In vivo Changes in Rat Liver Malic Dehydrogenase Capacities After Thyroidectomy.* (29942)

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Changes in rate of oxygen consumption in various thyroid states have been attributed to the effect of thyroid hormones on enzyme systems(1). Wolff and Ball(2) in their study of *in vitro* oxidation of succinate to oxaloacetate showed that malate oxidation is inhibited by thyroxine with no effect on the activity of fumarase. Specifically, Wolff and Wolff(3) have demonstrated *in vitro* that thyroxine competitively inhibits malic dehydrogenase (MDH) as well as other DPN-linked dehydrogenases. To elucidate the inhibitory action of thyroxine on MDH *in vivo* and to compare the enzyme changes with previously determined tissue oxygen consumption under similar experimental conditions(4), a time sequence study was undertaken.

Methods. Young adult male albino Sprague-Dawley rats weighing 125-175 g were maintained in the laboratory for 2 weeks prior to any experimental procedure. Fifty-six rats were thyroidectomized under ether anesthesia and given 1% $CaCl_2$ in their drinking water; 8 sham-operated animals served as controls. All animals were fed *ad libitum* on *Rockland Complete Rat Diet,* and fasted 25-35 hours before sacrifice by decapitation. Throughout an experimental period of 28 days, MDH capacity was determined by the method of Potter(5) and expressed in microliters of oxygen consumed per milligram of tissue nitrogen per hour (QO_2N).

The functional status of the thyroid gland was evaluated by body weight measurements together with 24-hour radioactive iodine uptakes (0.5 μc/rat) using a collimated crystal scintillation detector. Total tissue nitrogen of homogenate samples was determined using a modification of the Folin and Wu technique (6).

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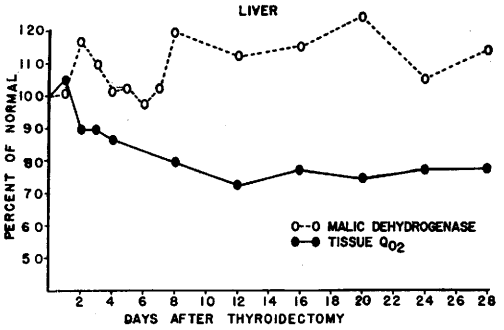

FIG. 1. Changes in malic dehydrogenase capacity and tissue oxygen consumption of liver after thyroidectomy.

Results and discussion. During the first 6 to 8 days of the experimental period, malic dehydrogenase activities were not consistent. This may have resulted from the surgical stress of thyroidectomy. Because of these inconsistent changes only those results obtained after the initial 6 to 8 days following thyroidectomy are considered in this study.

The relative changes in liver MDH capacities are shown in Fig. 1. No significant change from control capacity was observed on day 6 (98%). On day 8 the MDH capacity rose to a significant value of 121% of normal ($P = 0.08$) and remained significantly elevated throughout the experimental period except for day 24 (106%). A maximum increase of 125% in MDH capacity was observed on day 20 ($P = 0.01$). The absolute values for MDH capacities ranged from a control mean and standard deviation of 842 $\pm$ 30 to the experimental maximum of 1055 $\pm$ 24 QO_2N.

A mean I^{131} uptake of 4.2% $\pm$ 1.77% (mean $\pm$ S.D.) was obtained for the thyroidectomized animals in comparison with the uptake of 15.2% $\pm$ 2.9% for the control group. The experimental group failed to show an appreciable gain in body weight (20 g $\pm$ 8 g) whereas the control group increased 100 g $\pm$ 20 g.

No significant change in either liver dry weight values (28.0-30.3 mg per g tissue wet

weight) or tissue nitrogen values (33.5-37.4 mg nitrogen per g tissue dry weight) was observed.

A comparison of tissue MDH activities with previously determined oxygen consumption changes is given in Fig. 1. On day 8 post-thyroidectomy the liver MDH capacity rose to a significant value of 121% of control whereas the corresponding QO_2 continued to decrease to a value of 80% of the control. These values for MDH capacity and tissue QO_2 remained approximately at these levels throughout the remainder of the experimental period. There is apparently a complete lack of relationship between liver QO_2 and MDH activity since there was a progressive decrease in oxygen uptake from days 2 to 12 before plateauing, while the enzyme activity showed no change until an abrupt rise on day 8.

An *in vitro* study reported by Wolff and Ball(2) using heart homogenates showed a decrease in MDH capacity with addition of thyroxine to the system. The present *in vivo* study of liver revealed that a physiological reduction of circulating thyroxine after thyroidectomy resulted in an increase in MDH activity. Because of the difference in assay systems and tissues used, it is not certain whether the mechanisms involved in the two studies are the same.

Summary. Changes in MDH capacity of rat liver homogenates were followed for 28 days post-thyroidectomy. After an initial period of inconclusive results, liver showed an elevation in MDH capacity which occurred while the tissue QO_2 was decreasing. In this study of developing hypometabolism it is not possible to attribute the increased MDH capacities to a decreased oxygen consumption. Our findings do, however, support the concept that a thyroxine deficiency may have a stimulating influence on malic dehydrogenase capacity.

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A Stable Human Cell Line as a Host System for Sendai Virus.* (29943)

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Although Sendai virus (parainfluenza 1) has been thought by some investigators to be an agent of human disease (cf. 1,2), it has shown little capacity for multiplication in stable human cell lines. Cultivation of the virus and study of its multiplication usually have been performed in chicken embryos or in primary cultures of animal cells(3-9). In primary cultures of certain human cells it has been shown that a complete cycle of multiplication can be obtained(5,6,10,11), but even in primary cultures an incomplete cycle frequently occurs(10,11,12), and an incomplete cycle has been the regular result of inoculation of stable human cell lines(2,6,13, 14,15,16).

Data presented here demonstrate (a) that serial cultivation of Sendai virus can be accomplished in Chang's stable human conjunctiva cell line, (b) that the multiplication cycle in these cells is a complete one, (c) that once adapted to growth in conjunctiva cells the virus can then be cultivated readily either in conjunctiva cells or in chicken em-

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