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Glutathione Concentration of Livers and Muscles of Rats Following Injection of Hypophyseal Growth Hormone.*

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We have previously reported[1] that there is an increase in concentration of glutathione in muscles of mature rats after 15 daily injections of a potent growth hormone obtained by alkaline extraction of beef pituitary. In control animals similarly treated with a heat inactivated solution of the hormone we found no such change. Analyses of the livers showed no significant change. However, if animals were sacrificed a few hours after a single injection of the potent hormone we found a decided fall in the glutathione concentration of the liver with only a slight change, if any, in the muscle glutathione. We have no explanation to offer for this sudden change in the liver but believe that it may furnish a method for estimation of the potency of the growth hormone that is more rapid than the usual method by measuring growth after 20 days of injection. It may prove to have a more important significance since by its use the fundamental biochemical reactions induced by the growth hormone may be studied quantitatively and thus it may be possible to obtain additional information concerning the chemical reactions involved in the synthesis of tissues.

Mature female rats which had reached growth stasis normally were used. They were divided into 2 groups matched for weight. One group, the experimental, received a single injection of a growth hormone solution prepared according to the method of Evans.[2] In a previous trial daily injections of 1 cc. of this solution had induced an average growth of 50 gm. in 15 days in mature female rats. The control group received the same amount of the heat inactivated hormone. Both groups were injected then allowed to fast for periods varying from 8 hours to 24 hours, when they were killed. The livers and musculature of the posterior legs and loins were then quickly removed and prepared for analysis according to the method which we reported previously.[1] Glutathione was determined in the tungstic acid filtrate by iodometric titration after ascorbic acid had

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[1] Gregory, P. W., and Goss, Harold, *J. Exp. Zool.*, 1934, **69**, 13.

[2] Evans, H. M., *et al.*, *Memoirs Univ. Calif.*, 1933, **11**, 1.

TABLE I.

Glutathione Concentration in Livers and Muscles. Adult Rats After Injection of Potent and Killed Growth Hormone Solution

Exp. No.	cc. Hormone†	No. rats used	Killed after 1st injection	Liver GSH mg. %	Liver S.D	Liver Groups compared	Liver D / P. E.	Muscle GSH mg. %	Muscle S.D	Muscle Groups compared	Muscle D / P. E.
Normal Females.											
1	2 KGH	15	8 hr.	127.5±4.9	27.5	1-2	7.4	33.2±0.5	2.6	1-2	1.6
2	2 GH	15	8 "	83.1±3.3	21.6			31.6±0.8	4.6		
3	2 KGH then food	8	8 "	145.4±4.7	18.7			41.3			
4	2 GH then food	7	8 "	98.6±3.1	11.2	3-4	8.1	37.7			
5	2 KGH	15	12 "	125.3±3.8	21.1	5-6	16	33.3±0.4	2.4	5-6	2.2
6	2 GH	14	12 "	55.5±2.0	10.9			31.5±0.7	3.8		
7	1 KGH daily + food	16	5 days	144.8±3.7	21.4	7-8	3.2	34.6±0.6	3.2	7-8	6.4
8	1 GH daily + food	14	5 "	127.8±3.8	20.5			40.0±0.6			
Spayed Females.											
9	2 KGH	12	8 hr.	100.1±4.9	24.2	9-10	5.9	32.5			
10	2 GH	11	8 "	69.5±1.6	7.3			30.7			
11	2 GH then food	12	8 "	99.8±2.7	13.5			41.1			
12	2 GH	10	12 "	78.0±2.6	11.6						
13	2 KGH	15	24 "	152.6±3.7	20.4	13-14	14	34.3±0.4	2.4	13-14	4.2
14	2 GH	15	24 "	88.0±2.8	15.9			30.5±0.8	4.4		

† All animals except where noted were fasted after receiving the injection. GH refers to the potent growth hormone while KGH refers to the heated control solution in which the growth hormone was destroyed.

been removed by oxidation with 2,6-dichlorophenolindophenol. Details of the method are given in the paper referred to above.

Results are given in Table I. Besides the normal females we had at our disposal 75 mature female rats which had been spayed. These animals had reached their growth plateau normally and were suitable for this study. These results are also included in Table I. The potent hormone solution is designated "GH" and the heat inactivated solution as "KGH".

As early as 8 hours after a single injection the liver GSH concentration falls about 30%. At 12 hours the decrease amounts to about 55%. Similar decreases are found among the spayed rats although the data are not so complete. In groups 13 and 14, fasted for 24 hours after a single injection, the concentration of GSH in the livers of the experimental animals is still low. In experiments 3, 4, and 11 the animals were allowed food after the single injection. The presence of food seems to raise the GSH concentration of both liver and muscles.

If instead of a single injection the animals receive 5 daily injections of 1 cc. each and are killed 8 hours after the fifth injection we find a reversal of the concentrations. The liver GSH has returned to about normal while the muscle glutathione of the experimental group has increased to approximately the same level as we had previously found after 15 daily injections.

Lee and Schaffer[8] reported that the first rapid gain in weight following treatment with growth hormone was due in part to an increase in the water content of the tissue. We have made moisture determinations on a large number of livers and muscles from both normal and spayed females. It is interesting to note that there was a small but significant decrease in the moisture content of the livers of the potent hormone injected group. There was no significant difference in the moisture content of the muscles.

Further investigations are necessary to determine the cause of the decrease or increase of glutathione concentration following treatment with hypophyseal growth hormone. These results firmly establish an intimate correlation between the hormone and changes in the glutathione concentration of the tissues concurrently with the stimulation of increase in weight.

[8] Lee, Milton O., and Schaffer, Norwood K., *J. Nutrition*, 1934, 7, 337.