carbohydrates and fats; therefore, any lowering of sulfhydryl compounds in the liver or other tissues of the animal might well interfere with these phases of metabolism. Therefore, in a stressful situation it would be advantageous for an organism to maintain adequate levels of these sulfhydryl compounds in organs and tissues where activity is necessary. An example of such organs or tissues is the muscle where no change in the concentration of these compounds was observed. Barron(8) suggested that GSH may function in maintaining enzymes in their active sulfhydryl form. In a stressful situation where metabolism is increased, it is possible that this activity of GSH is also increased. Therefore, some of the changes observed in this study may be due to the conversion of reduced glutathione (GSH) to oxidized glutathione (GSSG) which was not measured by the method used.

Summary. Both hypothermia and restraint were independently capable of decreasing the concentration of liver NPSH. When these stresses were applied simultaneously, the effect of the two stresses was approximately additive. No significant change of NPSH was observed in the muscle and kidney. The possibility that the more immediate cause of the drop in concentration of liver NPSH was activation of the sympathoadrenal mechanism is discussed.

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Influence of Testosterone Propionate on Protein Metabolism of Thyroidectomized Rats. (21112)

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Administration of testosterone causes weight gain and a decrease of the urinary nitrogen excretion of the normal(1), castrated (2), adrenalectomized(3), and hypophysectomized(4,5) rat. The protein anabolic effects of testosterone thus occur in the absence of the hormones of the gonads, of the adrenal glands, and of the anterior pituitary gland. The protein anabolic effect of testosterone differs from that of thyroxine in as much as the latter in physiological doses, causes weight gain and nitrogen retention in the thyroidectomized rat(6), but is ineffective in the normal(6) or the hypophysectomized rat(6). In view of the fact that testosterone treatment fails to restore the serous granules of the submaxillary gland of the thyroidectomized rat (7) and fails to cause increase of the liver protein in the thiouracil-treated rat(8), but does cause weight gain and urinary nitrogen retention in the thiouracil-treated rat(9), it was considered of interest to determine whether testosterone propionate would exert an anabolic effect in the thyroidectomized rat.

Methods. Ten male rats, descendants of the Wistar strain, weighing between 257 and 292 g were used. The animals were thyroidectomized 2 months prior to the experiment. All animals were tube fed the "mixed" diet described by Ingle *et al.*(10) twice daily. The animals were gradually adapted to tube feeding, and then were fed a constant amount during the control and the experimental periods. The animals were kept in wire screened, individual metabolism cages in a constant temperature room. The 24-hour

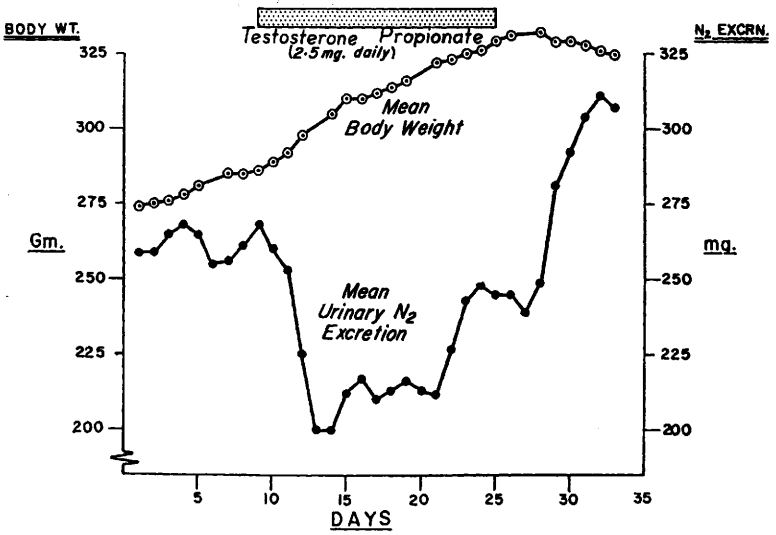

FIG. 1. Influence of testosterone propionate on body weight and urinary nitrogen excretion of thyroidectomized rats (mean of 10 animals).

urine specimens were analyzed daily by a micro-Kjeldahl method. The urinary nitrogen excretion and the weight of each animal were determined for a 9-day control period followed by a 16-day experimental period during which each animal received a daily dose of 2.5 mg of testosterone propionate by subcutaneous injection. The observations were continued for 8 days after the injections of testosterone propionate were stopped. After the completion of the experiment each animal was carefully inspected for completeness of the thyroidectomy.

