Without going into a detailed discussion of these structural alterations, I may say that these findings support my former view, namely, that nutritional disturbances in such vascular tissues are of fundamental importance in interpreting the results.[1] And furthermore, with our present knowledge such observations do not help to explain the nature of pathological processes such as arteriosclerosis, which result in structural alterations in blood vessels.

96 (506)

Modification of tissue oxidations in vitro.

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The purpose of this investigation was to determine the influence of certain substances upon oxidations by tissues *in vitro*, with a view of casting some light on the relation between such substances and tissue respiration after the administration of these substances to animals. The general method of investigation was similar to that practiced by Yeo.[2] Tissues and solutions of oxyhemoglobin of amphibians, reptiles, birds and mammals were employed. The tissues were placed in freshly prepared oxyhemoglobin solution made from fresh blood obtained from the same animal. The mixtures were made in test-tubes and for the most part air was not entirely excluded. The darkening of the hemoglobin solution as observed directly and the appearance of reduced hemoglobin as shown spectroscopically were taken as indicating the amount of reduction.

Preliminary experiments with mammalian tissues gave a value for different tissues somewhat different from that obtained by Bert,[3] who employed a different method. Also the results showed that tissues of warm blooded animals reduce such oxyhemoglobin solutions more actively than those of cold blooded animals; this observation agrees with the results of Battelli and Stern.[4] For the

[1] *Jour. of the Amer. Med. Assoc.*, 1908, l, 1035.

[2] *Jour. of Physiol.*, 1885, vi, 93.

[3] Leçons sur la physiologie comparée de la respiration, Paris, 1870, p. 46.

[4] *Jour. de physiol. et de path. gén.*, 1907, ix, 1.

later experiments muscle and liver were more extensively employed, because of their activity and their relative bulk. The tissues were prepared by cutting into gram cubes, or chopping finely, or crushing in a mortar. Both fresh and boiled extracts made from crushed tissues were studied.

It appears that the greater the area of tissue exposed, the more rapid the reduction of oxyhemoglobin. Fresh extract is slower in reducing oxyhemoglobin than the tissue itself; and boiled extract is without such effect.

The modifying influence of magnesium sulphate, magnesium chloride, sodium sulphate, sodium chloride, potassium chloride, calcium chloride, cane sugar and quinine sulphate on the reduction of the oxyhemoglobin solutions in the presence of the tissues and tissue extracts was then studied. Different concentrations of the substances were employed and as a rule reduction bore an indirect ratio to the concentration. Also some significance is attributable to the molecular character of the different salts for there are differences in the action of solutions of equal molecular concentration. But the physical character of the solution itself seems to be a very important factor. Cane sugar, calcium chloride and quinine sulphate not only exhibit a marked restraining action on the reduction of oxyhemoglobin, but they appear to favor its transformation into methemoglobin.

In general, the results indicate that reduction of oxyhemoglobin solutions under the conditions of these experiments is not a very true picture of the activities of tissues *in vivo*, for the activity varies directly with the time of removal of the tissue from the body. An extract of a perfectly fresh tissue is much less powerful than an extract of a tissue aseptically removed and preserved for a time before making the extract. In other words, the reducing property seems to be largely the result of *post mortem* changes. It seems clear that more delicate methods of experimentation are necessary for obtaining the desired information, and, therefore, another series of experiments with methods having for their object the preservation of the vitality of the tissues is now being conducted.