Effect of Purified Growth Hormone on Tumor Growth.* (17539)

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Alterations of hormonal processes have been suspected as being involved etiologically in neoplastic diseases. Several early experiments(1,2) indicate that anterior pituitary extracts stimulated the growth of inoculated tumors, while conflicting findings exist regarding the therapeutic success of similar extracts in inoperable cancer patients.(3,4) Stern(5) believes that "the anterior pituitary secretes two groups of hormones which are antagonistic as to their effect on tumor growth." Extracts containing the growth hormone principle are thought to stimulate neoplastic growth(6,7) while gonadotropic factors seem to inhibit tumor growth.(8,9) These divergent views may be attributed to differences in the experimental tumor and species of animal employed, as well as to the variable nature of the endocrine preparation used. This study was prompted by the recent availability of purified growth hormone (Armour†) in response to a new method of preparation,(10) and was undertaken to determine whether tumor growth could be influenced by the hormone. The activation of normal growth under the influence of the anterior hypophyseal hormone is well-known.(11,12)

Inbred "A" strain mice of both sexes were used. The animals weighed between 18 and 24 g, and were 2 to 3 months old. The mice received a diet of commercial pellets (Purina Lab Chow), weekly supplements of fresh lettuce, and were permitted access to food and water at all times. Tumors were transplanted by the trocar method, each animal receiving a fragment of neoplastic tissue in the right inguinal region. Sarcoma 37 and the familiar mammary adenocarcinoma were the test tumors. The latter tissue was not as satisfactory as the sarcoma, since there was the occurrence of late visceral metastases,(13) a tendency towards the formation of cysts containing white stringy material, and an earlier onset of visible necrosis than in the transplantable sarcoma.

Six days after tumor transplantation, the hormone therapy began. The animals included for the experiment had tumors of the following dimensions, 3.5 ± 1.5 mm × 3.0 ± 1.0 mm × 2.5 ± 0.5 mm. For the first two days, the daily dose was 0.1 mg growth hormone‡ in 0.2 ml distilled water (pH adjusted to 7.4 with sodium bicarbonate); from the third to the tenth day, the daily dose was 0.2 mg; the dose was increased to 0.5 mg on the eleventh day and continued at this level for 4 more days at which time the experiment was terminated. Throughout the experiment, the controls received corresponding amounts of crystalline bovine plasma albumin

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‡ A preliminary assay on plateaued female Long-Evans rats (about 200 g) showed that as little as 0.5 mg of the hormone caused a net increase of 10 g in weight over the controls in a 24-hour period.

TABLE I.
Effect of Purified Anterior Pituitary Growth Hormone on Tumor Growth.
Wt (in g) at autopsy.

Sarcoma 37						Mammary adenocarcinoma					
Controls			Hormone-treated			Controls			Hormone-treated		
3.45	0.56	1.68	2.14	2.29	0.91	2.37	2.55	2.95	1.60	2.30	1.90
3.02	0.22	1.88	2.25	1.69	1.29	2.03	1.55	1.75	1.10	1.15	1.70
2.27	0.55	1.76	2.98	2.90	1.32	1.30	1.30	1.53	2.40	1.10	0.70
1.89	1.07	2.42	2.42	2.13	2.01	1.60	1.35	2.42	1.00	1.28	0.95
1.71	2.58	1.58	1.41	0.29	1.37	1.20	0.45	1.35	1.75	0.47	1.25
1.64	3.57	1.36	1.37	0.41	2.01	1.55	1.40	1.58	1.95	1.43	0.65
2.14	2.67	1.23	2.00	2.83	2.17	0.80	1.10	1.57	1.20	0.63	1.20
1.06	2.14	1.15	1.74	0.76	1.74	0.77	0.70	0.90	1.25	0.72	1.10
0.73	1.92	1.08	2.01	1.48	0.94	0.13	0.60	1.28	1.25	0.49	0.55
0.88	2.02	1.69	1.39	1.12	1.70	0.12	1.40	0.87	0.75	1.03	0.70
1.73 ± 0.15*			1.70 ± 0.13			1.35 ± 0.12			1.19 ± 0.095		

* Mean values ± standard error.

(Armour). The mice receiving growth hormone showed a marked increase in weight during the first week of therapy. After this time, when the tumors were becoming necrotic, all groups suffered weight losses.

The animals were killed by decapitation; the tumor was peeled away from the subcutaneous connective tissue of the host, the interior exposed, and all visible necrotic material removed. The weights of the tumors are recorded in Table I.

It can be seen that the purified growth hormone did not show any appreciable effect, stimulatory or inhibitory, on the transplantable tumors used. Histological studies, which were kindly performed by Dr. E. Lowenhaupt of the Department of Pathology, revealed that tumors of all groups of animals, hormone-treated and controls, were of essentially similar appearance as regards relative proportions of necrotic tissue, numbers of mitotic figures and cell appearance.

Conclusion. Purified growth hormone does not influence the growth of sarcoma 37 and the mammary adenocarcinoma in "A" strain mice.

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Activation of Purified Prothrombin.* (17540)

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The activation of prothrombin has probably been discussed more extensively than any other problem in blood coagulation. It is an important process and exceedingly complex in nature. Calcium, thromboplastin, Ac-globulin and platelet derivatives participate in this vital function; and although it is not exactly clear how the activators work, it is apparent that they may be divided into two main classes; namely, those with thromboplastin activity in the traditional sense and those with accelerator or thromboplastin co-factor activity. Either class alone is a poor activator of purified prothrombin, but together they cause rapid conversion. To understand more exactly what forces these substances bring to bear on prothrombin it is essential that they be obtained in purified form and in sufficient quantity for study. This still needs to be accomplished, but in the meantime it may be possible to obtain indirect information concerning the mechanism of their action. For example, this