should be pointed out that the spectrum of ethylene diamine in this region resembles closely that of ammonia. On the basis of the chemical structure of nabam, however, it is probable that the compound in question is ethylene diamine.

Dimond and Horsfall (*12*) showed that small quantities of dimethyl amine greatly increased the toxicity of carbon disulfide to *Sclerotinia fruiticola*.

Results of the present experiments lead to the conclusion that the gaseous toxicants from nabam solutions are carbon disulfide and ethylene diamine. The effect at a distance from the solutions, observed by Rich and Horsfall (*7*) and confirmed herein, is thus to be attributed to these compounds. It may be inferred that carbon disulfide, in cooperation with certain amines, is responsible, at least in part, for the effect of the fungicidally active dithiocarbamic acid derivatives.

References

1. TISDALE, W. H., and WILLIAMS, I. Washington, D. C.: *U. S. Patent Office Index of Patents*, 740.
2. GOLDSWORTHY, M. C., GREEN, E. L., and SMITH, M. A. *J. Agr. Research*, **66**, 277 (1943).
3. PARKER-RHODES, A. F. *Ann. Applied Biol.*, **30**, 170 (1943).
4. DAVIES, W. H., and SEXTON, W. A. *Biochem. J.*, **40**, 331 (1946).
5. MCCALLAN, S. E. A., and WILCOXON, F. *Contribs. Boyce Thompson Inst.*, **3**, 13 (1931).
6. BARRATT, R. W., and HORSFALL, J. G. *Connecticut Agr. Expt. Sta. Bull.*, 508 (1947).
7. RICH, S., and HORSFALL, J. G. *Am. J. Botany*, **37**, 643 (1950).
8. SISLER, H. D. and COX, C. E. *Phytopathology* (Abstr.), **41**, 32 (1951).
9. ———. *Ibid.*, 565.
10. DENNIS, L. M., and NICHOLS, M. L. *Gas Analysis*. New York: Macmillan (1929).
11. VILES, F. J. *J. Ind. Hyg. Toxicol.*, **22**, 188 (1940).
12. DIMOND, A. E., and HORSFALL, J. G. *Phytopathology*, **34**, 136 (1944).

Manuscript received May 28, 1951.

Ascorbic Acid, a Coenzyme in Tyrosine Oxidation[1]

Robert R. Sealock[2] and Ruth L. Goodland

Department of Chemistry, Iowa State College, Ames

The crystalline antiscorbutic vitamin has been available since its isolation was announced in 1932. However, no adequate explanation of the chemistry of its biological functions has been established. Now at least one of its functions may be understood, for it has been found to be a necessary coenzyme in the metabolic oxidation of the amino acid tyrosine. Following the discovery of its need for complete utilization of tyrosine in the intact animal (*1*), it was shown that liver slices from scorbutic guinea pigs were unable to oxidize tyrosine (as normal slices were) unless the crystalline vitamin were added (*2*). With the *in vitro* addition of crystalline synthetic ascorbic acid, scorbutic liver slices were indistinguishable from normal slices in their ability to oxidize tyrosine as measured by oxygen consumption. Since surviving cells were present, an uncertainty remained as to whether the action of the vitamin was a direct enzymatic participation or some indirect effect.

Studies with cell-free scorbutic liver preparations gave indefinite answers, for with large numbers of animals the average values for tyrosine oxidation by deficient livers were almost equal to the average values obtained with normal livers. In occasional animals, the degree of tyrosine oxidation was increased by the addition of the vitamin. Painter and Zilva (*3*) have observed the increased disappearance of the tyrosine phenolic group with the addition of ascorbic acid to scorbutic liver preparations, which also were capable of extensive tyrosine metabolism.

In contrast, enzyme preparations from even normal animals completely lose the ability to oxidize tyrosine if the preparation is made in such a fashion that the total concentration of both free and bound ascorbic acid is reduced to an insignificant value. This removal of ascorbic acid may be accomplished by thorough dialysis, by certain types of acetone desiccation, by dialysis of other types of acetone powders, and by specific protein fractionations. With preparations of this sort the role of ascorbic acid is readily demonstrated. In order to achieve tyrosine oxidation, it is necessary to add α-ketoglutaric acid as amino group acceptor in the first stage of the reaction. This first stage is probably a nonoxidative transamination, as shown by experiments with tyrosine marked with heavy nitrogen in our own work and by use of ketoglutaric acid (*4*) and other experiments dealing with the transamination enzymes (*5, 6*).

The tyrosine oxidation was carried out by means of the usual manometric procedure, as previously described (*7*). Appropriate solutions of the enzymes combined with the necessary additives were incubated with tyrosine (5 μm), the oxygen consumption observed being corrected by subtraction of suitable controls. With the addition of the ketoglutarate in stoichiometric proportions (5–10 μm) and ascorbic acid in catalytic quantities (150–200 μg), the oxidation of tyrosine occurs with the uptake of 4 atoms of oxygen per mole of tyrosine present. Without the addition of the vitamin the oxidation proves insignificant, with much less than 1 atom of oxygen being consumed. With the total system present in adequate quantity the oxidation proceeds to completion in 1 hr.

