

pituitary alone was responsible for the appearance of the pigmented cells was demonstrated by the fact that the testes and adrenals of incompletely hypophysectomized rats possessing remnants of anterior lobe tissue alone did not show these changes.

Because of the morphological similarity between the pigmented structures in the adrenals and testes, it was thought that the cells in both the glands might be physiologically related. Various studies, however, have not lent support to this idea. Thus, hypophysectomized rats receiving pure gonadotropic hormone from a parabiotic partner⁴ had testes which showed no sign of pigmented cells, while the adrenals of these rats contained many such structures. Similarly, pigmented cells have been prevented from appearing in, or have been caused to disappear from, the testes of hypophysectomized rats by injections of antuitrin-S; but these injections failed to have any preventive action on the pigmented bodies in the adrenal.

Further studies are being planned to determine the nature, origin and fate of the pigmented cells and their responses to various substances.

Summary. Hypophysectomy in the rat caused invariably in the reticular zone of the adrenal and sometimes in the intertubular spaces of the testis the formation of cells containing yellow pigment granules. The nuclei of the cells usually showed varying degrees of pycnosis or were absent. Gonadotropic hormone prevented or corrected these changes in the testis, but failed to have any apparent effect upon the pigmented structures in the adrenal.

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A Comparison of the Potencies of Some Androgenic Sterols.

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This is a report of a study of the relative effects of six synthetic androgens* on the combs of capons. Some of these androgens had not been assayed previously by the procedure of Gallagher and Koch¹ which, in our hands, has proved to be the most satisfactory

⁴ Cutuly, E., McCullagh, D. R., and Cutuly, E. C., *Endocrinology*, 1937, **21**, 241.

* These substances were supplied through the courtesy of Dr. E. Schwenk of the Schering Corporation.

¹ Gallagher, T. F., and Koch, F. C., *J. Pharm. and Exp. Therap.*, 1935, **55**, 97.

method from the point of view of both convenience and accuracy. It must be remembered that the relative potency of these androgens would probably not appear to be the same if other biological test objects were employed. Since, however, the international androgenic unit has been defined in terms of growth of the capon's comb, it is for the present necessary to compare various products by this method.

Since it is known that a single injection of any of these sterols produces results which last for a rather short period, it seemed possible that some of the testosterone derivatives might have a more protracted action and thus prove much more satisfactory for clinical use than unmodified testosterone. Two of the critical points in the testosterone molecule are the 3 and the 17 carbon atoms since the keto and the hydroxy groups are found in these positions. The position of the unsaturated linkage also seems to be of significance in regard to the activity of these derivatives. The compounds employed in this investigation were chosen with these points in view.

The results of assays by the method of Gallagher and Koch¹ are recorded in Table I. According to this method of study, the formation of the oxime definitely decreases the potency of the 2 very active compounds testosterone and testosterone propionate. These oximes apparently are not readily metabolized to ketones by the capon. That the propionate is very active was not surprising since it has been formerly shown by Parkes² and others that, in the rat, testosterone propionate and testosterone acetate were many times more effective than the free hormone. This is probably due to the fact that after absorption the ester is slowly metabolized with the formation of the free hormone, thus giving the same effect as the frequent administration of hormone. The androstenediol employed was the Δ^5 androstenediol-3, 17. The fact that a very large dose produced only a very small comb-growth cannot be due to the fact that

TABLE I.
Results of Assay of the Androgens.

| Androgen used | Daily dose per bird in micrograms | Average comb-growth (Corrected to 57 mm.) | Calculated micrograms per bird unit |
|-------------------------------|-----------------------------------|---|-------------------------------------|
| Androsterone | 100 | 8.4 | 100 |
| Testosterone | 15 | 10.1 | 11 |
| Testosterone propionate | 15 | 8.0 | 17 |
| Testosterone oxime | 60 | 6.0 | 100 |
| Testosterone propionate oxime | 30 | 5.8 | 53 |
| Androstenediol | 250 | 7.2 | 310 |

² Parkes, A. S., *Lancet*, 1936, **2**, 674.

the double bond is in a different position than that of testosterone since the Δ^4 androstenediol-3, 17 has been shown to have little if any activity in the capon test.

