Recovery Oxidation in Muscle.—The electrical, mechanical and thermal events occurring during an isometric twitch in skeletal muscle, together with their probable biochemical explanation have been described in previous papers.[1 2] The present paper is intended as a brief review of the phenomena accompanying recovery.

Recovery Heat Production in Muscle.—The myothermal studies of A. V. Hill have afforded precise information concerning the magnitude and time course of recovery heat production in muscle. Its absolute magnitude in air or in oxygen is 1.5 times that of the initial heat. Most of the recovery heat is aërobic, since absence of oxygen reduces it to one-sixth[3] (p. 38) of its aërobic value. Since the initial heat is wholly anaërobic[3] (p. 42), the total aërobic heat produced in contraction is nearly the same as the total anaërobic.

The significance of the anaërobic fraction of the recovery heat is not clear. Hill[3] has suggested that it may be due to delayed neutralization of some of the products of contraction. In view of the considerations outlined in the rest of this paper, the possibility suggests itself that this heat may be the result of oxidations in which some substance other than oxygen serves as final hydrogen acceptor.

The rate of recovery heat production increases with increase in temperature within certain limits, the usual behavior of biochemical reactions, and is decreased by a rise in the hydrogen ion concentration. In excised frog muscle the rate of heat production in recovery is related to the "concentration of the substances whose removal constitutes recovery"[3] (p. 39). In any case, the total duration of recovery heat production is much greater than that of the initial heat. For example, after an isometric tetanus lasting 0.1 second, the initial heat production is over in about 1.3 seconds, while recovery heat production can be noted for some 300 seconds.

Oxygen Consumption in Muscle During Recovery.—An outline of the reactions occurring during recovery in muscle is given in a previous paper.[2] In general these are restitutive in nature. The relation of oxygen consumption to these processes has been established by the researches of Meyerhof,[4] which have shown that the oxygen consumption consequent upon muscular function occurs after but not during contraction. These observations accord well with Hill's findings described above. In rate and duration there is a parallelism between oxygen consumption and recovery heat production, and like the recovery heat, oxygen consumption is decreased by a rise in hydrogen ion concentration.[5]

Mechanism of Recovery Oxidation.—It has been known for a long time that the living cell can utilize oxygen to oxidize substances relatively stable under ordinary conditions, substances which may be kept in air for indefinite periods without oxidation. Xanthin is an example of such a body[6] (p. 331). It is very difficult to oxidize this substance to uric acid by any of the usual oxidizing reagents, and yet the reaction goes readily in air in the presence of xanthine oxidase. There are three possible mechanisms of doing this:

1. Activation of oxygen.
2. Activation of substrate.
3. Both.

At the beginning of the present century it was generally believed that biological oxidation was effected by means of activated oxygen. The historic background and experimental basis for this view is given in Kastle's excellent monograph.[7]

However, in consequence of the extensive researches of Wieland, Thunberg, Hopkins, Keilin, Dixon and others, the last fifteen years have seen a notable shift in point of view.

It is now thought by most investigators in this field that the first step in all biological oxidations is the activation of hydrogen atoms of the substrate by the several dehydrogenases known to be present.[6] In the opinion of Wieland, activation of oxygen is not an essential, but some experiments of Thunberg suggest that at least in some instances, both the activation of substrate and activation of oxygen are important. For example, the dehydrogenation of succinic to fumaric acid in the presence of succino-dehydrogenase is not inhibited by cyanides when methylene blue is the hydrogen acceptor, but is inhibited when the hydrogen acceptor is oxygen. Now it is known that activated hydrogen will react directly with methylene blue,[6] and that cyanides interfere with the activation of oxygen. Accordingly Thunberg[6] has inferred that the oxidation of succinic acid to fumaric acid by oxygen is a reaction involving two enzymes, succino-dehydrogenase and an oxidase.

It is known that animal tissues contain a number of more or less specific dehydrogenases[6] (p. 326), and while active oxygen may be required to accept from succinic acid the hydrogen activated by succino-dehydrogenase, this may not be a general phenomenon. In fact the work of Dixon and others has shown that xanthine oxidase will serve to so activate the hydrogen of xanthine and of aldehydes, that it will be taken up by molecular oxygen even in the presence of cyanides. In this case the oxygen is simply equivalent to methylene blue as an hydrogen acceptor, and reacts without activation. We are here dealing with what Thunberg calls a "catalytic three compound system," that is, a system containing as essentials substrate, dehydrogenase and oxygen.*

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*(Part Two of this contribution will appear in this column in next month's California and Western Medicine.)

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