by treating the heart-lung preparation with double dose of malonate are difficult to interpret. Succinate values are only slightly higher than with the single dose, and the high energy phosphate values are unchanged. There is thus no correlation between succinate accumulation and heart competence. The "failure" observed with the double dose was sudden, appearing before the whole dose was added, and was characterized by significant ECG changes. It may not be due to interruption of the Krebs cycle. It could well be due to hypertonicity of the serum, or binding of certain cations by malonate, or some unknown effect on myocardium. It has already been shown, for instance, that heart failure due to dinitrophenol cannot be attributed to its known action of uncoupling phosphorylation and oxidation(10). Other authors using different preparations have also noted an "anomalous" behavior of heart muscle to malonate(6,7,8).

Our experiments do not prove that succinate oxidation is not essential for cardiac function or that alternative pathways are functioning in malonate treated hearts. Malonate inhibition in our system may not be complete and succinate oxidation may not be the rate limiting step in the Krebs cycle. Further experimentation is necessary.

We have no explanation for variations in succinate accumulation after malonate. Preliminary experiments indicate that nutritional state of animals is of no significance.

Summary. Malonate in a concentration (0.03 M) which almost completely blocks the Krebs cycle in muscle mince, has no significant effect on performance of the isolated dog heart (heart-lung preparation) or on its high-energy phosphorus compounds. 0.06 M malonate produces also no change in the phosphorus compounds, there is even a slight increase in phosphocreatine. The double dose of malonate, however, produces a sudden cardiac dilatation before the full amount is administered. This is accompanied by a decrease in heart rate, ECG changes and arrhythmias. Significant increases in heart succinate with both doses constitute presumptive evidence that malonate diffuses into heart muscle but this accumulation of succinate shows variations and it cannot be correlated with cardiac performance.

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Anti-Infective Action of an Anabolic Steroid. (23876)

M. GHIONE (Introduced by Jerome M. Glassman)

Farmitalia, Laboratori Ricerche Microbiologia e Chemioterapia, Milano

Taubenhaus(1-4) and others showed that formation of granulation tissue in animals and response to infection were stimulated by testosterone; and this seemed to be related to anabolic rather than androgenic action of testosterone. Moreover, Sala and Baldratti(5) screened a series of steroids synthesized in this laboratory(6) and showed that in castrated rats some testosterone analogs possessed potent effect on weight of levator ani muscle and weak androgenic activity as measured by change in ventral prostate gland.

TABLE I. Effect on Nocardosis. 12 mice/exp.

Treatment	Dosage, mg/kg/day	Lethal time–50 (days)	95% confidence limits
Controls	—	3.1	2.2–4.2
4-chlorotestosterone	15	5.9	4.3–8.0*
Testosterone	15	4.0	3.2–4.9
Cortisone	25	1.9	1.4–2.6*
Cortisone + 4-chlorotestosterone	25 15	3.8	2.8–5.2†
Cortisone + testosterone	25 15	3.0	2.4–3.8†

* Significant difference between controls and the various treatments, $P < .05$.

† Significant difference between cortisone and the various treatments, $P < .05$.

4-chlorotestosterone was of particular interest in this respect because it also lacked corticoid, progestational and estrogenic activity and the thymolytic effect was greater than that induced by testosterone. In normal rats it neither caused testicular atrophy nor influenced spermatogenesis(7). As a result of these studies, experiments were undertaken to compare the effects of 4-chlorotestosterone with that of testosterone and cortisone on anaphylactic shock in guinea pigs and on experimental infections in mice and rabbits.

Method. For anaphylactic studies guinea pigs were sensitized by single subcutaneous injection of .01 to .02 ml horse serum. They were similarly injected daily with either 7.5, 15 or 30 mg/kg/day of 4-chlorotestosterone acetate for 10 days. At end of 2nd week all animals were challenged with 1 ml horse serum administered intravenously. Experimental nocardosis was produced in mice by intra-abdominal administration and in rabbits by intradermal administration of *Nocardia asteroides* suspension. Treatment, subcutaneously, was started immediately after infection was induced and was continued for 10 days thereafter. In another series of experiments mice were treated daily with the various agents 3 days prior to infection with intra-abdominally administered *Staphylococcus aureus* suspension and continued for 3 days thereafter.

