

and oxygen in a ternary catalytic complex, permitting the transfer of electrons, either singly or in pairs, from urate to oxygen.

Beinert has recently reported that in the oxidation of substrate by the flavo-protein, fatty acyl CoA dehydrogenase, two molecules of enzyme-bound flavin appear to act together (21). They are reduced together to a semiquinonoid state by one molecule of substrate which is thereby converted directly to product without passing through a detached free radical state. It is reasonable to suppose that in the reoxidation of the semiquinonoid enzyme intermediate by oxygen, two electrons are similarly transferred to the oxygen molecule without forming a detached perhydroxyl free radical. It is of interest that the oxygen-facultative, two-electron transfer oxidase, glucose oxidase, also contains two molecules of flavin per molecule of enzyme. If these coenzymes act in concert during the reduction of molecular oxygen to hydrogen peroxide without forming detached perhydroxyl, the absence of indiscriminate radical attack during the action of the enzyme may be explained.

The enzymes which catalyze terminal four-electron transfer to molecular oxygen are all metalloproteins (laccase, ascorbic oxidase, catecholase function of the phenolase complex, and cytochrome oxidase). In these cases, it is usually considered that either four consecutive transfers of single electrons to the bound oxygen molecule occur, or that the electron-transfer oxidase is so organized with respect to substrate that groups of electrons can be transferred simultaneously. This may be accomplished by means of clusters of oxidases bound to the oxygen molecule, each undergoing one-equivalent oxidation-reductions, or by means of two-equivalent (or higher) oxidation-reductions (14).

In the case of oxidases bearing copper or iron at their active centers, this might involve valence states higher than two or three (for example, respectively  $\text{Cu}^{+3}$ ,  $\text{Cu}^{+4}$ ,  $\text{Fe}^{+4}$ ,  $\text{Fe}^{+5}$ , or  $\text{Fe}^{+6}$ ). In such a

case, two-equivalent reduction of molecular oxygen becomes possible without formation of detached free radical intermediates. The evidence mentioned concerning the reactions of hemoproteins with peroxides (14), and electrophilic hydroxylations catalyzed by ferrous iron-oxygen systems (13, 15) suggests that molecular oxygen bound to cytochrome oxidase may undergo two two-electron reduction steps, each step forming a water molecule or hydroxyl anion (Eqs. 24, 25).



The relationship between such a mechanism for the terminal reduction of molecular oxygen to two molecules of water and mechanisms proposed for mixed-function oxidation (types ii and iii) is apparent and is being investigated. It is also apparent that such electron transfer and mixed function systems, acting in reverse with consumption rather than production of energy, afford interesting hypotheses for photosynthetic formation of molecular oxygen.

## Summary

The enzymes which catalyze reactions of molecular oxygen occur in three principle classes: (i) oxygen transferases, (ii) mixed function oxidases, and (iii) electron transferases. The first class catalyzes the transfer of a molecule of molecular oxygen to substrate. The second class catalyzes the transfer of one atom of the oxygen to substrate; the other atom undergoes two-equivalent reduction. The third class catalyzes the reduction of molecular oxygen to hydrogen peroxide or to water.

## References and Notes

1. W. von E. Doering and E. Dorfman, *J. Am. Chem. Soc.* 75, 5595 (1953).
2. An extended development and discussion of the ideas proposed here is in press (*Advances in Enzymol.*). I wish to thank the U.S. Public Health Service, the American Cancer Society,

and the National Science Foundation for support, at the University of Oregon Medical School, of research concerned with phases of oxygen metabolism.

