Effect of Pituitary Growth Hormone in Mice*

HENRY D. MOON, MIRIAM E. SIMPSON, CHO HAO LI, AND HERBERT M. EVANS

(Institute of Experimental Biology, Division of Anatomy, and the Department of Biochemistry, University of California, Berkeley, Calif.; Division of Pathology, University of California School of Medicine and Veterans Administration Hospital, San Francisco, Calif.)

The carcinogenic and growth-promoting effects of long-term administration of pituitary growth hormone in normal adult female rats have been reported previously (1, 3, 4, 5). The present report is concerned with the effects of large amounts of pituitary growth hormone in young mice of several different strains injected for a maximum period of 194 days.

MATERIALS AND METHODS

Mice of strains A, C3H and C57 black, 3-4 months old, were used as the experimental animals. In strains A and C3H, ten males and ten females were injected with physico-chemically pure pituitary growth hormone; identical numbers of male and female mice were used as uninjected controls. In the C57 black strain, five males and five females were injected with growth hormone; the same number of uninjected mice of each sex were used as controls. All experimental animals were injected intraperitoneally daily for 6 days each week for a maximum period of 194 days. The initial daily dosage of growth hormone was 0.04 mg.; this was increased at intervals to a maximum dosage of 2.0 mg. daily. This dosage of growth hormone is very high in relation to the body weight—approximately 20 times that used in female rats in which tumors occurred (1, 3, 4, 5) (Chart 1). The animals were weighed every 5 days. At autopsy all organs were examined under a dissecting binocular microscope, removed, weighed, and fixed in formalin. Representative sections of all tissues were taken for microscopic study.

OBSERVATIONS

During the early stages of the experiment the rate of growth of the mice receiving growth hormone did not differ from that of their controls. As the dosage of growth hormone was increased, the female mice of all three strains showed a greater gain in weight than those of their controls (Table 1). The male mice of all three strains receiving growth hormone showed no significant alteration in their growth curve, as compared to that of the controls. The average total body length for both male and female mice of all three strains was slightly greater in the mice receiving growth hormone than in their respective controls. The hearts, lymph nodes, spleens, livers, kidneys, and adrenal medullas of the injected animals were larger than those of the controls.

As shown in detail below there was no increase in the incidence of neoplasms in the three strains of mice injected with growth hormone.

Strain A male mice.—There were no neoplasms in either the experimental mice or their controls. The hearts, lymph nodes, spleens, and kidneys of the mice injected with growth hormone were larger than those of the controls and roughly proportional to the total body weight. The livers also were larger than those of the controls (Table 2), and the hepatic cells were hypertrophied and exhibited greater nuclear pleomorphism and hyperchromatism. The adrenal glands of the injected animals showed medullary hypertrophy.

Strain A female mice.—There were no neoplasms in either the experimental mice or their controls. The hearts, lymph nodes, spleens, and kidneys of the mice injected with growth hormone were larger than those of the controls and roughly proportional to the total body weight. The livers also were larger than those of the controls (Table 2), and the hepatic cells were hypertrophied and exhibited greater nuclear pleomorphism and hyperchromatism. The adrenal glands of the injected animals showed medullary hypertrophy.

Strain C57 male mice.—Noneoplasms occurred in either the mice injected with growth hormone or their controls. The hearts, lymph nodes, spleens, and kidneys of the animals receiving growth hormone were hypertrophied. The livers of these animals showed changes similar to those noted in the males. The adrenal medullae were hypertrophied in the injected mice.

Strain C3H male mice.—No neoplasms occurred in either the mice injected with growth hormone or their controls. The hearts, lymph nodes, spleens, and kidneys of the mice receiving growth hormone were hypertrophied. The livers were also enlarged; the hepatic cells showed greater pleomorphism than those of the controls. The adrenal medullae were hypertrophied in the injected group.
CHART 1.—Effect of growth hormone on body weight of mice
**Strain C3H female mice.**—Mammary carcinomas occurred in two mice receiving growth hormone and in two controls. The hearts, lymph nodes, spleens, and kidneys of the mice injected with growth hormone were hypertrophied. The livers were also enlarged and showed cellular pleomorphism to a greater degree than the controls. The adrenal medullae were hypertrophied in the experimental group.