From these results it may be argued that ascorbic acid is necessary to the enzyme responsible for the first oxidative step, as may be concluded from the results obtained with liver slices (*2*). In light of this finding it also may be concluded that the vitamin is a coenzyme in this step, a conclusion which is further supported by the finding that the velocity of the oxidation is dependent upon the concentration of ascorbic acid present. In fact, it has been possible to calculate the dissociation constant between the coenzyme and the apoenzyme by the classical procedures of enzyme chemistry (as will be described elsewhere).

Since transamination appears to be the first step in the reaction sequence, it is obvious that *p*-hydroxy-

[1] The generous assistance of the Nutrition Foundation is gratefully acknowledged.

[2] Deceased.

phenylpyruvic acid should be regarded as the intermediate involved in the uptake of the first oxygen atom. With this compound substituted for the amino acid and with α-ketoglutaric acid omitted, the same enzyme preparations cause the oxidation of the tyrosine keto acid, provided that sufficient ascorbic acid is added to the system. Without the vitamin insignificant oxidation is obtained. Thus it may be argued that ascorbic acid plays its part in tyrosine metabolism by acting as a coenzyme in the oxidation of the deaminated amino acid.

The exact mechanism of this chemical reaction is unknown, but an attractive working hypothesis may be presented, based upon the reversible enediol oxidation reduction center of the vitamin. The enzyme would be regarded as removing hydrogen from the tyrosine keto acid by means of the dehydroascorbic acid form of the vitamin, with subsequent transfer to oxygen and regeneration of dehydroascorbic acid. Specific experiments testing this hypothesis and more detailed discussion will appear in a subsequent communication.

References

1. SEALOCK, R. R., and SILBERSTEIN, H. E. *Science,* **90**, 517 (1939).
2. LAN, T. H., and SEALOCK, R. R. *J. Biol. Chem.,* **155**, 483 (1944).
3. PAINTER, H. A., and ZILVA, S. S. *Biochem. J.,* **46**, 542 (1950).
4. LA DU, B. N., JR., and GREENBERG, D. M. *J. Biol. Chem.,* **190**, 245 (1951).
5. CAMMARATA, P. S., and COHEN, P. P. *Ibid.,* **187**, 439 (1950).
6. HIRD, F. J. R., and ROWSELL, E. V. *Nature,* **166**, 517 (1950).
7. SEALOCK, R. R., and GOODLAND, R. L. *J. Biol. Chem.,* **178**, 939 (1949).

Manuscript received July 13, 1951.

Book Reviews

Principles of Human Geography (Huntington's). 6th ed. Revised by Earl B. Shaw. New York: Wiley; London: Chapman & Hall, 1951. 805 pp. $6.25.

The late Ellsworth Huntington's *Principles of Human Geography,* in its several earlier editions, has been one of the major texts in the field of geography for many years, and the able editing and revision of the sixth edition by Dr. Shaw should continue its use. Shaw has injected many of his own viewpoints and the results of some of his own research into the book, combining them skillfully with Huntington's forceful ideas and writing.

The *Principles* of Huntington and Shaw is in the tradition of the French masters of human geography, Vidal de la Blache and Brunhes, in its search for universals. Man's relationships with the several physical or natural elements of the environment are the center of attention; intercultural relationships are distinctly subordinate. Subject matter is categorized in terms of elements such as climate, landforms, and soils, and relationships are primarily the natural influences upon man rather than the effects of man. The role of the physical environment is presented in a distinctly positive manner, although man is by no means relegated to complete subservience in this environment. Environmental determinism as such is categorically denied.

Huntington's theses concerning the close relations between climates and the energy of peoples and their civilizations receive ample presentation as the most extreme form of man's dependence upon nature. It is regrettable that this form of environmental determinism, actually a highly debatable issue on which little solid agreement exists at present, should have been discussed in such a positive manner. Direct effects of climate in such areas as the Congo basin have as yet been insufficiently isolated from other influences on the health of man, both related and unrelated to climate.

Although the natural elements of our environment as causative factors in world geography get the lion's share of attention compared to the treatment of the cultural elements (cf. *Culture Worlds,* by R. J. Russell and F. B. Kniffen, SCIENCE, **114**, 400 [1951]), this book is in no sense a text on physical geography, as nature is discussed only insofar as it relates significantly to man. But relationships rather than areas form the organizational framework, and, in a concluding section, where major countries are discussed on a regional or areal basis, brevity results in rather unsatisfactory discussion. Vivifying presentation of facts and ideas, which highlight many pages elsewhere, are here absent.

The book is helped by a handsome format, well-chosen photographs, and a minimum of typographical error. With a few exceptions, the mapping is adequate.

DONALD PATTON

Department of Geography
University of Maryland

The Mountain of Giants: A Racial and Cultural Study of the North Albanian Mountain Ghegs. Carleton S. Coon. Cambridge, Mass.: Peabody Museum of American Archaeology and Ethnology, Harvard University, 1950. 105 pp., 16 plates. $4.75.

In the author's words, "This is not a work of ethnography, but one of somatology" (p. 5) that perhaps too narrowly announces merely an attack upon "the Dinaric problem." In fact, Dr. Coon's long-delayed publication of field work done 20 years before should interest many specialists variously concerned