3. H. S. Mason, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 55C.
4. —, W. L. Fowles, E. W. Peterson, *J. Am. Chem. Soc.* 79, 2914 (1955).
5. The expression *oxygen transferase* was first used (4, 6) in the present connection in order to maintain a historical continuity in the oxidase field. The general debate on mechanisms of biological oxidation which took place between the schools of Warburg and Wieland, among many others, was concerned in part with the problem of enzymic oxygen transfer. Since tracer study has now demonstrated that oxygen transfer does occur enzymically, the expression *oxygen transferase* is being used categorically within the limits of a specific definition given in the text. The term *oxygenase* has recently been suggested for these enzymes (7, 8) because it is succinct, because it is consistent with *hydrogenase* and because enzymic transfer is being employed in connection with groups or radicals rather than molecules. It is hoped that a consensus of interested investigators on this matter of nomenclature will soon be reached.
6. O. Hayaishi, M. Katagiri, S. Rothberg, *J. Am. Chem. Soc.* 77, 5450 (1955).
7. O. Hayaishi, personal communications.
8. O. Hayaishi, S. Rothberg, A. H. Mehler, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 53C.
9. By *substrate* is meant the reagent other than molecular oxygen, which is itself a substrate.
10. S. Udenfriend, C. Mitoma, H. S. Posner, Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 54C.
11. M. Hayano *et al.*, *Arch. Biochem. and Biophys.* 59, 529 (1955); M. L. Sweat *et al.*, *Federation Proc.* 15, 237 (1956).
12. T. T. Tchen and K. Bloch, *J. Am. Chem. Soc.* 78, 1516 (1956), Abstr. 130th Meeting, American Chemical Society, Atlantic City, N.J., September 1956, p. 56C.
13. H. S. Mason and I. Onoprienko, *Federation Proc.* 15, 310 (1956).
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15. H. S. Mason, I. Onoprienko, D. Buhler, *Biochim. et Biophys. Acta* 24, 225 (1957).
16. R. Bentley and A. Neuberger, *Biochem. J. (London)* 52, 694 (1952).
17. I. Onoprienko and H. S. Mason, unpublished results.
18. R. Bentley and A. Neuberger, *Biochem. J. (London)* 45, 584 (1949).
19. H. R. Mahler, H. M. Baum, G. Hubscher, *Science* 124, 705 (1956).
20. H. R. Mahler, *Advances in Enzymol.* 17, 233 (1956); B. Chance and G. P. Williams, *Advances in Enzymol.* 17, 65 (1956); W. W. Wainio and S. J. Cooperstein, *Advances in Enzymol.* 17, 329 (1956).
21. H. Beinert, *Biochim. et Biophys. Acta* 20, 588 (1956).

taught uninterruptedly until his retirement in 1942.

An ardent disciple of his predecessor, William Graham Sumner, who introduced, in 1875, the first course in sociology in an American university, he devoted much of his research, following the latter's death in 1910, to bringing to completion the huge project which Sumner had begun and which was finally published as the four-volume *Science of Society*, in 1927. Keller, a prodigious writer, was the author of 12 other volumes. Noteworthy among them are *Homeric Society* (1902), *Colonization* (1908), *Societal Evolution* (1915), *Man's Rough*

# A. G. Keller, Distinguished Sociologist

One of the great figures at Yale University for nearly half a century, Albert G. Keller, emeritus professor of the science of society, died on 31 October 1956.

Born in Springfield, Ohio, he received his B.A. degree in 1896 and his Ph.D. degree in 1899, at Yale University. He immediately joined the Yale faculty and

*Road* (1932), and *Net Impressions* (1942). He also edited various books—collections of Sumner's essays in particular—and published scores of articles and hundreds of notes and reviews.

Like Sumner, Keller was a pioneer in stressing the objective and scientific approach to the study of social phenomena. The two men founded what might be called "cultural sociology," a comparative study of the institutions and patterned forms of behavior of social groups. At the risk of oversimplification, it may be said that Sumner's major single contribution was the concept of the folkways (*Folkways*, 1906) and Keller's, that of extending the principle of evolution into the social range (*Societal Evolution*, 1915). Sumner defined folkways as habits of the individual and customs of the society which arise from efforts to satisfy needs. They become regulative for succeeding generations and take on the character of a social force. Although deeply rooted in tradition, they are modifiable and change in response to changing life-conditions. Keller demonstrated that adjustment is the crucial fact in social life, that man's mode of adjustment is mental and social rather than organic, and that it may be measured by his civilization or culture. Societal adjustment, he further held, is achieved, in the main, automatically, through the operation of massive impersonal forces of which the individuals concerned are rarely more than dimly aware.

