made. The division of the animals in this way, as well as the selection of animals above 12 months of age, has made some of the groups rather small, and in such groups our results must be considered as tentative. Our findings suggest, however, that there was a relatively equal incidence of liver tumors in the nonbreeding animals of both sexes, 6 per cent (1 of 16 animals) in the males and 10 per cent (1 of 10 animals) in the females. In breeding animals the incidence of hepatomas was 27 per cent (16 of 60 animals) in the males and zero (none of 47 animals) in the females. Breeding, therefore, favorably influenced the development of tumors in the males and unfavorably influenced the development of tumors in the females. There was no great difference in the average age at which the neoplasms appeared.

**SUMMARY**

1. The incidence of hepatomas was observed in 133 untreated breeding and nonbreeding strain C3H mice.
2. In breeding males the incidence was 27 per cent (16 of 60 animals), as compared to 6 per cent in nonbreeding males (1 of 16 animals).
3. No tumors were found in 47 breeding females, whereas 10 per cent of the 10 nonbreeding females developed them.
4. The small number of animals in some groups makes confirmatory experiments desirable.

**REFERENCES**

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