It seemed possible that further information might be gained by the injection of these compounds in larger single doses. Capons were therefore injected with single doses of 10-bird units of each substance and the curve of growth and regression was measured. In each case the dose was dissolved in one cubic centimeter of sesame oil and injected into the pectoral muscles. Five birds were used in each test and all substances were tested under the same conditions. The results are graphically summarized in Fig. 1.

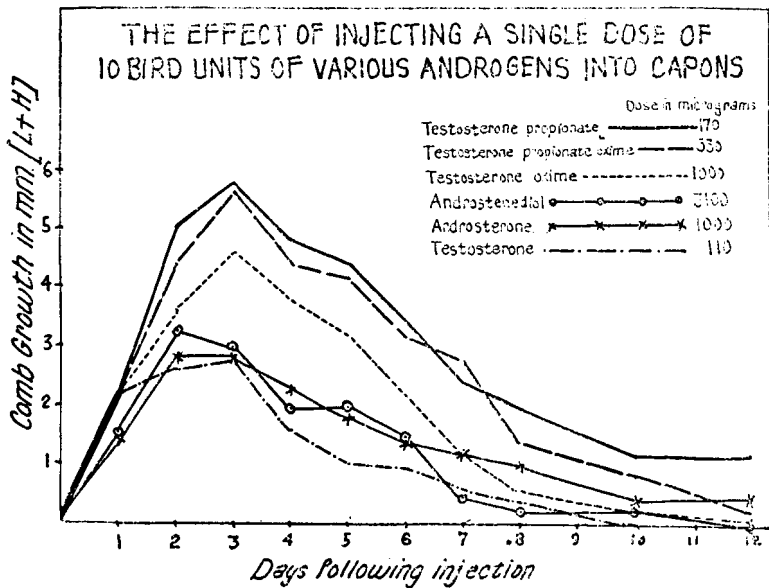


FIG. 1.

Since there was no sign of activity after the third day, it would seem that in every case the material was absorbed and either excreted or inactivated by that time. In the assay of androsterone by the Gallagher and Koch procedure, the injection of one unit on each of 5 consecutive days caused a growth of 8.4 mm., whereas the greatest growth obtained (using an average of 5 birds) with a single dose of 10 units was less than 6 mm. The 2 testosterone esters injected in single doses were much more effective than were the other compounds. The curves for testosterone, androsterone, and androstenediol were either flat or nearly so after the second day, the curves for the oxime, the propionate, and the propionate oxime

of testosterone all continued to show considerable growth between the second and third days. This protracted action would indicate that the esters are the more practical compounds for clinical use.

Summary. Androsterone, testosterone, testosterone propionate, testosterone propionate oxime, testosterone oxime, and androstenediol have been compared in regard to their effect on the combs of capons.

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Active Sensitization of White Mice.

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According to the only known studies dealing specifically with active anaphylaxis in mice,^{1, 2, 3} a certain number of mice given a single prior injection of horse serum may be expected to show anaphylactic reactions when reinjected after the usual incubation period, but a higher proportion of the animals will react if 2 sensitizing injections have been made. In an attempt to attain the maximum degree of sensitivity, we gave different groups of normal mice, one 2, 3, or 4 intraperitoneal or intravenous doses of horse serum or egg white. The mice were then tested for sensitivity by the intravenous or intraperitoneal injection of the appropriate antigen at varying intervals after the last sensitizing dose, but usually after 12-21 days.

The results observed with mice sensitized to horse serum and tested by intravenous doses ranging between 0.5 cc. and 1.5 cc. are summarized in Table I. The effect of repeated sensitizing injections in increasing the liability to severe anaphylactic reactions seems clearly indicated. Only in groups of mice that received 3 or 4 antigen doses prior to the shocking dose were reactions observed in all the animals, and the best results were obtained with mice given 4 sensitizing inoculations. Severe or fatal reactions occurred in only about 40% of mice sensitized by 2 injections, but this percentage increased to 89% in the mice sensitized by 4 injections. In the latter group occurred the highest proportion of deaths (48%).

¹ Braun, H., *Munchener med. Wochenschr.*, 1909, **37**, 1880; *Z. f. Immunitats.*, 1910, **4**, 590.

² Ritz, H., *Z. f. Immunitats.*, 1911, **9**, 321.

³ Von Sarnowski, *Z. f. Immunitats.*, 1913, **17**, 577.