The work of both scholars was integrated in the monumental *Science of Society*, which traced the development and adjustment of social institutions from early beginnings, drawing material from primitive, as well as modern, societies, and basing conclusions on tens of thousands of instances or cases.

This dispassionate analysis, classification, comparison, sequence-making, and law-derivation in the field of human affairs was a novel approach in their time, when the traditional study of mankind consisted in appeal to the supernatural, appeal to authority, reliance on intuition, pure logic, and the like, with no thought of subjecting notions to rigorous verification, and when indeed, at least in certain quarters, it was regarded as

quite improper to consider men and society as natural phenomena. "Undergraduate students," Keller once wrote, "know little about method, and care less. What they imbibe, however, from tender years, is deduction, always deduction. They are not taught much about causes—impersonal causation—but ever is agency set before them, chiefly in the guise of the great man, the hero to worship. They are fed upon grand shaky major premises and imposing visions of idealized lives of great men, and other edifying and ethical mythology. Through such constructions Sumner [and Keller too] drove a mighty bludgeon. Of course there was lamentation and resistance as the pieces flew, but young men are far from being supine fools and besides, they are not averse to a racket; and many of them followed Sumner through the hole he had made and came out into a freer air on the far side."

A born teacher, with the knack of putting ideas, even abstract ones, into forceful language, Keller exerted a tremendous influence on generations of Yale students. In his long years at Yale he estimated that he had taught 16,000 of them. Teaching he regarded as a man-sized job, to be done to the best of one's ability, faithfully and conscientiously; a human job that should rank above the paper job of research and publication. He demonstrated that he could do both extremely well, but, to his mind, teaching was the greater of the two.

The distinguishing traits of his teachings, as they were impressed on his students, were to challenge every idea and tradition by reference to cold facts; to conceive present crises—political, economic, social—in the light of a long stretch of social evolution; to mistrust all panaceas, exercises in logic, and subjective and mystical revelations of ethical principles and transcendent philosophies; to dig the major premise out of every generalization, particularly out of the noble ones; to work unceasingly; never to compromise for the sake of diplomacy; and, above all, to discipline oneself.

Keller held that all good elementary teaching in college must be more or less dogmatic. "To begin with the balancing of theories," he asserted, "is idiotic. The

only way in which a student may healthily set out is from some definitely and clearly presented position; then subject it to all the criticism possible. But there must be something solid to set foot upon, and I do not know what could be better adapted to the purpose than the matured conclusions, from long and intimate acquaintance with the facts, of a mind whose single interest is the truth. What matter if later study and experience cause one to question such conclusions? He has at least something positive to correct or reject; and is challenged by his very respect for what he has been strongly taught, not to abandon it for less than serious reason."

In part because of a shy and retiring nature, which he hid behind a kind of surface bluntness, and in part because he felt they took time away from his work, Keller shunned membership in professional organizations and most outside activities. Although he was one of the founders of the American Sociological Society, he attended its meetings for only a few years and later resigned. His memberships consisted only of Phi Beta Kappa, the Sigma Xi, and the university club.

A lone wolf in many respects, Keller was distinguished by his personal and intellectual honesty, which led him to deal openly with others and to abhor all political maneuvering; by his scientific integrity, which made him impatient of fools and charlatans (of whom there have been more in the social sciences than in disciplines further advanced toward preciseness); by his paradoxical combination of a fundamental tolerance of attitude with a dogmatism of exposition, which proved effective in long years of successful undergraduate teaching; by his stability and toughness of mind, his utter lack of pretense, and his austerity. Defects reside in these as in all virtues, as Keller would have been the last to deny, but the picture that emerges is that of a genuine scientist, imbued with a deep humility in the face of the mountain of the unknown beside the molehill of the known.

MAURICE R. DAVIE

*Department of Sociology, Yale University, New Haven, Connecticut*

