SUMMARY

Two new inbred lines of Syrian hamsters are described in their 13th to 20th and 24th to 34th generations of brother-sister mating. One of the two lines, identified as BIO 4.24, shows a high incidence of adrenal tumors (in about 50% of the animals). The other, BIO 45.5, shows a significantly lower incidence (in about 17% of the animals). Histologically, these were the types of adrenal tumors previously described in this species. In 12 other inbred strains the adrenal tumor incidence averaged 23%. The BIO 4.24 line (high incidence of adrenal tumors) also showed a higher incidence of histological anomalies of sex glands and pituitary which, however, was not related to the adrenal neoplasms. There was also present a high incidence of obesity in females which was not correlated with the observed anomalies of the endocrine system. Genetic factors seem to explain the previously reported highly variable incidence of spontaneous adrenal tumors of hamsters.

INTRODUCTION

Adrenal tumors are not rare in Mesocricetus auratus auratus. From the review of Russfield (11), tumors of the adrenal cortex seem to be one of the most characteristic spontaneous lesions in this species. The frequency of such spontaneous adrenal cortical neoplasms has been variously reported from different colonies as low (1), moderate (2), and high, and more frequent in males than in females (3, 4). The latest review of the subject by Kirkman and Algard (7) also notes that there are contradictions in spontaneous tumor incidences reported from different laboratories. These authors explain this variance in terms of age differences among the animals studied.

This report deals with a description of the adrenal gland in 2 inbred strains of hamsters, BIO (4.24) and BIO (45.5). One (4.24) is characterized by a high incidence (24 of 53 animals) of adrenal tumors, the other (45.5) is characterized by a low incidence (6 of 35 animals) of such tumors. In 12 other inbred strains, from each of which at least 20 animals were histologically studied (from 21 to 45 animals per strain), the incidence of adrenal tumors ranged from 18% (line X.68) to 35% (line 4.22) and averaged 23%. In all lines (except 54.7 and 4.24) the males had more frequent adrenal tumors than the females.

MATERIALS AND METHODS

These observations were derived from part of a study of the aging of Syrian hamsters. In this project, 80 animals (40 males and 40 females) of each of 11 inbred lines of hamsters were kept under standard conditions (a maximum of 5 to a cage, sexes separated) in an air-conditioned animal room. Ab-Sorb-Dri bedding was used; the animals received Old Guilford breeder chow and tap water ad libitum. Every 6 months or at shorter intervals during the latter part of the study, depending on spontaneous mortality, 10 males and 10 females were killed. Complete autopsies were done; the organs were weighed and fixed in formaldehyde. Sections stained with hematoxylin-eosin were made of those organs being studied. In the 2 lines reported here, there were available at the time of this study complete autopsies on 30 males and 23 females of the BIO 4.24 line and 20 males and 15 females of the 45.5 line.

RESULTS

General Characterization of the 2 Strains. The 4.24 line was previously described (5) when inbred for 17 generations. This line has now been inbred for 34 generations. While at the time of our first report females of the 4.24 line were noted as being the “largest” animals among any of the lines studied, it is now evident that there is in this line a high incidence of obesity. The average litter size is still approximately 6.5, the same as at the time of the earlier description. The animals of the 45.5 line are presently inbred by brother-sister mating for 22 generations. The average litter size in this line was 5.5. No striking anomalies have been noted so far in this line.

The mean survival time of 67 animals of the 45.5 strain was 561.6 days (S.D., 238), and that of 79 of the 4.24 animals was 619.7 days (S.D., 117.8). The extreme mean

FEBRUARY 1970
survival times of the other lines studied were from 464 to 711 days.

The BIO 45.5 line is characterized by a cream color and an average body weight and growth curve; the BIO 4.24 line is agouti and has a high incidence of obesity, more marked and more frequent in females than in males.

Characterization of Hamsters Studied. In line 4.24 the animals autopsied for this study represented 24 to 32 generations of inbreeding. There were 20 males and 23 females. The average age of the males was 79.2 weeks (range, 42 to 114 weeks) and of the females, it was 81.35 weeks (range, 28 to 109 weeks). The average body weight of the males was 134 g (range, 83 to 192 g), and of the females, it was 143 g (range, 102 to 210 g). In line 45.5 the animals studied represented the 13th to the 20th generations of inbreeding. There were 20 males and 15 females. The average age of the males was 78.9 weeks (range, 34 to 119 weeks) and of the females, it was 79.3 weeks (range, 36 to 116 weeks). The average body weight in the males was 99 g (range, 74 to 132 g), and in the females it was 100 g (range, 74 to 127 g).

Description of Adrenal Glands. Many more enlarged adrenal glands occur in strain 4.24 than in strain 45.5. Table 1 summarizes the types of lesions observed in the adrenals of the 2 lines. Amyloidosis occurred in about one-third of the adrenals studied (Fig. 1) with roughly equal frequency (26% in line 4.24 and 37% in line 45.5).

Table 1
Incidence of adrenal lesions among animals of 2 inbred strains of hamsters (BIO 4.24 and BIO 45.5)

<table>
<thead>
<tr>
<th>Type of lesion</th>
<th>Lesions observed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Strain 4.24</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>11</td>
</tr>
<tr>
<td>Extracapsular nodules</td>
<td>16</td>
</tr>
<tr>
<td>A-B cell hyperplasia</td>
<td>11</td>
</tr>
<tr>
<td>A-B cell tumors</td>
<td>12</td>
</tr>
<tr>
<td>Cortical nodules</td>
<td>9</td>
</tr>
<tr>
<td>Cortical tumors</td>
<td>1</td>
</tr>
<tr>
<td>Unclassified tumors</td>
<td>8</td>
</tr>
<tr>
<td>Distribution of adrenal tumors</td>
<td>30 adrenal tumors in 24 out of 53 animals</td>
</tr>
</tbody>
</table>

aConsidered as hyperplastic phenomena.
bConsidered as tumors (benign adenomas).

