Further Observations on the Survival Time of Mice Bearing Chemically Induced Fibrosarcomas*

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Recent data have shown that the survival time of mice of the Prunt inbred strain bearing chemically induced fibrosarcomas is influenced by litter seriation (2, 3). It was determined that female mice developing fibrosarcomas with latent periods of less than 100 days lived longer when they belonged to late rather than early litters of the same breeding mice (188 mice) (2). This shift in survival time was not observed in female mice which developed tumors with latent periods between 101 and 200 days (148 mice) (3).

TABLE 1

<table>
<thead>
<tr>
<th>EFFECT OF LITTER SERIATION ON SURVIVAL TIME OF MICE BEARING METHYLCHOLANTHRENE-INDUCED SARCOMAS</th>
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<tr>
<td>LATEST PERIOD</td>
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<td>&lt;100</td>
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<tr>
<td>DIFFERENCE</td>
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To date, similar observations on survival times with chemically induced fibrosarcomas on 556 female mice of the Prunt strain have been made. Of these, 205 developed fibrosarcomas with latent periods of less than 100 days, and 351 developed similar tumors between 101 and 200 days following the subcutaneous injection of 1 mg. of methylcholanthrene dissolved in 0.1 cc. of sesame oil at 60 days of age. These data include the data of the two previous studies on survival time (2, 3). Survival time is determined by the time between the appearance of a definite progressively growing tumor at the site of the injection of methylcholanthrene and the death of the animal. All mice showing nodules which regressed following their appearance are excluded from this analysis. All mice included in the study had tumors at the time of death. Even though the tumor may not have been the exclusive cause of death, it must have contributed to that end. Sections of all tumors were examined histologically.

The data are given in Table 1 and graphically in Chart 1. The number of mice in the late litters (beyond the fifth) is still small. Consequently, in order to make a statistical analysis of trends, data for mice of early litters (the first three) and of later litters (4-11) are grouped together and comparisons made between these two classes for each of the two groups. One group consisted of mice developing fibrosarcomas with latent periods of less than 100 days, and the second group of mice with tumors with latent periods of between 101 and 200 days. Seventy-four mice belonging to litters 1-3, with chemically induced fibrosarcomas of latent periods less than 100 days, lived an average of 69.3 days. This gave a median value of 66.0±2.5 days. The formula for probable error,

\[
P.E. = \frac{\text{QUARTILE DEVIATION FROM MEDIAN}}{\sqrt{n}}
\]

(where n is number of mice), was used to test levels of significance. One hundred and thirty-one female mice belonging to litters 4-11 within the same latent period class (latent period < 100 days) lived, on an average, 92.8 days. This is a median value of 99.0±2.4 days. There is a difference of 33.0±3.4 days between the two groups. This is 9.6×P.E. Thus, there is a significant increase of survival time with female mice belonging to litters 4-11, as compared to female mice belonging to litters 1-3.

In the two groups of female mice developing fibrosarcomas with latent periods between 101 and 200 days, the following values on survival times were obtained: 156 female mice belonging to litters 1-3 showed an average survival time value of 72.7 days. These data include the data of the two previous studies on survival time (2, 3). Survival time is determined by the time between the appearance of a definite progressively growing tumor at the site of the injection of methylcholanthrene and the death of the animal. All mice showing nodules which regressed following their appearance are excluded from this analysis. All mice included in the study had tumors at the time of death. Even though the tumor may not have been the exclusive cause of death, it must have contributed to that end. Sections of all tumors were examined histologically.

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days. This is a median value of 72.0 ± 2.0 days. In the group belonging to litters 4–11, 195 female mice had average survival time values of 70.6 days. This gave a median value of 69.0 ± 1.5 days. The difference between the two groups 72.0 ± 2.0 - 69.0 ± 1.5 is only 3.0 ± 2.5 days, or 1.2 X P.E., which is not significant.

The difference between the two groups of female mice belonging to litters 1–3 (230 mice) is 72.0 ± 2.0 - 66.0 ± 2.5 days or 6.0 ± 3.2 days which is 1.8 X P.E. However, the difference between the two groups of female mice belonging to litters 4–11 (526 mice) is 69.0 ± 2.4 - 69.0 ± 1.5 or 30.0 ± 2.8 days. This is 10.7 X P.E., which is significant.

The present data provide further evidence on the previous conclusion based on smaller numbers that the survival time of female mice bearing chemically induced fibrosarcomas is significantly increased in successive litters—provided the latent period for the appearance of the fibrosarcomas is less than 100 days (2, 3). Why this increased survival time is present in mice of successive litters for the early appearing tumors and not for mice with latent periods between 101 and 200 days is not clear from the available data.

It has been shown in other studies of chemically induced fibrosarcomas (4, 5) that the number of mice developing fibrosarcomas with invasion into the body cavity is gradually reduced in mice of successive litters. It is now clear that this reduction in the invasiveness of fibrosarcomas with litter seriation is not due to changes in the survival time of mice—the mice actually live longer in successive litters with tumors of latent periods of less than 100 days and live as long in successive litters when the latent periods of chemically induced fibrosarcomas is between 101 and 200 days.

Female mice of advanced litters (4–11) differ more in survival time values of chemically induced fibrosarcomas than do female mice belonging to early litters (1–3) (median difference, 30.0 ± 2.8 days, compared to 6.0 ± 3.2 days). This divergence in a biological characteristic is perhaps indicative of a fundamental biologic function whose nature is not yet indicated.

Shimkin (1) reported in 1941 that the mean length of survival of CSH and L strain mice with induced subcutaneous sarcomas was 4.36 ± 0.10 weeks, irrespective of whether the palpable tumors appeared early or late following the injection of the carcinogen. The present data do not confirm this conclusion.

SUMMARY

To date, 556 female mice of the Prunt inbred strain (a) have received subcutaneous injections, at 60 days of age, of 1 mg. of methylcholanthrene dissolved in 0.1 cc. of sesame oil; (b) have developed fibrosarcomas at the site of the injection, and (c) have died. The present study deals with observations on survival time, the time between the appearance of the fibrosarcomas and the death of the mice. Of these mice, 205 developed fibrosarcomas with latent periods of less than 100 days, and 351 with latent periods of between 101 and 200 days. Mice belonging to late litters live longer with chemically induced fibrosarcomas than mice of early litters, provided that the tumors have a latent period of less than 100 days. This increase does not occur when the latent period of tumors is between 101 and 200 days. Thus, female mice of advanced litters (4–11) differ more in survival time values of chemically induced fibrosarcomas than do female mice belonging to early litters (1–3). This divergence in a biological characteristic is indicative of a fundamental biologic function whose nature is not yet indicated but perhaps may be included under the phenomenon of "tissue specificity."

REFERENCES

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