Effect of Androgen on Concentration of Certain Amino Acids in the Rat Prostate.* (17341)

HORACE N. MARVIN AND JORGE AWAPARA.

From the University of Texas, M. D. Anderson Hospital for Cancer Research, Houston, Texas.

Although recent reports[1] have appeared describing the effects of hormones on the biochemical constituents of organs stimulated by those hormones, no information is available relative to the influence of hormones on the free amino acids of such tissues. As part of a large program of growth investigation, it became of interest to make such a study.

Young, adult male rats (140-160 g) of the Sprague-Dawley strain were used. Orchidectomy was performed through a mid-ventral incision with the rats under light ether anesthesia. A period of 15 days was allowed for prostatic atrophy. The castrated rats which received androgen were given 0.5 mg of testosterone propionate (Oreton†) in 0.25 ml of corn oil subcutaneously each day for periods of 1, 4, 8, and 12 days. All animals were fasted 24 hours, killed by decapitation, and the ventral lobes of the prostates were removed. A sufficient number of glands was pooled to furnish a total of 300-500 mg of tissue. The tissues were prepared and analyzed by paper chromatography according to the method of Awapara.[2] Qualitative separation of the various amino acids was done by the two-dimensional method, and one-dimensional quantitative determinations were carried out for alanine, glycine, glutamic acid, and aspartic acid. The results of the former procedure are shown in Fig. 1, and the values obtained by the latter method are given in Table I.

It can be seen that following castration there are fewer amino acids determinable by the qualitative technic, and with replacement therapy the variety progressively approaches the normal. This can be interpreted in at least two ways: a) there is an absolute disappearance of certain amino acids, and b) the concentration of these amino acids is reduced below the sensitivity of the method. The latter explanation seems to be the more reasonable. Quantitation of the 4 principal amino acids shows that castration is followed by a marked reduction in their concentrations. It is apparent also that 8-12 days of replacement therapy with 0.5 mg of testosterone propionate each day is necessary before the amino acid concentrations approximate the normal levels. These data cannot be compared with the findings of the authors previously quoted because in those experiments the injections of androgen were begun on the day of castration and, therefore, no time was allowed for atrophy.

In Fig. 1 it can be seen that the normal prostate has at least 4 peptides (14 A, B, C, D) not seen in the glands of castrates or castrates receiving androgen. It is also of interest to note that the prostate of the castrate animal has a substance, probably a peptide, which disappears after 4 days of treatment with androgen. The physiologic significance of these peptides is not at all clear and must await further study. An unidentified substance (Fig. 1, No. 15) was found to be present in every case. Preliminary studies in this laboratory suggest that this substance is cystine.

Androgen replacement stimulates growth and renews the secretory activity of atrophic prostate glands. Since these changes are concomitant with a progressive increase in the concentration of free amino acids, it may be concluded that growth is associated with an increased propensity of tissue for concentrating and retaining these substances. This concept would appear to be important in

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1 Davis, J. S., Meyer, R. K., and McShan, W. H., *Endocrinology*, 1949, **44**, 1.

† The Oreton used was supplied by the Schering Corporation through the courtesy of Dr. Irwin Schwenk.

2 Awapara, J., *J. Biol. Chem.*, 1949, **178**, 113.

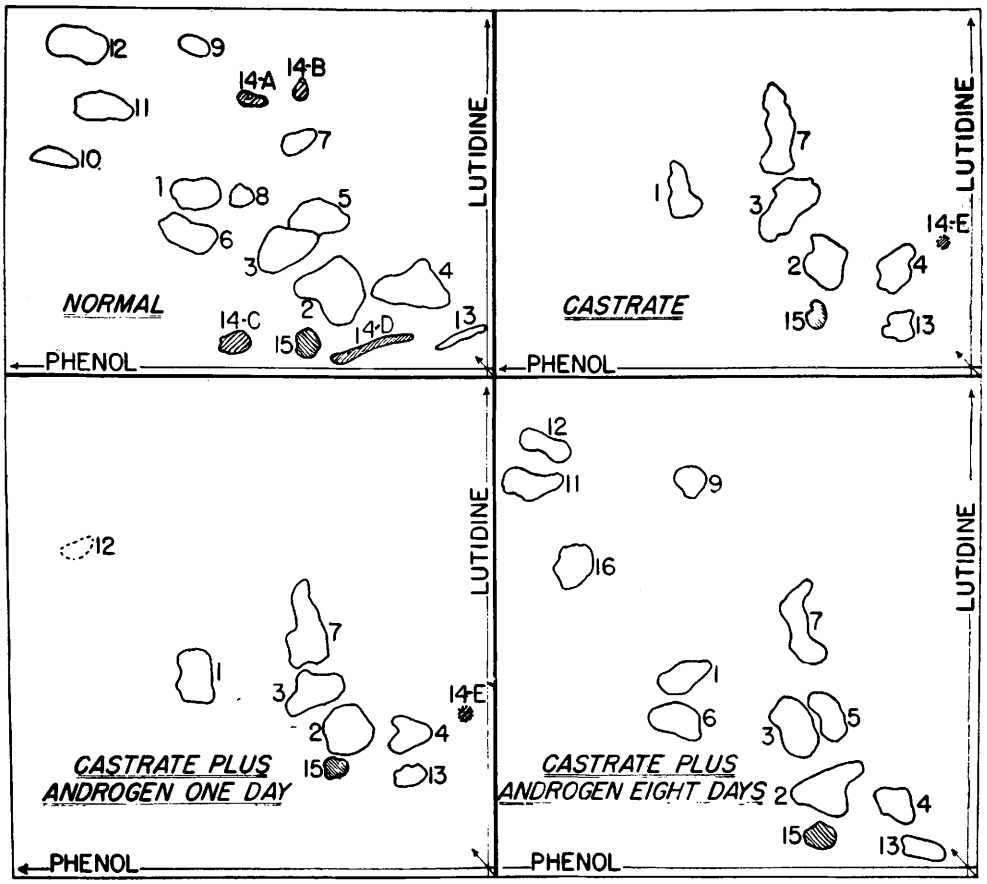

FIG. 1.