Results. The results are recorded in Fig. 1. Testosterone caused a significant decrease in the urinary nitrogen excretion, and induced increased weight gain in the thyroidectomized rats. These changes are not evident until the third day of treatment. The urinary nitrogen excretion begins to increase on the 13th day of treatment, and this increase is maintained during continued treatment ("escape"). Following the cessation of treatment the urinary nitrogen excretion increases further, to levels higher than those of the control period; this "rebound" is associated with weight loss.

Discussion. Testosterone propionate induces weight gain and nitrogen retention in the thyroidectomized rat fed a constant amount of an adequate diet. The response of the thyroidectomized rat is similar to that of the normal, castrated, adrenalectomized, and hypophysectomized rat. The "escape" as manifested by increasing urinary nitrogen excretion and decreasing weight gain during treatment, as well as the "rebound" in urinary nitrogen excretion with a decrease in weight when the testosterone administration is stopped, occurs in the thyroidectomized rat just as it does in the normal(11), castrate(3), and adrenalectomized(3) rat. However, the action of testosterone in the thyroidectomized rat differs in one respect from that of the normal, castrated, adrenalectomized, or hypophysectomized rats. In the latter groups of animals the decrease of urinary N excretion occurs within 24 hours following the start of treatment, whereas this decrease in the thyroidectomized animals was not evident until 3 days after the start of treatment. The reason for this delayed effect was not evident, but may be due to a decreased rate of absorption of the hormone in the hypothyroid animals.

As was shown previously(6), small, physiologic doses of thyroxin induce protein anabolism (N retention) in the thyroidectomized, but not in the hypophysectomized rat. This fact, together with the observation that thyroidectomy causes loss of eosinophilic granula-

tion in the anterior pituitary and that the eosinophilic granulation is restored by treatment with thyroid hormone(12), suggests that the protein anabolic effect of thyroid hormone may be an indirect effect exerted by inducing growth hormone secretion of the anterior pituitary. The action of testosterone on the other hand must be a direct one, mediated neither through the anterior pituitary nor through the thyroid.

Conclusions. Testosterone propionate after an initial latent period of 3 days causes a decrease in the urinary nitrogen excretion associated with an increased weight gain in the thyroidectomized rat fed a constant intake. Escape during continued treatment, and a "rebound" after the cessation of treatment occurs in the thyroidectomized rat just as it does in the normal, castrated or adrenalectomized rat.

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Physiological Disposition of 2-Phenyl Quinoline-4-Carboxylic Acid (Cinchophen) in Man. Method for its Estimation in Biological Material. (21113)

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Cinchophen (2-phenyl quinoline-4-carboxylic acid) has been extensively used as an analgesic, antipyretic and uricosuric agent. However, its use has diminished in recent years because fatal hepatitis has occasionally occurred during therapy with this drug. In spite of the once widespread use of cinchophen, relatively little information exists concerning its physiological disposition and fate in man. The development of a specific and sensitive method for the estimation of cinchophen in biological material has made it possible to study the fate of the drug in man. Data concerning the absorption, excretion, rate of biotransformation and distribution will be presented in this paper.

Methods. Estimation of cinchophen in biological materials. Cinchophen is isolated from biological materials by extraction into benzene at pH 4.0. The drug is returned to pH 9.0 buffer, acidified and assayed spectrophotometrically at 345 mμ. *Procedure for plasma.* To one to 3 ml plasma in a 60-ml glass-stoppered bottle add an equal volume of 0.4 M citric acid and 30 ml benzene* containing 1.5% isoamyl alcohol.* Shake for 10 minutes and centrifuge the bottle. Transfer 20 ml of the benzene phase to another 60-ml glass-stoppered bottle containing 5 ml of borate buffer pH 9.0 and shake for 5 minutes. Transfer 4 ml of the aqueous phase to a

* Solvents (Reagent grade) are purified by successive washings with 1N NaOH, 1N HCl, and 3 washings with water.