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RATE OF DISAPPEARANCE OF GROWTH HORMONE FROM THE PLASMA OF RATS AFTER A SINGLE INTRAVENOUS INJECTION

By

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A study was made of the rate of disappearance of growth hormone from the plasma of normal rats after a single intravenous injection. The rate of disappearance of intravenously injected growth hormone from the plasma of rats has been reported by Van Dyke, Simpson, Li & Evans (1950). They administered purified growth hormone to hypophysectomized rats in a single intravenous injection and measured the concentration of hormone in the plasma after 15, 30 and 60 min. In their experiment the level of growth hormone in the plasma fell exponentially with a biological half life of 26 min.

PROCEDURE

Male albino rats weighing about 300 gm. were anaesthetized with ether and injected intravenously via the saphenous vein with 3 mg. of purified growth hormone prepared by Dr. C. H. Li as described by Li, Evans & Simpson (1945). After 15, 30, 90, 180 and 420 min. some of the animals were again anaesthetized with ether and blood was collected from the abdominal aorta into a heparinized syringe. The plasma was separated by centrifugation and immediately lyophilized. This lyophilized plasma was assayed for growth hormone content by the tibial cartilage width method of Evans, Simpson, Marx & Kibrick (1943). A standard assay curve was prepared for this study using the same growth hormone preparation that was used in the experiment. A total amount of 3.3-5.3 ml. of plasma was injected intraperitoneally into each of the standard assay rats once daily for 4 days. On the 5th day the animals were autopsied and the growth hormone content of the injected plasma was determined by comparing the average width of tibial cartilage with the standard curve (Fig. 1).

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Effect of pituitary growth hormone on width of the proximal epiphyseal cartilage of the tibia of the hypophysectomized female rat.

Disappearance of growth hormone from the plasma after a single intravenous injection of 3 mg. into 300-gm. male rats.

RESULTS

The results are presented in Table 1 and Fig. 2. The controls were hypophysectomized at the same time as the injected rats and received no treatment. After 15 minutes (3 mg. into a 300 gm. rat) the plasma level of growth hormone was 112 µg. per ml. and after 3 hours the level was 9 µg. per ml. During this
Table 1.
Growth hormone content of plasma 15, 30, 90, 180 and 420 min. after intravenous administration of 3.0 mg. of purified growth hormone into 300-gm. male rats.

<table>
<thead>
<tr>
<th>Time after injection of growth hormone</th>
<th>Total amount of plasma injected per assay rat</th>
<th>No. of assay rats</th>
<th>Tibial cartilage width of assay rats</th>
<th>Average cartilage width</th>
<th>Growth hormone content per. ml. of plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>min.</td>
<td>ml.</td>
<td></td>
<td></td>
<td>µ</td>
<td>µg.</td>
</tr>
<tr>
<td>15</td>
<td>4.0</td>
<td>3</td>
<td>179, 220, 282</td>
<td>227</td>
<td>112</td>
</tr>
<tr>
<td>30</td>
<td>3.3</td>
<td>3</td>
<td>177, 186, 266</td>
<td>210</td>
<td>79</td>
</tr>
<tr>
<td>90</td>
<td>5.3</td>
<td>3</td>
<td>180, 186, 200</td>
<td>189</td>
<td>25</td>
</tr>
<tr>
<td>180</td>
<td>5.3</td>
<td>3</td>
<td>142, 144, 159</td>
<td>149</td>
<td>9</td>
</tr>
<tr>
<td>420</td>
<td>4.0</td>
<td>3</td>
<td>125, 128, 138</td>
<td>130</td>
<td>0</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td>20</td>
<td>135, 129, 120, 100, 112, 121, 124, 120, 124, 126, 130, 136, 131, 112, 115, 128, 138, 114, 114, 133.</td>
<td>123 ± 2.2</td>
<td></td>
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The data indicate that growth hormone is removed from the body fluids exponentially as a function of time. It should be pointed out, however, that such a large dose of growth hormone is unphysiological. The initial concentration of growth hormone, as determined by extrapolation, was found to be 140 µg. per ml. of plasma at zero time. A 300 gm. rat has 7.2 ml. plasma volume (Berlin, Huff, Van Dyke & Hennessy, 1949). By multiplying the plasma volume (7.2 ml.) by the initial concentration (140 µg. per ml.) it is found that only about 1000 µg. or 1/3 of the dose is present in the plasma. This suggests that growth hormone is not restricted to the plasma volume but is more widely distributed in the body fluids.

**SUMMARY**

The disappearance of a single intravenous injection of growth hormone from the plasma of normal rats has been studied. The fall in concentration of the
hormone was determined by injecting lyophilized samples of the plasma into hypophysectomized rats. The assay method used was the tibial epiphyseal cartilage width assay of Evans, Simpson, Marx & Kibrick (1943). The concentration of the injected growth hormone fell exponentially as a function of time with a biological half life of 40 min.

From extrapolation to zero time it is estimated that only about $1/3$ of the injected dose could be found in the plasma immediately after the injection.

REFERENCES