The adrenal morphology observed conformed to previous descriptions in the literature (8–10). The following proliferative lesions were noted: extracapsular nodules, which are rounded masses of cells with the usual characteristics of adrenal cortex encased in connective tissue and lying outside the cortex (Fig. 3); subcapsular nodules composed of 2 types of cells, which in mice have been called A and B cells, the former being long, spindle-shaped cells resembling fibroblasts, the latter, larger plump cells which resemble normal adrenal cortical cells (Figs. 2, 4, 5); cortical nodules composed of only 1 cell type with marked resemblance to normal adrenal cortex. These cortical nodules lie inside the cortex and have no capsule of their own. They are differentiated from the rest of the cortex by a different nuclear cytoplasmic ratio; and unclassified tumors, which are usually large masses of plump, voluminous translucent cells resembling those of the medulla. Studies for the further histochemical characterization of these tumors were not done; differentiation from cortical tumors is not possible with certainty. In a few instances (3 cases) of large tumor masses (in 1 case invading the kidney), it was no longer possible to determine the origin of the proliferating cells; hence, these tumors were classed separately (Fig. 6). None of the tumors was transplanted. From their morphological appearance and the absence of metastases, we infer that these are benign adenomas.

The pituitaries of these animals were also studied histologically. In the 45.5 (low adrenal tumor) strain no anomalies were found. There were microadenomas in 4 females of the 4.24 (high tumor) strain. There was intermediate lobe hyperplasia in 6 females and, questionably, in 1 male of the 4.24 strain. While these lesions were limited to animals of line 4.24, they did not occur more frequently in animals with adrenal tumors or in obese animals.

Histological study of the testicle showed variability ranging from atrophy to active spermatogenesis. Because there were only small numbers of animals in each of these groups in both strains, no statistically significant differences were found. Testicular morphology did not seem to be related to the presence or absence of adrenal tumors. The ovaries of the 2 strains were similar (equal distribution of follicles, corpora lutea, and ova). There were 2 small ovarian tumors in the 4.24 (high tumor) strain. One was a theca granulosa cell tumor, the other, a tubular adenoma. The uteri were found to be stimulated or resting in equal proportions in both strains.

There was no relation between the weights of the adrenal glands and the body weights of the animals, as there was also no relation between the weights of the gonads and the adrenals or the weights of the seminal vesicles and uteri and the adrenals.

All absolute organ weights in the 4.24 strain were higher than in the 4.45 strain. With the exception of some adrenal tumors, the relative organ weights (g/100 g body weight) were the same in both lines.

In both strains, tumor-bearing animals were older than those without tumors. In line 4.24 the average age of tumor-bearing females was 94 weeks and of tumor-bearing males, 92 weeks. The average ages of animals without tumors were 64 weeks for females and 68 weeks for males. In line 45.5 the single female with a tumor was 112 weeks old, and the average age of the females without tumors was 76.5 weeks.

The 5 tumor-bearing males had an average age of 78 weeks, compared to 6.7% in the low tumor line.

In both strains, tumor-bearing females was 94 weeks and of tumor-bearing males, 92 weeks. The average ages of animals without tumors were 64 weeks for females and 68 weeks for males. In line 45.5 the single female with a tumor was 112 weeks old, and the average age of the females without tumors was 76.5 weeks. The 5 tumor-bearing males had an average age of 78 weeks, compared with 72 weeks for males without adrenal tumors. Tumor incidence for males was approximately the same in both lines (33% versus 25%). In the high tumor strain (4.24), however, 61% of the females had adrenal tumors, as compared to 6.7% in the low tumor line.
DISCUSSION

The existence of a high incidence of spontaneous adrenal tumors in an inbred line of Syrian hamsters suggests that genetic factors may account for the reported variability of the incidence of these tumors in this species.

The histological nature of the tumors occurring in our "high adrenal tumor" strain BIO 4.24 is the same as the morphology of adrenal tumors previously reported in Syrian hamsters (10). The exception was seen in 8 "unclassifiable" tumors. Because medullary tumors are rare in hamsters, it would seem unlikely that these tumors are pheochromocytomas, but this possibility needs to be explored further.

Our purely morphological studies permit the conclusion that the adrenal tumors were not correlated with either the pituitary gonadal or secondary sex organ structure. Females in the high adrenal tumor strain are clearly more prone to tumor development than males, and the pituitary pathology in the high adrenal tumor strain suggests increased estrogen levels (6). Biochemical endocrine studies are necessary to ascertain the true nature of these suggested imbalances and possibly their relationship to oncogenesis.

The literature on oncogenesis and endocrinology in the hamster is confused and contradictory. Our observations suggest that with increased knowledge of genetic factors and availability of inbred strains of hamsters, some of the existing problems may be clarified.

ACKNOWLEDGMENTS

The assistance of Dr. C. W. Nixon and Miss Maureen Connelly is greatly appreciated. They supervised and maintained the inbred hamster lines used in this study.

REFERENCES

An Inbred Line of Syrian Hamsters with Frequent Spontaneous Adrenal Tumors

F. Homburger and A. B. Russfield


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/30/2/305

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.