Results. Table I shows that 4-chlorotestosterone effectively prolonged survival time of mice infected with *N. asteroides*. Testosterone was ineffective and cortisone hastened deaths. Although 4-chlorotestosterone or testosterone in combination with cortisone extended the survival time beyond that observed with cortisone alone, this effect was not significantly different from that obtained with untreated controls. Similarly, 4-chlorotestosterone doubled the survival time of mice infected with *S. aureus* (Table II) and was more effective in this respect than tetracycline.

In rabbits with cutaneous nocardosis 15 mg/kg/day 4-chlorotestosterone hastened healing of abscess by intensification of regenerative process and stimulation of granulation. 10 mg/kg/day cortisone, on the other hand, intensified the disease process and produced rapidly spreading purulent lesions. When 4-chlorotestosterone was administered together with cortisone the effect of the latter was prevented, healing was accelerated, necrosis was limited and proliferation of the surrounding tissue was stimulated.

4-chlorotestosterone in doses up to 30 mg/kg/day had no protective action in guinea pigs sensitized to horse serum. Actually, the mortality rate and tissue injury were markedly increased. The serum proteins, however, were not significantly affected.

Discussion. The non-specific body response to allergic or infective stimuli occurring in animals treated with 4-chlorotestosterone was significantly higher than that observed for controls. This non-specific stimulation was observed also in animals treated with cortisone; the proinfective action of cortisone, however, appeared to be nullified, without production of histologic changes. These conditions were particularly evident for *N. as-*

TABLE II. Effect on Staphylococcal Infection. 12 mice/exp.

Treatment	Dosage, mg/kg/day	Lethal time–50 (days)	50% confidence limits
Controls	—	5.3	2.2– 8.0
4-chlorotestosterone	15	10.5	6.6–16.6*
Tetracycline (Achromycin)	1	5.8	4.0– 8.4
Tetracycline + 4-chlorotestosterone	1 15	9.8	6.6–14.6*

* Significant difference between controls and treatment, $P < .05$.

teroides and *S. aureus* infected animals whose survival times were significantly prolonged. *In vitro,* however, 4-chlorotestosterone did not inhibit development of the infecting strains. According to these data the particular anti-infective action of 4-chlorotestosterone is not attributed to a direct chemotherapeutic effect but rather to a stimulating action of the steroid on organic reactive systems; particularly those inhibited by cortisone and conditioning the organic response to allergic or infective stimuli.

Summary. 4-chlorotestosterone is an anabolic steroid comparable to testosterone, but with less androgenic potential. It enhances the intensity of anaphylactic shock in guinea pigs, prolongs survival time of mice infected with *Nocardia asteroides,* or *Staphylococcus aureus,* hastens healing of cutaneous nocardosis in rabbits, and nullifies the proinfective action of cortisone.

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Comparison of Porphyrin Producing Enzyme Activities in Harderian Glands of Mice and Other Rodents.* (23877)

ROGER H. DAVIDHEISER† AND FRANK H. J. FIGGE
Department of Anatomy, University of Maryland School of Medicine, Baltimore

It was observed that the Harderian glands of rats, hamsters, and most mice fluoresced red, while the Harderian glands of rabbits and guinea pigs did not(1-5). It had been assumed, and was later found, that the red fluorescent Harderian glands contained relatively greater quantities of porphyrin than those that did not fluoresce red. The enzymes for producing porphyrin must, however, be present in all Harderian glands because free protoporphyrin has been extracted from Harderian glands that were not red fluorescent. It was, therefore, of interest to determine the quantitative aspects of porphyrin producing enzymes in Harderian glands of various rodents. It was especially desirable to compare amounts of enzyme activity present in rat and hamster, where the glands are usually red fluorescent, with the amount of enzyme in Harderian glands in guinea pigs and rabbits, where these glands are usually not red fluorescent. In some rodents, where Harderian glands are white fluorescent, the porphyrin is present in such small quantities that its red fluorescence is masked by presence of blue-green fluorescent material. The blue-green and red fluorescence spectra are complimentary and the glands appear to be white fluorescent. In the rabbit, the Harderian gland consists of a dark and a white fluorescent portion. The white fluorescent portion contains by far the most porphyrin, but not nearly as much as the Harderian glands of rats and hamsters.

The results of these experiments on quantitative aspects of porphyrin producing enzymes in Harderian glands of rodents indicate that while these enzymes were present in rabbit and guinea pig Harderian glands, the enzyme activity in the rabbit gland was less than half that of the rat or hamster. In the guinea pig the enzyme activity was only 20%

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