intensity of the yellow color (amount of bilirubin present). The time was decidedly shorter in the average specimen with a high index than when the index was low. The occurrence of an immediate reaction seemed in most instances to be a part of the expression of this decrease in the reaction time rather than of some independent phenomenon, such as a chemical difference in the nature of the bile pigment present. There were a few rather conspicuous exceptions to this orderly arrangement, and the authors believe that the presence of substances, other than bile pigments, which give the diazo reaction must be considered as a possible explanation for them.

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Tissue Respiration and Endocrine Function. III. Influence of Thyroidectomy on Tissue Respiration.*

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Opinion differs in regard to the exact method by which the thyroid hormone exerts its influence on body metabolism. Plummer and Boothby,[1] Kendall[2] and others have accepted the view that its action is within the cells themselves and believe that it acts as a catalyst. Kunde[3] has shown that when daily repeated doses of thyroid substance are given to dogs a progressive increase in metabolism occurs as time advances, reaching a maximum in 3 weeks or more after the initial dose. This investigator states further that the height of response to a quantity of the thyroid substance depends upon some condition of the body cells, which become less and less resistant to repeated doses of the thyroid hormone, and that the catalytic theory of Plummer is inadequate to explain hyperthyroidism experimentally induced in dogs.

Data previously reported from this laboratory[4] would indicate that the apparent catalysis of the fundamental processes of metabolism induced by thyroid substance is, in part at least, indirect, *i. e.*,

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1 Plummer, H. S., and Boothby, W. M., *J. Am. Med. Assn.*, 1924, lxxxiii, 1333.

2 Kendall, E. C., *Endocrinology*, 1924, iii, 156.

3 Kunde, M. M., *Am. J. Physiol.*, 1927, lxxxii, 195.

4 Dye, J. A., and Waggener, R. A., *Am. J. Physiol.*, 1928, lxxxv, 1.

that it exerts its influence upon the body cells by increasing the amount, potency or some other property of the oxidation catalysts normally present. As measured by the indophenol oxidase activity, there is a diminution of from 10 to 50% in the respiratory power of the cells from tissues of cretin pups and lambs.

The present experiments were undertaken to determine the oxygen consumption of surviving tissues from cretin pups (thyroidectomized when 5 weeks of age, tissues studied 7 months later) as compared with their normal litter-mates of the same sex. If the diminished metabolic rate of the thyroidectomized animal is reflected in the surviving tissue, it follows that normally the thyroid hormone must accumulate in the cells, if its action is to be considered as catalytic in nature, or that it must affect, in some way, one or more of the normal constituents of the cells. Foster[5] reported a diminution of from 25 to 30% in the oxygen consumption of surviving strips of diaphragm muscle from thyroidless rats.

The oxygen consumption of finely minced skeletal muscle, in atmospheric oxygen, was measured by means of a differential volumeter, to be described later. The suspension fluid employed was a N/15 disodium phosphate solution in normal saline, which after adding the minced tissue (1 gm. to 3 cc.), now acid in reaction, gave a pH of 7.27. The water bath was kept at 39° C. ± 0.01. Representative readings for normal and experimental tissues from a single experiment are shown in the following table.

EXPERIMENT 11.

Oxygen consumption of surviving skeletal muscle of normal and thyroidectomized pups.

Animal	*M. biceps femoris* *M. semitendinous*						*M. adductor magnus* *M. semimembranous*					
	Time 10′	20′	30′	40′	50′	60′	10′	20′	30′	40′	50′	60′
Average cretin	107	209	306	389	451	526	94	186	271	345	411	462
Average control	155	305	462	610	726	825	155	308	443	550	638	710
Av. cretin % / Av. control	69.0	68.5	66.2	63.8	62.1	63.7	60.0	60.4	61.2	62.7	64.4	65.1

Substrate: 0.9 % NaCl; N/15 disodium phosphate. pH 7.27.
All volumes are reduced to 0° C., 760 mm.

These data, which we have readily duplicated in other experiments, show that for skeletal muscle of cretin pups, 7 months after thyroidectomy, there is a diminution of from 25 to 60% in their

[5] Foster, G. L., PROC. SOC. EXP. BIOL. AND MED., 1927, xxiv, 334.

power to consume atmospheric oxygen; an average of from 30 to 40%. These low values would support the view that the thyroid hormone exerts an influence upon the oxidative systems of the cells. Further work is in progress.

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Tissue Respiration and Endocrine Function. IV. Influence of Thyroidectomy on Succinoxidase Activity of Surviving Tissues.*

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The oxidation of succinic acid is a very suitable reaction for studying the oxidation capacity or respiration of a tissue, particularly muscle. Einbeck,[1] Moyle,[2] and others have shown that perfectly fresh muscle normally contains succinic acid; Thunberg,[3] Batelli and Stern,[4] *et al.*, have demonstrated in muscle and other tissues a very powerful enzyme for the oxidation of this acid; the activity of this enzyme is not diminished, in fact may be enhanced, by washing the tissues, a procedure which almost completely inhibits the action of other oxidizing systems either by its direct action upon the enzyme systems or by removing their normal substrates; and lastly, through the work of Thunberg, Einbeck and Fleisch[5] we are familiar with the details of the chemical changes occurring in this oxidative reaction. These investigators have shown that when succinic acid, $C_4H_6O_4$, is oxidized by the tissues it is transformed to fumaric acid, $C_4H_4O_4$, one atom of oxygen reacting with each molecule of the acid without the addition of water. Fleisch has further shown that the succinoxidase is probably composed of a dehydrogenase which is capable of transporting active hydrogen to any suitable acceptor, *e. g.*, active oxygen, methylene blue, etc., but before the former can function as a hydrogen acceptor it must first be activated by another enzyme. Warburg[6] believes that this depends

* This work was aided by a grant from the Heckscher Research Foundation of Cornell University.

1 Einbeck, H., *Z. Physiol. Chem.*, 1913, lxxxvii, 145; *Ibid.*, 1914, xc, 301.

2 Moyle, D. M., *Biochem. J.*, 1924, xviii, 351.

3 Thunberg, T., *Skand. Arch. Physiol.*, 1909, xxii, 430.

4 Batelli, F., and Stern, L., *Biochem. Z.*, 1911, xxx, 172.

5 Fleisch, A., *Biochem. J.*, 1924, xviii, 298.

6 Warburg, O., *Biochem. Z.*, 1921, cxix, 134; *Ibid.*, 1923, cxxxvi, 266.