**Strain C57 black male mice.**—There were no tumors in either the experimental or control mice. The mice injected with growth hormone showed hypertrophy of hearts, lymph nodes, spleens, and livers. The hepatic cells were hypertrophied; there was moderate nuclear pleomorphism. The adrenal medullae were larger in the experimental mice than in the controls.

**Strain C57 black female mice.**—There were no tumors in either the experimental mice or their controls. The hearts, lymph nodes, spleens, livers, kidneys, and adrenal medullae were hypertrophied in the experimental group.

**Summary**

The administration of pituitary growth hormone to young male and female mice of the A, CSH, and C57 black strains did not cause an increased incidence of tumors. The amount of growth hormone in relation to body weight administered to these mice was extremely high. The efficacy of growth hormone in these mice was shown by the greater gain in body weight in females and by visceral enlargement.

**Table 1**

<table>
<thead>
<tr>
<th>Mice</th>
<th>Treatment</th>
<th>Maximum gain at autopsy (gm.)</th>
<th>Total length at autopsy (cm.)</th>
<th>Gain</th>
<th>Range per cent</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>A male</td>
<td>Growth hormone (9)*</td>
<td>193</td>
<td>262</td>
<td>8.6</td>
<td>19.1—21.4</td>
<td>37</td>
</tr>
<tr>
<td>A female</td>
<td>Growth hormone (9)*</td>
<td>194</td>
<td>250</td>
<td>20.1</td>
<td>19.1—21.2</td>
<td>37</td>
</tr>
<tr>
<td>CSH male</td>
<td>Growth hormone (5)*</td>
<td>193</td>
<td>372</td>
<td>20.8</td>
<td>20.5—21.2</td>
<td>41</td>
</tr>
<tr>
<td>CSH female</td>
<td>Growth hormone (6)*</td>
<td>192</td>
<td>244</td>
<td>20.3</td>
<td>19.6—21.0</td>
<td>40</td>
</tr>
<tr>
<td>C57 bl. male</td>
<td>Growth hormone (5)*</td>
<td>194</td>
<td>266</td>
<td>18.8</td>
<td>18.0—19.6</td>
<td>31</td>
</tr>
<tr>
<td>C57 bl. female</td>
<td>Growth hormone (5)*</td>
<td>194</td>
<td>266</td>
<td>19.0</td>
<td>16.6—19.4</td>
<td>31</td>
</tr>
</tbody>
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*The figures in parentheses show the number of mice which survived for the total duration of the experiment and were used for determining the average measurements.

**Table 2**

<table>
<thead>
<tr>
<th>Mice</th>
<th>Treatment</th>
<th>Heart (mg.)</th>
<th>Spleen (mg.)</th>
<th>Thymus (mg.)</th>
<th>Liver (mg.)</th>
<th>Kidney (mg.)</th>
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</thead>
<tbody>
<tr>
<td>A male</td>
<td>Growth hormone (9)*</td>
<td>154—201</td>
<td>1,13—136</td>
<td>19—20</td>
<td>2.0—2.5</td>
<td>5.0—7.0</td>
</tr>
<tr>
<td>A female</td>
<td>Growth hormone (9)*</td>
<td>154—201</td>
<td>1,13—136</td>
<td>19—20</td>
<td>2.0—2.5</td>
<td>5.0—7.0</td>
</tr>
<tr>
<td>CSH male</td>
<td>Growth hormone (5)*</td>
<td>118—140</td>
<td>85—125</td>
<td>19—25</td>
<td>2.0—3.0</td>
<td>5.0—7.0</td>
</tr>
<tr>
<td>CSH female</td>
<td>Growth hormone (6)*</td>
<td>118—140</td>
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**References**


4. ———. Neoplasms in Rats Treated with Growth Hormone. II. Adrenal Glands. Ibid., pp. 304—70.

5. ———. Neoplasms in Rats Treated with Growth Hormone. III. Reproductive Organs. Ibid., pp. 540—56.
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