to exercise. The results suggest that exercise increases glucocorticoid biosynthesis but does not affect plasma levels in animals with an intact thyroid gland. Exercise only affects the plasma levels of thyroidectomized animals regardless of whether T_4 is present or not. This indicates that the thyroid is important in maintaining corticosterone levels during exercise but that T_4 is not involved in this regulation.

The data presented here demonstrates that the thyroid gland is essential for normal glucocorticoid production. It further shows that exercise stimulates this production in both intact control and thyroidectomized animals. The release or metabolism of corticosterone seems dependent upon an intact thyroid gland since plasma levels of the corticoid are decreased during exercise if the thyroid is absent. The administration of T_4 is not sufficient to renew these levels. At the present time there are no clearcut answers to some questions raised by these findings, but with research we are presently conducting, we hope to provide the needed solutions.

Testosterone in Human Saliva

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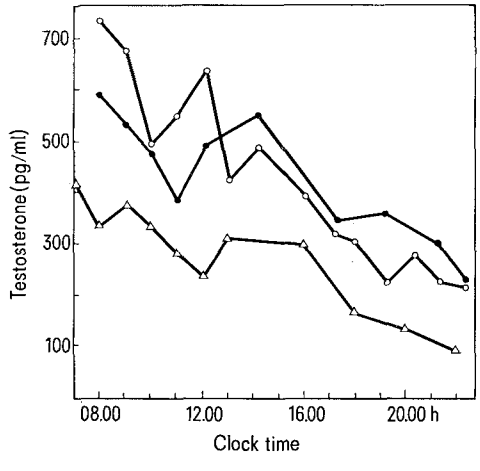
Summary. Testosterone has been detected in whole human saliva. Levels averaged (± SE) 295 ± 36 and 195 ± 25 pg/ml in adult males and females, respectively, and usually were undetectable in children. In adult males, the excretion of testosterone in saliva appeared to follow a circadian rhythm.

Both the structure and function of the submandibular gland in the rodent[2–5] and pig[6–8] are influenced by androgens, indicating that this gland is a target organ for these hormones. Moreover, the submandibular gland in the rat[9,10], mouse[11] and dog[12] exhibits some steroid synthetic ability, involving either the oxidative or reductive metabolism of testosterone. In spite of the numerous investigations of androgen-dependent characteristics of salivary glands and the studies on steroid metabolism by gland tissue, there appear to be no reports of the presence of testosterone in human saliva. There is reason to suspect that the major androgens found in serum might also be secreted in saliva since the glucocorticoids cortisol and cortisone have been reported present in human parotid saliva[13].

The present investigation was designed to determine the influence of sex and age on the concentration of testosterone in whole human saliva, and the possibility of a circadian rhythm in salivary levels of testosterone in the adult male.

Materials and methods. Between 10.00 and 15.00 h, a sample of unstimulated whole saliva (1–2 ml) was collected from each of 12 males (25–55 years of age), 12 females (25–35 years of age) and 12 children (5–10 years of age) of both sexes. To determine if levels of testosterone in saliva varied with time of day, samples were collected from 07.00 to 22.00 h at hourly intervals from 2 adult males. One of the males was sampled on 2 consecutive days. Saliva was stored at −20 °C until assayed for testosterone. Testosterone concentrations were determined in duplicate by radioimmunoassay as previously described[14], except that an antiserum raised in sheep immunized with testosterone-3-carboxy-methyloxime conjugated to bovine serum albumin was employed in the assay system. Differences between mean salivary levels of testosterone in males, females and children were tested for significance by analysis of variance followed by a Duncan's new multiple range test.

Results and discussion. Testosterone in whole saliva averaged (± SE) 295 ± 36 pg/ml for adult males and



The concentration of testosterone in whole saliva from 2 adult males at various times of the day. Saliva samples were collected hourly for 16 h from subject No. 1 on 2 consecutive days (●—●) and (○—○) and from subject No. 2 on 1 day (△—△).

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195 ± 25 pg/ml for adult females. The difference between these 2 levels was significant ($p < 0.05$) and levels in both males and females were significantly ($p < 0.05$) higher than in the children. In 9 of the 12 children the level of testosterone in saliva was undetectable, with values falling below the sensitivity of the assay (108 pg/ml). Salivary levels of testosterone averaged 124 ± 7 pg/ml for the remaining 3 children. The direction of age and sex differences in the concentration of testosterone in saliva are consistent with the known differences in serum testosterone levels. The sex difference in serum testosterone, however, is greater than that for testosterone in saliva. Serum testosterone levels in women do not vary with the stage of the menstrual cycle and average 400 pg/ml[15]; in men serum testosterone levels are in the range of 5.0–6.5 ng/ml[16]. It appears that in women the levels of testosterone in saliva are about one half those in serum while in men they are less than one tenth of the serum levels. It is possible that transport of testosterone from blood to saliva is a factor limiting the levels that can be achieved in saliva.

We observed that salivary levels of testosterone varied considerably with time of day in the adult male (Figure). In both subjects, levels were highest between 07.00 and 08.00 h and then gradually declined throughout the day reaching a low at 22.00 h. A circadian rhythm in serum testosterone in men is well documented[17–19] with peak levels in early morning and lowest levels in late evening. Our data on testosterone levels in saliva suggest a similar circadian rhythm.

The physiological role of testosterone in the saliva is not clear. It could affect cells of the oral mucosa and studies of testosterone effects on these cells must take into account the fact that the hormone may be available both from the blood and from the saliva.

Of possible importance is the potential clinical value of using testosterone levels in saliva to assess the endocrine status of a patient with respect to testosterone. In serum, testosterone is bound to a testosterone binding protein with only about 2% of the testosterone being free. Of the total testosterone in serum, only the free testosterone is metabolically active. If it is assumed that the free testosterone enters salivary gland cells and eventually appears in saliva either free or bound to a protein, then the levels of testosterone in saliva may be indicative of the availability of testosterone to other tissues in the body. This information would be far more useful than the measurement of total testosterone in serum which is not necessarily related to the testosterone available to target cells. Since only 2% of testosterone on average is available to cells at any particular time, subtle changes in binding capacity of the binding globulin and subsequent changes in free testosterone can have profound effects. The procedures required for measurement of free testosterone and binding capacity in serum are too complex and time consuming to be used as a routine clinical test. The possibility that radioimmunoassay determination of testosterone in a sample of saliva will yield equivalent information is worthy of investigation.

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The Influence of Somatostatin on Drug-Induced Prolactin Release in the Monkey[1]

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Summary. The infusion of linear somatostatin did not block prolactin release induced by either perphenazine, TRH or serotonin. Somatostatin infusion, however, potentiated prolactin release induced by perphenazine and TRH but not that induced by serotonin.

A polypeptide hormone which inhibits growth hormone release has recently been isolated and characterized from the hypothalamus[3]. This hormone, called somatostatin (SRIF), can block not only basal secretion of growth hormone[4] but also that provoked by drugs[5], sleep[6] and hypoglycemia[7]. Somatostatin's inhibitory action on pituitary hormone release does not appear to be entirely specific for growth hormone since it has been reported to suppress the TRH-induced TSH release but not the basal levels of TSH[7,8]. It also inhibits the secretion of both glucagon and insulin[4,9]. Somatostatin appears to have little influence on basal levels of prolactin in

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