Chart showing the distribution of free amino acids as demonstrated by two-dimensional paper chromatography. The numbered areas indicate the positions of the following substances: 1. alanine; 2. glutamic acid; 3, glycine; 4. aspartic acid; 5. serine; 6. glutamine; 7. taurine; 8. threonine; 9. tyrosine; 10. proline; 11. leucine; 12. phenylalanine; 13. glutathione; 14. A, B, C, D, E, unidentified peptides; 15. unidentified (cystine ?); 16. valine.

understanding the stepwise mechanism of protein synthesis in growth. One might question the contribution of prostatic secretion, *per se*, to the increase in amino acid levels. Unpublished data in this laboratory obviate this possibility, in that no free amino acids have been demonstrated in prostatic fluid by the same procedure used above.

TABLE I.
Effect of Castration and Androgen Replacement on Amino Acids in Rat Prostate.

Treatment	Prostate wt,* mg	Amino acid concentration mg/100 g tissue			
		Aspartic acid	Glutamic acid	Glycine	Alanine
Castrate—15 days	45 (9)	12	16	9	—
Castrate + androgen 24 hr	55 (6)	13	20	12	—
Castrate + androgen 4 days	178 (4)	12	29	16	9
Castrate + androgen 8 days	562 (2)	23	57	25	43
Castrate + androgen 12 days	762 (2)	44	100	44	36
Normal	700 (2)	58	102	45	40

* The figures in parentheses are the numbers of glands from which the mean weight given was obtained.

Summary. A decrease in the amounts and numbers of free amino acids determinable by paper chromatography is associated with prostatic atrophy after castration. Replacement therapy in the castrated animal is followed by a progressive increase toward normal. The relation of these findings to growth processes is briefly discussed.

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The Electroencephalogram in Parkinsonism. (17342)

HENRY NEWMAN, ROBERT MCNAUGHT, AND FRANCIS O'DONNELL.

From the Departments of Medicine and Surgery, Stanford University School of Medicine, San Francisco, Calif.

It is generally recognized that the pathological process in Parkinsonism centers about the basal ganglia. The electrical activity of this region was studied by Meyers and Hayne[1] by direct insertion of insulated electrodes. They found normals to have a striatal rhythm faster than that of the cortex, while patients with Parkinsonism showed sequences of 25 cycle rhythm not recorded from the cortex. Spiegel[2] found the potentials from the cat's thalamus to be much like those from the cortex. Using an electrode driven into the sphenoidal bone Grinker and Serota[3] found 4 to 6 cycle waves as well as alpha rhythm. Using nasopharyngeal electrodes, Barnett[4] failed to find any 4 cycle activity.

Using conventional scalp electrodes, Yeager and Baldes[5] reported 4 cycle waves not synchronous with the tremor in patients with Parkinsonism. Jasper and Andrews[6] found no slow waves in two patients with unilateral Parkinsonism, but did record such activity from 2 patients with advanced bilateral disease. They concluded that the slow activity was present in cortical leads only when tremor was bilateral. Schwab and Cobb[7] recorded similar potentials from patients with Parkinsonism, but were of the opinion that the slow waves were artifacts from head movement, since they were able to suppress them by mechanically restraining the head. In view of these conflicting opinions, it seemed worth while to investigate the problem further.

The basal leads which we employed consisted of silver cannulae, insulated save at the tip with bakelite varnish, which were inserted, after topical cocainization, through the nostrils and into the sphenoidal sinuses, where the tips lay against the posterior wall. X-ray examination showed the tips to be in close proximity to the floor of the sella turcica in the majority of cases. In addition to the two sphenoidal leads, scalp electrodes of hypodermic needle type[8] were placed on each side in the frontal, central, and occipital regions, and the two mastoid regions were grounded. The potentials were amplified by a Grass 4 channel electroencephalograph. Recordings were made between the two sphenoidal electrodes, as well as between the sphenoidal electrodes and the pairs of scalp electrodes. Unipolar recordings from the sphenoidal and scalp electrodes were also made.

In general, where both sphenoidal electrodes made good contact, which occurred about half the time, the intersphenoidal potentials resembled most those recorded from the central scalp electrodes, showing mostly 20 cycle ac-

1 Meyers, Russell, and Hayne, Robert, *Trans. Am. Neurol. Assn.*, 1948, p. 10.

2 Spiegel, E. A., *Am. J. Physiol.*, 1937, **118**, 569.

3 Grinker, R. R., and Serota, H., *J. Neurophysiol.*, 1938, **1**, 573.

4 Barnett, A., *J. Lab. and Clin. Med.*, 1941, **26**, 1659.

5 Yeager, E. L., and Baldes, E. J., *Proc. Staff Meet. Mayo Cl.*, 1937, **12**, 705.

6 Jasper, H. H., and Andrew, H. L., *J. Neurophysiol.*, 1938, **1**, 87.

7 Schwab, R., and Cobb, S., *J. Neurophysiol.*, 1939, **2**, 36.

8 Newman, H. W., *Stanford Med. Bull.*, 1949, **7**, 61.