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

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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.

upon the presence of iron. The oxygen activator only is inhibited by HCN.

The utility of this reaction lies especially in the fact that, through washing of the finely minced tissue, succinoxidase can be studied alone since succinic acid, in the form of its sodium salt, can be added to the substrate in optimum concentrations. Skeletal muscle from normal and cretin pups (thyroidectomized when 5 weeks of age, the tissues were studied 7 months later) was finely minced, forced through a fine sieve, washed with vigorous shaking for 8 minutes in 50 volumes of distilled water, filtered, rewashed twice more in the same manner, strained and pressed through fine-meshed gauze to remove as much water as possible, and their avidity for oxygen in the presence of succinic acid studied. In no case were the tests made sooner than 4 hours after the death of the animal.

The respiratory power of the tissues was measured by determining the volumes of oxygen consumed from atmospheric air, the oxygen serving as the hydrogen acceptor. For this purpose the differential volumeter used in the study of tissue respiration was employed. One-half gm. of the washed tissue was floated in 3 cc. of the substrate (N/30 disodium phosphate, 1% sodium succinate), the mixture having a pH of 7.45-7.5.

The data contained in the following table are a few representative readings from one experiment only. Similar values have been obtained in our other experiments, these will be reported in full at a later date. The oxygen uptake of washed muscle in the presence of succinic acid is more vigorous than that of unwashed surviving tissue. Without exception, the tissues from the cretin animals showed a diminution in their power to oxidize succinic acid. These

EXPERIMENT 11.

Oxygen consumption of washed skeletal muscle from normal and thyroidectomized pups, using succinic acid as a substrate.*

Animal	*M. Biceps femoris* *M. semitendinous.*				*M. adductor magnus.* *M. semimembraneous.*				
	Time 10′	20′	30′	40′	10′	20′	30′	40′	50′
Average Cretin	205	397	610	787	179	351	509	652	761
Average Control	244	482	683	875	217	436	630	786	925
Av. Cretin % / Av. Control	84.0	82.4	89.3	90.0	82.5	80.5	80.7	82.0	82.6

*Substrate: 1% sodium succinate. N/30 disodium phosphate buffer. pH 7.4-7.5. All volumes are reduced 0° C., 760 mm.

vary from an average of 5% for pup 26, not a typical cretin, to 15% for pup 24 and 30% for pup 22. With all animals included, there is a diminution of 16% in the cretins.

These results offer additional support to the view that the thyroid hormone exerts an influence on the oxidizing systems normally present in the cells.

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Responses of the Kidney and Spleen to Subcutaneously Injected Epinephrin.

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Halsey and Lemann[1] found that hypodermic injection of epinephrin in asthmatic patients may cause relaxation of the bronchial musculature without synchronous rise in blood pressure. This observation reopened the question of the differing sensitivity of various epinephrin receptors. C. A. Dragstedt and Huffman[2] recorded in dogs the simultaneous effects of continuous intravenous injections of epinephrin on blood pressure and intestinal motility during and after anesthesia and in the absence of drugs and anesthetics. Except under deep anesthesia, the authors were able to obtain definite blood pressure rises without intestinal inhibitions. Durant and McNinch[3] externalized the spleens of two young dogs by the Barcroft-Stephens method and took blood pressure and oncometric (spleen) tracings while the animals were unanesthetized. Intravenous injection of minimal amounts of epinephrin produced blood pressure rise and splenic constriction, but no intestinal inhibition.

Luckhardt and Koppányi[4] developed a method which greatly facilitated the attack of our problem. This method consists of subcutaneous injection of epinephrin and massage of the injected area. Such massages produced marked blood pressure rises, but, deepening the anesthesia promptly abolished the effects of massage upon blood pressure. When the effectiveness of massages of the epinephrinized areas upon the blood pressure is thus abolished, one can observe the action which such massages exert on different organs.

[1] Meyer and Gottlieb's Pharmacology, translated by Halsey. 346.

[2] Dragstedt, C. A., and Huffman, *Am. J. Physiol.*, lxxxv, 129.

[3] Durant and McNinch, *Am. J. Physiol.*, lxxxv, 364.

[4] Luckhardt and Koppányi, *Am. J. Physiol.*, lxxxi, 436.